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Individual differences in avoidance learning: the role of adverse childhood experiences and intolerance of uncertainty

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Abstract

Avoidance of stimuli perceived as threatening is an essential element of all anxiety-related disorders. Conditioned avoidance paradigm used to study avoidance investigates how individuals learn to respond to aversive stimuli by trying to prevent its frequency or intensity. While studies exist on the general mechanisms underlying avoidance, research on individual differences in avoidance is scarce but important not only for deepening our understanding of avoidance learning but potentially forming a basis for further studies researching the long-standing question why some individuals develop anxiety disorders while others do not. For example, people with more adverse childhood experiences (ACE) are more likely to develop an anxiety-related disorder but the mechanism behind this process remains largely elusive. Moreover, not everyone with the same amount of adverse childhood experiences develops an anxiety-related disorder. One factor that might increase people's tendency to avoid threatening stimuli is their level of intolerance of uncertainty (IU). Hence, the aim of this study was to 1) investigate the relationship between conditioned avoidance and ACE; 2) the relationship between conditioned avoidance and IU; and 3) the moderating role of IU on the relationship between conditioned avoidance and ACE. Based on our sample of 195 participants, cluster analysis revealed individuals did differ in how often they avoided the aversive stimulus, but these differences could not be predicted by scores on ACE questionnaire or Intolerance of uncertainty scale (IUS). Further research is needed to determine whether individuals differing in adaptive conditioned avoidance differ in their tendency to avoid non-threatening stimuli, and whether any other individual differences can predict these individual differences.

Key words: conditioned avoidance, intolerance of uncertainty, adverse childhood experiences, individual differences, experimental psychopathology

In the face of potential threat or harm, people tend to behave defensively (LeDoux & Daw, 2018). Defensive behaviors range from actively tackling the threat to avoiding it altogether. Avoidance of an object, person, or situation the individual perceives as a potentially harmful is one of the most perplexing defensive behaviors (LeDoux et al., 2017). While avoidance of threatening stimuli can be an adaptive survival response (Kenrick & Shiota, 2008), excessive avoidance that is disproportionate to the actual threat, plays a crucial role in anxiety-related disorders (Loijen et al., 2020), such a PTSD (Zandvakili et al., 2020), specific phobias (Eaton et al., 2018; Grös, & Antony, 2006), social anxiety disorder (Heeren & McNally, 2018), and generalized anxiety disorder (Asher et al., 2021; Kashdan et al., 2014).

Research on conditioned avoidance has shed light on some of the general underlying cognitive mechanisms of avoidance learning (Pittig et al., 2020; see Krypotos et al., 2015 for a review). The most common theories and procedures view avoidance as the result of classical and instrumental conditioning (Pittig et al., 2020). In classical conditioning, associations are gradually formed between a neutral stimulus and an aversive unconditioned stimulus (US), resulting in the previously neutral stimulus becoming a conditioned stimulus (CS). In a typical conditioned avoidance paradigm, once participants have learned the CS-US association (fear conditioning), they are enabled to avoid the US by performing an experimenter-defined response (pressing a button) during the CS presentation. This type of avoidance is an essential feature of all anxiety-related disorders; the CS-US association persists if the person avoids the CS because they are not able to disconfirm their belief that the US always follows the CS. For example, a person might have learned to associate men (a previously neutral stimulus) with experiencing trauma (US), resulting in her avoiding all interactions with men (now CS). The learned defensive behavior often generalizes to novel stimuli that resemble the CS; a phenomenon called avoidance generalization.

However, while conditioned avoidance research deepened our understanding of the avoidance acquisition and generalization, it has mostly assumed that when faced with the CS-US association. all individuals develop the same avoidance response, which does not correspond to clinical findings (Krypotos et al., 2018). For example, not all victims of trauma develop PTSD; not everyone who had been bitten by a dog develops a specific phobia; and not everyone with a negative social experience develops social anxiety disorder. In short, individual differences in avoidance learning remain largely unknown (Krypotos et al., 2018). Indeed, "theories of avoidance learning […] are utterly silent with regard to the role of individual differences factors" (Krypotos et al., 2015: 11), which calls for "extensions of the [conditioned avoidance] paradigm including the test of individual differences" (Krypotos et al., 2018: 99). Hence, research on "individual differences in avoidance responses [is] critical in determining vulnerability or resistance to anxiety disorders" (Antunes et al., 2020: 1). This means that not only is knowledge of such differences in avoidance learning relevant for deepening our understanding of processes underlying avoidance, but that greater understanding of individual differences in avoidance learning could help expand our knowledge on the sources of individual differences in anxiety related disorders, characterized by excessive avoidance (Pittig et al., 2018; Krypotos et al., 2018; Hofmann, & Hay, 2018).

A more thorough understanding of individual differences in avoidance learning then, is crucial for two reasons. Firstly, by deepening our knowledge about the fundamental processes underlying individual differences such findings will greatly contribute to the contemporary theories of avoidance learning and its role in psychopathology. This is important since most current theories are group-based, ignoring individual fluctuations in avoidance learning (Pittig et al., 2020). Secondly, and practically relevant, novel empirical findings could form a basis for future translational studies investigating effectiveness of different therapeutic techniques for maladaptive avoidance based on individual differences. If we know which individuals develop an avoidance response more quickly, and avoidance is a key element in anxiety related disorders, than we can tailor treatment of anxiety disorders based on these individual differences in avoidance learning, making it much more individualized than it currently is.

Some studies have investigated individual differences in avoidance, such as in rape avoidance behavior (McKibbin et al., 2011), avoidance in the context monetary loss (Samanez-Larkin et al., 2008), and individual difference in conditioned avoidance learning in rats (Hodes et al., 1985, Brush, 1991), which are not necessarily translatable to humans (Keeler & Robbins, 2011). One recent study which investigated two individual differences in conditioned avoidance learning specifically found that individuals exhibiting a higher level of intolerance of uncertainty (IU) tend to avoid more frequently than those scoring low on IU (San Martin et al., 2020). However, this conclusion was based on a relatively small sample size (N=101), making generalization of results difficult. A study testing the role of IU in conditioned avoidance would be valuable because it could inform future interventions in the healthy population. If individuals with a higher level of IU turn out to avoid more frequently, individuals with a higher level of IU could be offered prevention programs aiming at decreasing their intolerance of uncertainty and, consequently, avoidance frequency. Hence, the first aim of this study is to investigate whether individuals with a higher level of IU tend to learn to avoid more frequently, in a larger sample than previous studies.

Another individual factor that might contribute to development of avoidance in humans are adverse childhood experiences (ACE), a subset of childhood adversities that is commonly used as one measure of traumatic experiences and has gained increasing attention in the past years because of its high validity and reliability (Kuhar & Kocjan, 2021). ACE have been linked to a whole host of psychological disorders (for a review see: Kalmakis & Chandler, 2015; Hughes et al., 2017; Petruccelli et al., 2019; De Venter et al., 2013), including anxiety related disorders (Sareen et al., 2013; Chapman et al., 2007). Some studies even suggest that individuals with more adverse childhood experiences are likely to avoid more frequently (Hagan et al., 2017; Monnat & Chandler, 2015). More generally, some studies found a greater tendency to avoid one's internal experiences in those who experienced trauma (Kroska et al., 2018). However, the aim of none of these studies was to experimentally investigate the role of individual differences in the process of conditioned avoidance learning, which should be researched if we want to improve the effectiveness of clinical interventions for anxiety disorders. The interest of most previous studies was to retrospectively observe individual characteristics of people who had already developed an anxiety disorder. The aim of this study, however, is to test whether healthy individuals (without psychiatric diagnoses) who experienced more ACE tend to avoid aversive stimuli more frequently than those who experienced less ACE.

Lastly, evidence shows that not everyone who has experienced a similar number of adverse events develops mental disorders (Dolbier et al., 2021; McKeen et al., 2021). Hence, we hypothesize that individuals with the same number of ACE will not learn to avoid equally frequently as well. Specifically, since IU is a general risk factor for developing anxiety-related disorders (Watts & Ferreira, 2021), we hypothesize that individuals with the same amount of ACE, but higher levels of IU, avoid aversive stimuli more frequently than those with lower levels of IU. Knowledge of this could contribute to a better understanding of risk and resilience factors for development of avoidance, one of the main elements of anxiety-related disorders. In addition, such knowledge could contribute to improving existing (or developing new) interventions for those with traumatic experiences who struggle with avoidance by applying techniques for increasing their tolerance of uncertainty. In other words, findings about IU as a potential moderating factor of the association between ACE and avoidance could help ameliorate the effect of ACE on avoidance by improving the victims' tolerance of uncertainty.

Considering the somewhat inconclusive and lacking current empirical results regarding the individual differences of avoidance, the main aim of this study was to reexamine the relationship between avoidance, adverse childhood experiences, and intolerance of uncertainty. We investigated whether individual differences in conditioned avoidance can be predicted by the amount of ACE. Secondly, we intended to test whether the level of intolerance of uncertainty moderates the effect of adverse childhood experiences on avoidance frequency.

We hypothesized greater avoidance frequency is associated with having experienced more adverse childhood events. We further hypothesized the level of intolerance of uncertainty moderates the relationship between the number of adverse childhood experiences and avoidance frequency. Specifically, it was hypothesized individuals with the same amount of ACE, but lower levels of IU learn to avoid the US less frequently.

Method

Participants

Required power to find a small main effect (f = 0.10) was estimated with an ad-hoc power analysis using G*Power (Kang, 2021). To calculate the required power, we used as our test a fixed effect, omnibus, one-way analysis of variance (ANOVA). It was determined that in the case that we chose two groups in the measured variable avoidance proportion (proportion of trials that participants avoided in relation to all trials) after having conducted a cluster analysis, 200 participants would be needed to reach the power of (1-β) = .71 at $\alpha = .05$. With three groups, 201 participants would be needed to reach the power of (1-β) = .78 at $\alpha = .05$, and with four groups, 200 participants would be needed to reach the power of (1-β) = .81 at $\alpha = .05$. Using social media, personal communication, and university SONA system, we recruited participants aged between 18 and 35. The exclusion criteria included pregnancy, cardiovascular conditions, other serious medical conditions, current psychiatric disorders, having received medical instructions to avoid stressful situations, having hearing problems, color-blindness, or lack of fluency in English. Participation was voluntary. Compensation was granted to Utrecht University students using the SONA system in the form of 1 participation point (approximately 1 hour of work). For non-psychology students, there was a possibility of winning 50 € in exchange for participation in the study, if they provided their personal contact information (an email address) at the end of the experimental task.

A sample of 197 participants was acquired. Two had to be excluded because they did not meet the age inclusion criteria. This left us with a final sample of 195 participants of which 62.1 % were female and 37.9 % male. The age ranged from 19 years to 35 years with a mean age of 24.41 (*M*=24.4, *SD*=2.85). Most participants (57.4%) had a bachelor level of education (*N*=112), 26.2 had completed higher education (*N*=51), and 16.4% had a secondary education (*N*=32). The average evaluation of US arousal was low (*M*=31.27, *SD*=36.53). Most participants evaluated the US as unpleasant (*M*=77.72, *SD*=22.90). The average volume level was lower than instructed (*M*=60.03, *SD*=18.69) and 11.8% removed headphones during the experimental task.

Measurements

Adverse Childhood Experiences

To measure the number of adverse childhood experiences of participants, the Adverse Childhood Experience Questionnaire by Felitti et al. (1998) was used (see Appendix A). This questionnaire consisted of 10 items measuring childhood trauma. Participants were instructed to place a checkmark next to each statement about an adverse experienced based on whether they had experienced it prior to their 18^{th} birthday. Some scores had to be reversed in accordance with the manual. The questionnaire has an acceptable internal consistency in a variety of samples (Bruskas, 2013; Ford et al., 2014; Mersky et al., 2017; Wingenfeld et al., 2011; Zanotti et al., 2017). Additionally, convergent validity with the Childhood Trauma Questionnaire (CTQ) was found to be satisfactory both in the clinical and non-clinical samples (Wingenfeld et al., 2011).

Intolerance of uncertainty

To measure intolerance of uncertainty the Intolerance of uncertainty scale (IUS) by Freeston et al. (1994) was used (see appendix B). This questionnaire included 27 statements about a person's ability to cope with uncertainty. Participants were instructed to indicate how strongly they identified with statements on a 5-point Likert scale (1 = "not at all characteristic of me" to 5 = "entirely characteristic of me."), resulting in a total score between 27 and 135. Some scores had to be reversed in accordance with the scale's manual. The internal consistency of the English version of the IUS is excellent ($\alpha = 0.94$) and the test-retest reliability is good ($r = 0.74$) (Buhr and Dugas, 2002).

Conditional and generalization stimuli

The conditional stimulus (CS) was represented by pictures of an office room with a desktop lamp. There were three types of CS: the red, yellow, or green lamp. CS + av was followed by the unconditional stimulus (US) that could be avoided by pressing the space bar. CS + unav was followed by the US that could not be avoided. CS - was the safe stimulus not followed by the US. The colors of the CS+unav and CS- were counterbalanced across participants to avoid color being a confounding variable. There were four generalization stimuli (GSs) in the task, two of them colored between yellow and red, and the other two colored between yellow and green (based on San Martin et al., 2020).

Unconditional stimulus

The US was the first second of the aversive sound from the data on the International Affective Digitized Sounds (IADS) (Stevenson & James, 2008).

Relief rating

A horizontal visual analogue scale appeared on the screen 4 s after the stimulus presentation on all trials and lasted for 6 s. Participants were asked: "How pleasant was the relief that you felt?", with the option "Neutral" on the left and "Very pleasant" on the right end of the scale. Participants rated the level of relief by clicking a point on the scale they felt represented their level of relief.

US-expectancy rating

US-expectancy was measured by an ordinal scale with 6 questions about the level of US expectancy for each of the three CSs after each trial. Participants were asked: "On a scale from 1 to 10 (1 = not at all, 10 = very much), how much were you expecting to listen to a loud sound after the presentation of green/yellow/red").?" Expectancy ratings in the avoidance conditioning phase separated expectancies of each color under the hypothetical condition of clicking or not clicking the space bar: ("On a scale from 1 to 10 (1 = not at all, 10 = very much), how much were you expecting to listen to the sound if you did/didn't press the button during green/yellow/red") (adapted from San Martín et al., 2020).

Fear Rating

The level of fear of the CS was measured after each block, once per each CS with an ordinal visual analogue scale. Participants were asked: "How fearful did you find the color you just saw?". Participants could choose any value between 1 (not fearful at all) and 10 (very fearful), by choosing any point on the scale with the computer mouse.

Unpleasantness of the US rating

During the fear conditioning phase, participants were asked to rate the level of unpleasantness of the sound (the US) they had heard. This question was posed to them only after the first block of the first phase to ensure the US was indeed perceived as aversive to the participants. Participants were asked: "How unpleasant did you find the sound you just heard?". The values ranged from 1 (very pleasant) to 10 (very unpleasant). They could answer by clicking on any point on the ordinal VAS with their computer mouse.

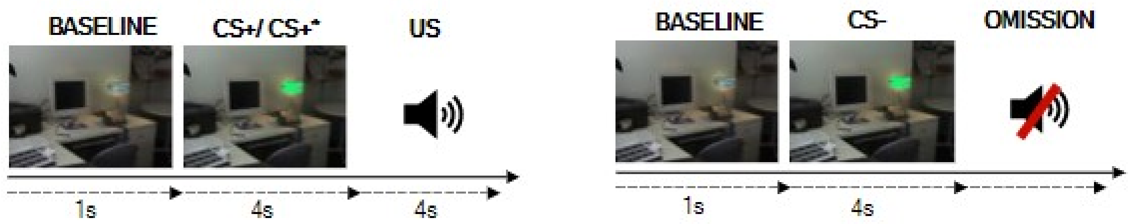
Procedure

The study was approved by the Ethics Review Board of the Faculty of Social and Behavioral of Utrecht University, reference number 21-2190. The experimental task was programmed in software Gorilla (Anwyl-Irvine et al., 2020). The study was preregistered on OSF and is accessible via this link: https://osf.io/txcp3/?view_only=6c61fd4d3e9a480cbeab9cd4966db0b0. Participants were given access to the online study via a link. They were first presented with the information letter and consent form. If consent was not given, the study ended. Then, they were asked to answer questions regarding exclusion criteria (answered with yes or no). If any of the criteria were met, the study ended. If consent was given, participant was shown a screen with instructions for filling out the Positive and Negative Affect Scale (Watson et al., 1988), and began with the task.

The experimental task consisted of three phases. In fear acquisition phase conditioned avoidance paradigm was introduced to participants (see figure 1). They were informed that they would be presented with multiple stimuli, some of which may be followed by an aversive sound. Then, they were instructed to plug in their headphones and adjust their volume to 70% of the maximum. This phase consisted of 4 CS + av, 4 CS + unav trials, and 8 CS – trials which formed two blocks, each block consisting of 8 trials. All trials started with a 1s presentation of the office room with the desktop lamp switched off. Then, the lamp lit up in one of the three colors for 4s. This was followed by a 4s presentation of the US. After each block, participants were presented a 5-point Likert-scale to rate subjective aversiveness of the US, the level of fear they experienced when being presented with the CS, and the level of US-expectancy.

Figure 1

Fear acquisition phase

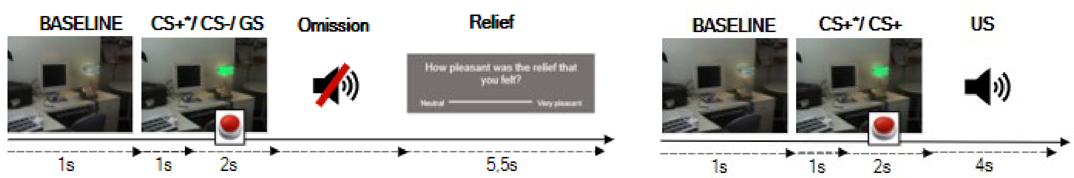


Note. The left figure represents the timeline of CS+ trials. The right figure represents the timeline of the CS- trials. Adapted from "Further characterization of relief dynamics in the conditioning and generalization of avoidance: Effects of distress tolerance and intolerance of uncertainty" by San Martín, C., Jacobs, B., & Vervliet, B. (2020). *Behaviour research and therapy*, *124*, 103526.

This was followed by the avoidance conditioning phase (see figure 2). All trials started with a 1s presentation of the office room with the desktop lamp switched off. Then the lamp lit up in one of the three colors for 4s. Participants were given the possibility to avoid the US by pressing the space bar, which was cued by a 2s presentation of a red button on the screen, appearing 1s after the presentation of the CS. On US trials, this was followed by a 4s presentation of the US. At the end of each block, participants were asked to rate the level of fear they experienced when being presented with the CS, and the level of US-expectancy.

Figure 2

Avoidance conditioning and avoidance generalization phase



Note. The left figure represents the non-US trials. The right figure represents the US trials. Adapted from "Further characterization of relief dynamics in the conditioning and generalization of avoidance: Effects of distress tolerance and intolerance of uncertainty" by San Martín, C., Jacobs, B., & Vervliet, B. (2020). *Behaviour research and therapy*, *124*, 103526.

In the generalization phase, it was tested to what degree participants learned to generalize avoidance behavior to novel stimuli similar to the initial conditioned stimulus (see figure 2). This phase consisted of three blocks of 7 trials, of these 3 being the CS and 4 being the novel GS, not followed by the US. At the end of each block, participants were again asked to rate the level of the US aversiveness, the level of fear of the CS, and the level of US-expectancy. The timeline of stimuli presentation was the same as in phase 2. A schematic of the experimental design including the number of trials per block can be seen in table 1.

Table 1

Schematic of the experimental design

	Pavlovian Phase	Instrumental Phase	Generalization Phase
Block 1	CS+ → US (2) CS+* →US (2) CS- → - (4)	CS+ → US (4) CS+*→ US (4) CS- → - (4)	CS+ → US (1) CS+* → US* (1) CS- → - (1) G1 → * → - (1) G2 → * → - (1) G3 → * → - (1) G4 → * → - (1)
US Expectancy Rating, Fear Rating, CS Aversiveness Rating,			
Block 2	CS+ → US (2) CS+* → US (2) CS- → - (4)	CS+ → US (4) CS+*→ US* (4) CS- → -(4)	CS+ → US (1) CS+* → US* (1) CS- → -(1) G1 → * → - (1) G2 → * → - (1) G3 → * → - (1) G4 → * → - (1)
US Expectancy Rating, CS Fear Rating, CS Aversiveness			

Block 3	CS+ → US (1) CS+* → - (1) CS- → - (1) G1 → * → - (1) G2 → * → - (1) G3 → * → - (1) G4 → * → - (1)
US Expectancy Rating, CS Fear Rating, CS Aversiveness Rating	

Note. Schematic of the experimental design used. The numbers within the brackets denote the number of trials for each stimulus. CS+ Conditional Stimulus followed by Unconditional Stimulus without avoidance availability, CS+* Conditional Stimulus followed by US with avoidance availability, CS- Conditional Stimulus non followed by US, G Generalization Stimulus, US* Unconditional Stimulus avoidance availability, * avoidance availability, - there is no avoidance availability. Adapted from San Martín, C., Jacobs, B., & Vervliet, B. (2020). Further characterization of relief dynamics in the conditioning and generalization of avoidance: Effects of distress tolerance and intolerance of uncertainty. *Behaviour Research and Therapy*, *124*, 103526. Adapted with permission.

After completing the task, participants were presented with the rest of the questionnaires. The questionnaires relevant for this study were the Adverse Childhood Experience Questionnaire (Felitti et al., 1998) and the Intolerance of Uncertainty Scale (IUS) (Freeston et al., 1994). Also used for testing different hypotheses were Trait Anxiety Scale (Spielberger et al., 1983), Anxiety Sensitivity Index (Reiss et al., 1986), Distress Tolerance Scale (Simons & Gaher, 2005), and the neuroticism subscale of the Big 5 Personality Traits Inventory (John & Srivastava, 1999). Participants were asked about demographic factors (age, sex, occupation, ethnicity, educational status) and were debriefed. At the end of each block, participants were again asked to rate the level of the US aversiveness, the level of fear of the

CS, and the level of US-expectancy. At the end of the experiment, they were asked to provide their email if they wished to participate in a lottery to win 50 €.

Statistical analyses

Data reduction

All analyses were performed in the software IBM SPSS, version 26. The total score for ACE was calculated by summing scores on all questions. Proportion of avoided trials (avoidance proportion score) was computed by counting the trials in which participants avoided the CS and averaging it per block and per stimulus.

Manipulation checks

Variables were not standardized as this is not required when variables are measured on the same scale (Fischer & Milfont, 2010). US-expectancy and fear ratings for phase 1 were analyzed via separate 3 (stimulus: CS+av, CS+un, CS-) x 2 (time: block 1 vs 2) within-subject repeated measures analyses of variance (RM-ANOVAs) factor with 3 levels (CS + av vs. + unav, vs. CS -), and time being a factor with 2 levels (block 1 vs. block 2). For phase 2, proportion of avoided trials was calculated per each stimulus per each phase. In the avoidance conditioning phase, we conducted four RM ANOVAs. The same two RM-ANOVAs as in phase 1 were conducted with the one for US-expectancy having an additional "question" factor with two levels (US-expectancy under assumption participant avoided vs under assumption they did not avoid). For avoidance proportion, 2 (time) x 2 (stimulus: CS+av, CS-) RM-ANOVA for relief and 2 (time) x 3 (stimulus) RM-ANOVA were conducted. In the avoidance generalizationFor phase 3, four RM-ANOVAs were conducted with: 7 (stimulus: CS+av, CS+un, CS-, GS1-GS4) x 3 (time: block 1-3) x 2 (question) design for US-expectancy; 6 (stimulus: all stimuli expect CS+un) x 3 (time) design for relief; 7 (stimulus) x 3 (time) design for fear; and 7 (stimulus) design for avoidance. For each RM-ANOVA Greenhouser-Geisser correction was applied when assumption of sphericity was violated.

Pairwise comparisons were Bonferroni-corrected within each RM-ANOVA model to protect against inflated type I errors.

Cluster analysis

Cluster analysis was conducted to determine whether data formed meaningful clusters in terms of avoidance proportion in the avoidance conditioning phase using two approaches, hierarchical and k-means clustering. Hierarchical clustering was chosen because it does not require an a priori decision about the number of clusters, and Ward's method specifically was chosen because it creates equal-size clusters (Saraçli et al., 2013). The chosen distance for hierarchical clustering was Squared Euclidean distance because it is compatible with k-means clustering (Sasirekha & Baby, 2013). K-means method was used because of its effectiveness in clustering large data sets (Celebi et al., 2013). Participants were ordered into clusters with k-means clustering method with the macro qcluMacroRnd, which repeated the method 100 times, each time with a different, randomly-selected leaders. To compare the solutions obtained with the two clustering methods, criterion function value for each of these solutions was calculated and the solution with the lower value was chosen, keeping the number of clusters constant. Of the three solutions (each with a different number of clusters) with the lowest criterion function values, one clustering solution was chosen based on the dendrogram, scree plot and silhouette. Using this solution as the group-defining variable, three one-way between-subjects ANOVAs with standardized scores of avoidance proportion, ACE and IU as outcome measures were conducted.

Results

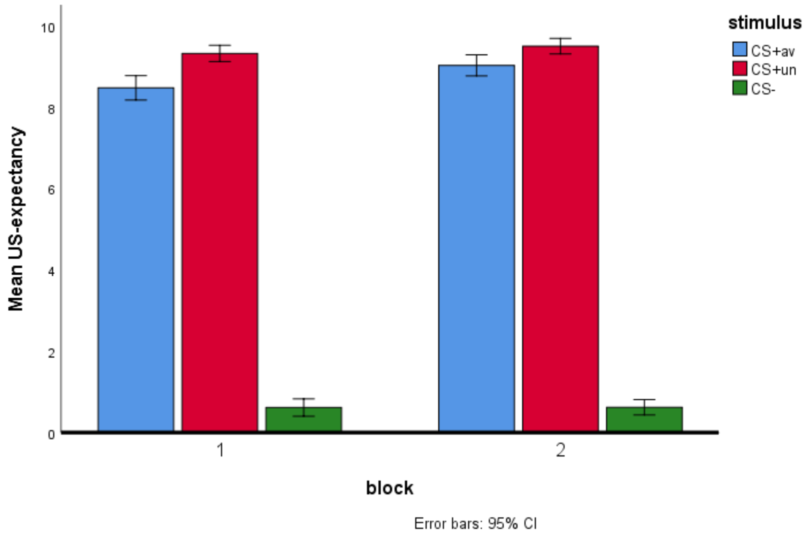
Manipulation checks

Fear acquisition phase

US-expectancy. There was a significant main effect of stimulus (F(1.46, 284.65) = 2308.10, $p < 0.001$, $\eta_p^2 = 0.92$). US-expectancy was the highest for CS+unav (M=9.42, *SE*=0.09), lower for CS+av (*M*=8.76, *SE*=0.12), and the lowest for CS- (*M*=0.62, *SE*=0.08), with differences between all pairs being significant (p<0.001). There was a significant main effect of time ($F(1, 194)=18.29$, $p < 0.001$, $\eta_p^2 = 0.09$) with US-expectancy in block 1 (*M*=6.14, *SE*=0.06) being significantly lower than US-expectancy in block 2 (*M*=6.39, *SE*=0.06). The interaction effect was significant ($F(1.63, 316.71) = 4.97$, $p = 0.007$, $\eta_p^2 = 0.03$), meaning the effect of stimulus on US-expectancy differed between blocks (see figure 3).

Figure 3

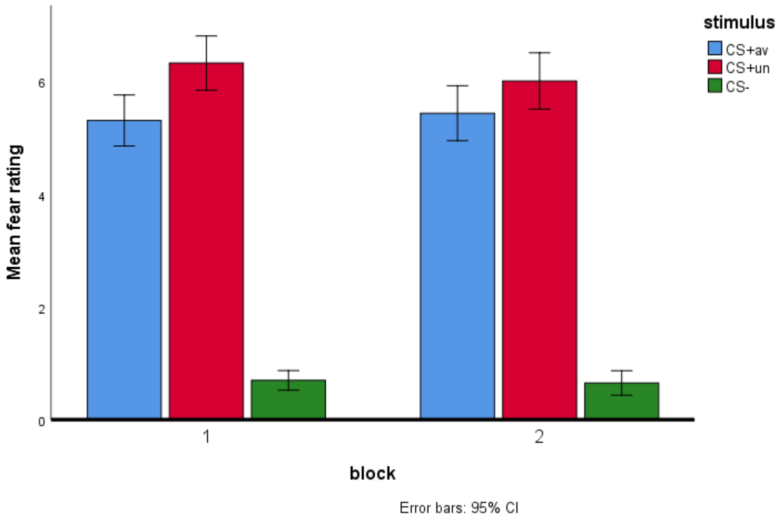
Interaction effect of stimulus and block on US-expectancy in fear acquisition phase



Fear rating. There was a significant main effect of stimulus ($F(1.37, 264.75) = 464.43$, $\eta_p^2 = 0.71$, $p < 0.001$), with fear rating being higher for CS+un(*M*=6.18, *SE*=0.24) and CS+av (*M*=5.38, *SE*=0.22) than for CS- (*M*=0.67, *SE*=0.08). The effect of time was not significant ($p = 0.47$). There was a significant interaction effect ($F(1.75, 339.51) = 3.29$, $p = 0.04$, $\eta_p^2 = 0.02$), meaning thee effect of stimulus on fear rating differed between blocks (see figure 4).

Figure 4

Interaction effect of stimulus and block on fear rating in fear acquisition phase



Avoidance conditioning phase

US-expectancy. The main effect of stimulus on US-expectancy was significant (F(1.88, 364.52) = 1046.44, p < 0.001, η_p^2 = 0.84), with US-expectancy for CS+av (M=4.07, SE=0.16) being lower from US-expectancy for CS+un (M=8.52, SE=0.12) and higher from US-expectancy for CS- (M=0.60, SE=0.09). Bonferroni-corrected pairwise comparisons showed all differences were significant, p<0.001. The main effect of time on US-expectancy was not significant (p = 0.19). The main effect of question on US-expectancy rating was significant (F(1, 194) = 104.68, p < 0.001, η_p^2 = 0.35), with US-expectancy for level 1 of factor question (expectancy assuming participant did not avoid) being higher (M=4.99, SE=0.9) than US-expetancy for level 2 of the factor question (expectancy assuming participant avoided) (M=3.80, SE=0.10). The interaction between time and stimulus was significant (F(1.80, 348.69) = 50.69, p<0.001 η_p^2 = 0.21), indicating the effect of stimulus differed across blocks. The interaction between time and question was significant (F(1, 19) = 15.34, p < 0.001, η_p^2 = 0.07), indicating the effect of the factor question differed across blocks. The interaction between the factors question and stimulus was significant (F(1.84, 356.92) = 99.01, p<0.001, η_p^2 = 0.34), indicating the effect of stimulus depended on the question asked. The interaction between question, time, and stimulus was significant ($F(1.93, 374.60) = 5.87$, $p = 0.003$, $\eta_p^2 = 0.03$) (see figure 5 and 6).

Figure 5

Interaction effect of stimulus and block on US-expectancy under the assumption the participant did not avoid in avoidance conditioning phase

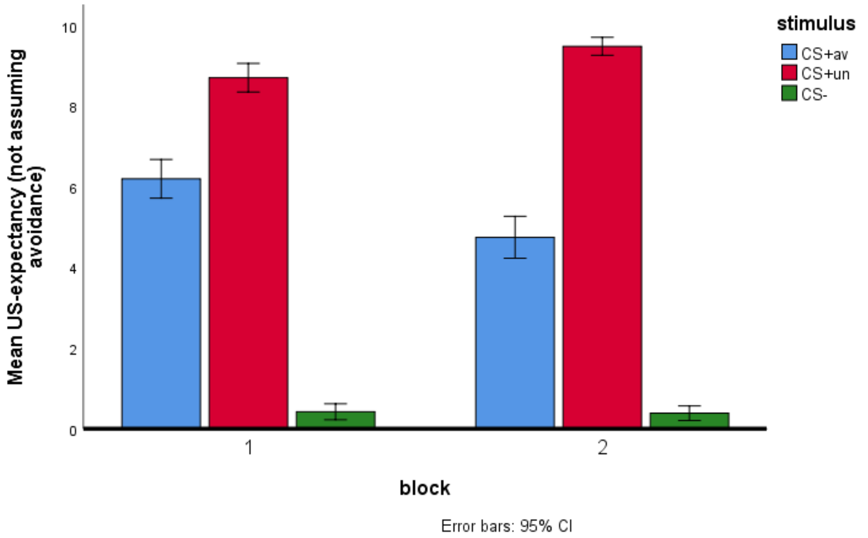
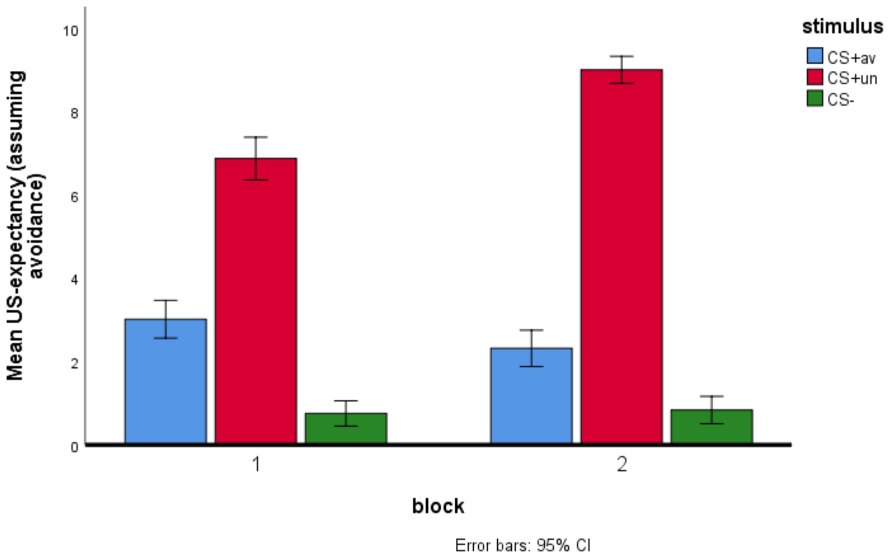


Figure 6

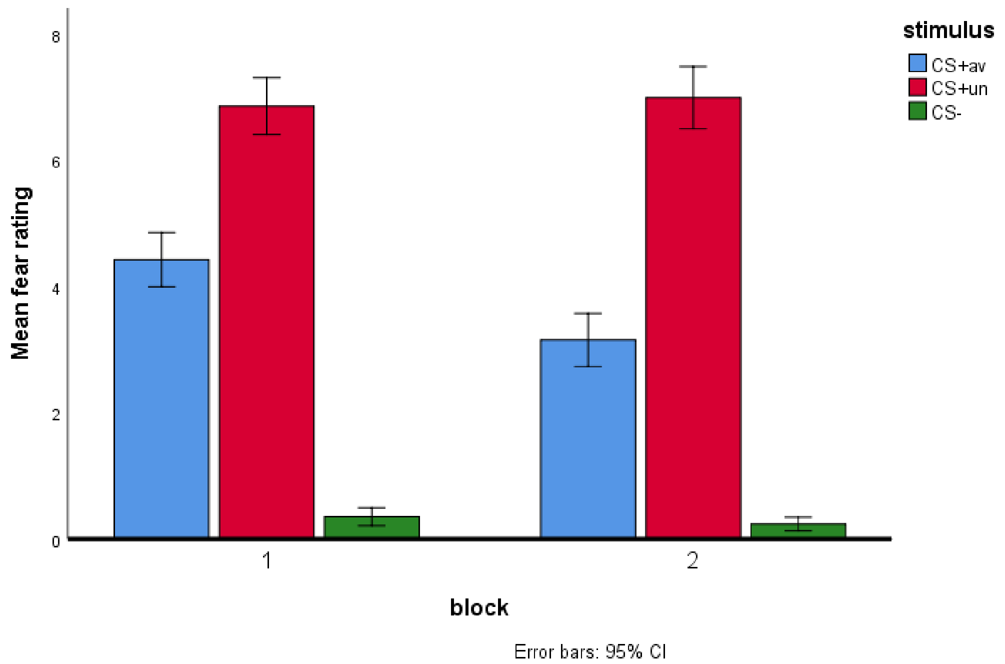
Interaction effect of stimulus and block on US-expectancy under the assumption the participant avoided in avoidance conditioning phase



Fear rating. There was a significant main effect of stimulus (F(1.84, 356.86) = 542.99, p<0.001, η_p^2 =0.74), with fear ratings being the highest for the CS+unav (M=6.93, SE=0.23), lower for the CS+av (M=3.79, SE=0.19), and the lowest for CS- (M=0.30, SE=0.06). Bonferroni corrected pairwise comparisons showed that all differences in fear rating between stimuli were significant (p<0.001). There was a significant main effect of time (F(1, 194) = 18.98, p<0.001, η_p^2 = 0.90), with fear ratings in block 1 (M=3.88, SE=0.14) being higher than in block 2 (M=3.46, SE=0.14). There was a significant interaction effect between stimulus and time (F(1.87, 363.36) = 29.35, p<0.001, η_p^2 = 0.13), meaning that the effect of stimulus differed across the two blocks (see figure 7).

Figure 7

Interaction effect between stimulus and block on fear rating in avoidance conditioning phase



Relief rating. There was a significant main effect of stimulus (F(1)=69.65, p < 0.001, η_p^2 = 0.26), with relief rating being higher for CS+av (M=5.54, SE=0.18) than for CS- (M=3.74, SE=0.20). There was no significant main effect of time (p = 0.19) or interaction effect (p = 0.06).

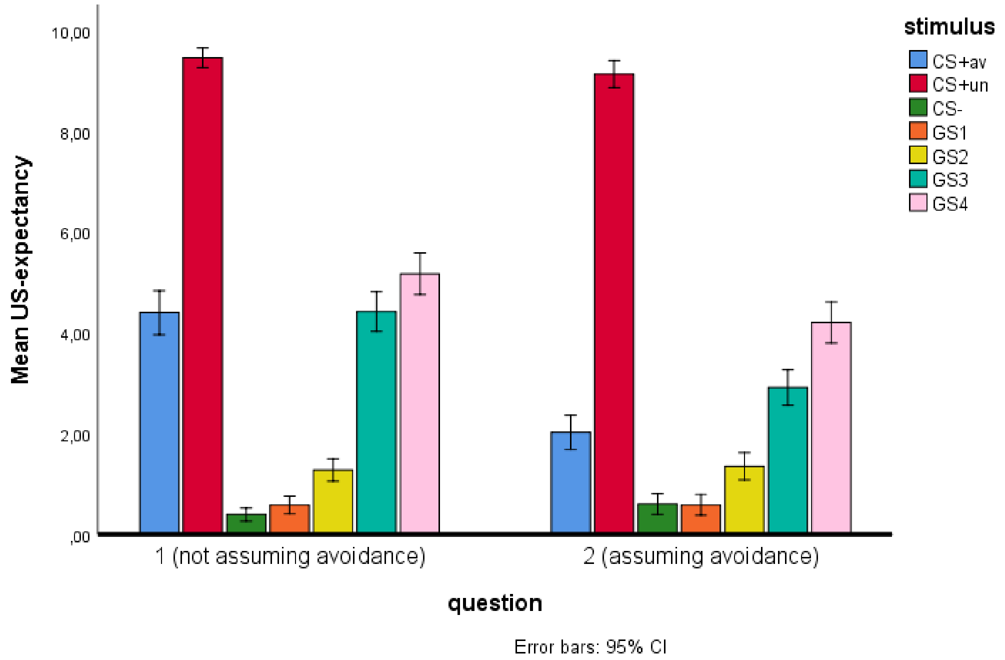
Avoidance proportion. There was a significant main effect of stimulus (*F*(1.57, 305.18) = 774.29, $p < 0.001$, $\eta_p^2 = 0.80$), with avoidance proportion being the highest for CS+unav (*M*=75.71, *SE*=1.99), lower for CS+av (*M*=74.42, *SE*=2.16), and the lowest for CS- (*M*=6.41, *SE*=0.93). Bonferroni corrected pairwise comparisons showed avoidance proportion differed significantly between CS+av and CS- (*MD* = 68.01, *SE* = 2.35, $p < 0.001$), as well as between CS+un and CS- (*MD* = 69.30, *SE* = 2.16, $p < 0.001$), but not between CS+av and CS+un (*MD* = 1.28, *SE* = 1.41, $p = 1.00$). There was a significant main effect of time (*F*(1, 194) = 9.52, $p = 0.002$, $\eta_p^2 = 0.05$), with avoidance proportion in block 1 (*M* = 49.92, *SE* = 1.57) being lower than in block 2 (*M* = 54.44, *SE* = 1.50). There was no significant interaction effect between time and stimulus ($p = 0.14$).

Generalization phase

US-expectancy. There was a significant main effect of stimulus (*F*(3.23, 626.88) = 725.01, $p < 0.001$, $\eta_p^2 = 0.80$), with US-expectancy being the highest for CS+un (*M* = 9.30, *SE* = 0.118) and the lowest for CS- (*M* = 0.50, *SE* = 0.07). Bonferroni corrected pairwise comparisons showed US-expectancy differed significantly ($p < 0.001$) between all pairs of stimuli except between CS- and GS1 ($p = 1.00$). There was a significant main effect of question (*F*(1, 194) = 80.06, $p < 0.001$, $\eta_p^2 = 0.29$). US expectancy under the assumption the participant had not avoided (*M* = 3.67, *SE* = 0.09) was higher than US-expectancy under the assumption they had avoided (*M* = 2.97, *SE* = 0.09). There was a significant interaction effect between stimulus and question (*F*(3.44, 666.55) = 45.45, $p < 0.001$, $\eta_p^2 = 0.19$), indicating the effect of stimulus on US-expectancy differed between the two questions (see figure 8).

Figure 8

Interaction effect between stimulus and question on US-expectancy in generalization phase



Fear rating. There was a significant main effect of stimulus (F(2.59, 502.13) = 386.267, p < 0.001, η_p^2 = 0.67). Fear rating was the highest for CS+un (M = 7.20, SE = 0.25) and the lowest for CS- (M = 0.33, SE = 0.06), with significant differences between all pairs of stimuli (p < 0.001).

Avoidance proportion. There was a significant main effect of stimulus (F(3.65, 707.90) = 204.76, p < 0.001, η_p^2 = 0.51), with avoidance proportion being the highest for CS+un (M = 77.78, SE = 2.467), followed by avoidance proportion for CS+av (M = 66.15, SE = 2.76), and for CS- (M = 11.62, SE = 1.90). Bonferroni corrected pairwise comparisons showed fear rating differed significantly between all pairs of stimuli (p < 0.001), except for the difference between avoidance rate of CS+av and GS4 (MD = 3.76, SE = 2.43, p = 1.00); and the difference between avoidance of CS- and GS1 (MD = 1.71, SE = 1.51, p = 1.00).

Relief rating. There was a significant main effect of stimulus (F(3.11, 602.97) = 62.51, p < 0.001, η_p^2 = 0.24). Relief rating was the highest for GS4 (M = 5.75, SE = 0.20) and GS3 (M = 5.23, SE = 0.21), and the lowest for CS- (M = 3.39, SE = 0.22), GS1 (M = 3.53, SE = 0.22), GS2 (*M* = 3.95, *SE* = 0.20), and CS+av (*M* = 4.71, *SE*=0.20). Fear rating differed significantly between all pairs of stimuli ($p < 0.01$), except for the difference between relief rating for CS- and GS1 (*MD* = 0.14, *SE* = 0.11, *p* = 1.00).

Cluster analysis

Ward's method with Squared Euclidean distance

Based on the dendrogram obtained with Ward's method, a two-cluster or a three-cluster solution seemed the most appropriate (see Appendix C). We decided for the solution based on the most popular way of obtaining a partition of data into clusters, that is by performing a straight line cut of the dendrogram at an "appropriate" level and then treating each separate branch as a cluster (Kettenring, 2006). Two new variables were created identifying participants' cluster membership.

K-means

Based on the scree plot and silhouette (see Appendix C) obtained by k-means clustering method, a three-cluster solution appeared to be the most appropriate. The value of the silhouette was the largest at three clusters and the scree plot had the most noticeable turn at three clusters as well.

Comparison of solutions

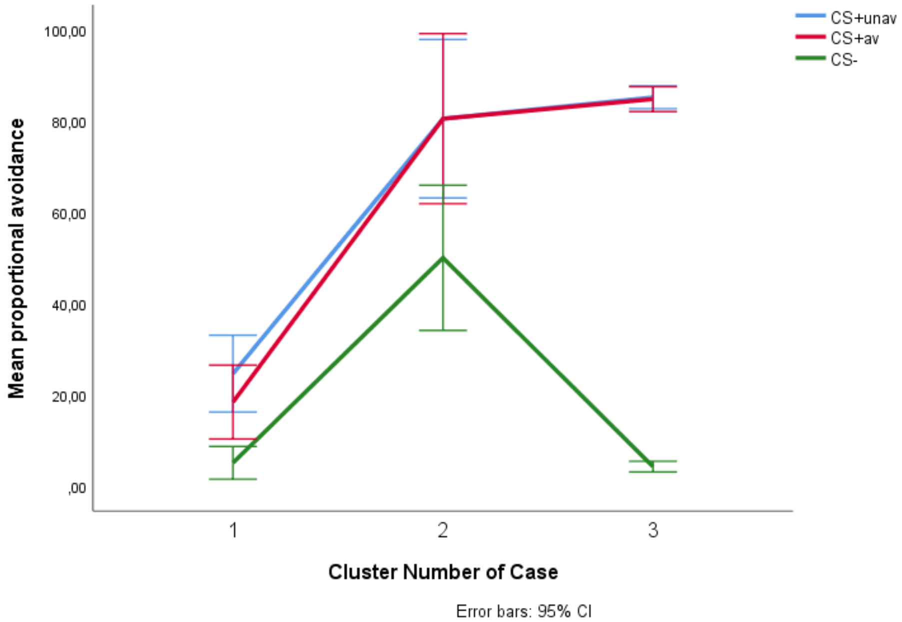
Based on the criterion function values, the preferred solutions were the two-cluster Ward's method solution; the three-cluster k-means solution; and the four-cluster k-means solution. The Adjusted Rand Index for all three comparisons was low (<0.6), meaning Ward's method and k-means method provide very different results. This might indicate that there is no clear natural structure in the data. Based on the dendrogram, scree plot and silhouette, the three-cluster k-means solution was chosen.

Description of the chosen solution

Cluster 1 (low avoidance cluster) includes participants very low on avoidance of CS- and low to medium on avoidance of both CS+. Cluster 2 (medium to high avoidance cluster) includes participants medium on avoidance of CS- and high on avoidance of both CS+. Cluster 3 (polarized cluster) includes participants very low on avoidance of CS- and very high on avoidance of both CS+ (see figure 9).

Figure 9

Avoidance proportion mean for three-cluster k-means solution



Between-subjects ANOVAs

The three clusters obtained with k-means method differed significantly in proportion avoidance of CS+un ($F(2)=154.94$, $p < 0.001$), of CS+av ($F(2)=165.89$, $p < 0.001$), and of CS- ($F(2)=117.46$, $p < 0.001$). Significant differences existed in avoidance proportion of CS+un between clusters 1 and 2 ($MD=55.97$, $SE=6.58$, $p < 0.001$); and clusters 1 and 3 ($MD=60.67$, $SE=3.45$, $p < 0.001$); but not between clusters 2 and 3 ($p = 1.00$). In avoidance proportion of CS+av significant differences existed between clusters 1 and 2 ($MD=62.22$, $SE=6.97$, $p < 0.001$); and clusters 1 and 3 ($MD=66.52$, $SE=3.66$, $p < 0.001$); but not between clusters 2 and 3 ($p = 1.00$). Lastly, for avoidance proportion of CS-, significant differences existed between clusters 1 and 2 (*MD*=45.00, *SE*=3.32, $p < 0.001$); and clusters 2 and 3 (*MD*=45.84, *SE*=3.00, $p < 0.001$); but not between clusters 1 and 3 ($p = 1.00$). However, no pair of clusters differed significantly in the score on ACE (p=0.47) or IUS (p=0.69). Since there were no differences between clusters on these two variables, analysis on the moderating role of IUS on the relationship between ACE and avoidance proportion was not performed.

Discussion

Avoidance is a key feature of anxiety disorders, yet little is known about individual differences contributing to differential levels of avoidance in healthy individuals. To address this question, this study we tested whether healthy individuals differ in conditioned avoidance and whether these differences can be predicted by the level of intolerance of uncertainty and adverse childhood experiences.

In line with previous research using the same conditioned avoidance paradigm (San Martin et al., 2020), results showed participants mostly learned the CS-US contingencies they were expected to learn. In both the fear acquisition and avoidance conditioning phase, US-expectancy was higher for both CS+s than for CS-, and was higher in block 2 than block 1. This indicates participants' ability to differentiate which stimuli were followed by the US increased after block 1 when CS+av and CS+unav were repeatedly followed by the US, while CS- was not. While both the fear and relief rating were as well higher for CS+s than for CS-, they did not increase across tim, which might be a result of them having reached the ceiling level of fear and relief, or of fear and relief not being always reflective of US-expectancy.

Moreover, the fact that avoidance and US-expectancy proportion were higher for CS+s than for CS- in avoidance and generalization phase indicates participants successfully learned the US has the least possibility to be avoided. However, it was unexpected that in both phases, participants expected and avoided CS+un more than CS+av. One possible reason for this is that participants wrongly believed the space bar pressed after the CS+un malfunctioned and that this was way the US could not be avoided despite having pressed the space bar. Another possibility is they simply preferred to press the space button just in case because pressing the button was not costly for individuals, also known as the “better safe than sorry” strategy (Lommen et al., 2010). Furthermore, participants successfully learned to generalize their knowledge of US-expectancy, relief, fear and avoidance to similar novel stimuli. Taken together, results show contingencies were learnt successfully, which was expected based on previous studies using the conditioned avoidance paradigm (San Martin et al., 2020; Krypotos et al., 2018; Lommen et al., 2010); Pittig et al., 2020). However, results did not support our main hypothesis. While individuals from different clusters did on average differ in how often they avoided the aversive sound, they did not differ in their score on ACE and IUS.

Research and clinical implications

Several implications follow from these results. One of the research implications stems from the observation that participants successfully learned the contingencies. This finding presents additional empirical support for the validity of the conditioned avoidance paradigm in testing behavioral avoidance in humans. However, the fact that our results were not in line with our main hypotheses and previous research findings (San Martin et al., 2020; Monnat & Chandler, 2015), could indicate one of the following problems. It might be that no effect exists, but this is difficult to reconcile with similar existing literature in which significant effect have been reported. The problem is more likely a methodological one. Our method might not have been sensitive enough to register an existing effect, meaning that different methods should be employed to study this research question in the future, especially using different, more real-life aversive stimuli people tend to avoid in everyday life. The online form of the experiment might have also affected the results, since the experimental task in previous studies was conducted in the controlled environment of the lab where participants might have been more attentive and engaged in the task (San Martin et al., 2020). And lastly, from our results it only follows that no significant individual differences in conditioned avoidance were found with the specific method used in this study. Had we used a multiverse statistical approach, that is reported outcomes of many different statistical analyses, not just one, different results obtained with various methods could be compared (in the domain of fear conditioning, this approach is introduced and used for example by Lonsdorf et al. (2022). While beyond the scope of this study it is recommended to be done in future research to increase transparency and robustness of the results.

Limitations

The current study faces several limitations. Most importantly, because it was conducted online, there was a higher possibility of confounding variables affecting results, such as participants not following the instructions as precisely as they would in the lab. However, this is a common problem in online studies and not a specific limitation of the conditioned avoidance paradigm (Anwyl-Irvine et al., 2020). Secondly, while the aversive sound used as the US had been shown to be reliable in previous studies (Droit-Volet et al., 2010), it might lack in external validity (Seow & Hauser, 202). That is, even if clusters of participants did differ significantly in proportion avoidance, ACE and IU, this effect might not have been detected using this particular aversive stimulus.

Conclusion and future directions

The current study investigated the role of adverse childhood experiences and intolerance of uncertainty in conditioned avoidance. While contingencies were successfully learned and significant differences in avoidance frequency between clusters obtained by cluster analysis, these differences could not be predicted by the two proposed individual factors. Future research should aim to develop more reliable aversive stimuli that more closely resemble aversive stimuli people encounter in everyday life.

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Appendix A

Adverse Childhood Experiences (ACE) Questionnaire

1. Prior to your 18th birthday:

   Did a parent or other adult in the household often or very often…

   Swear at you, insult you, put you down, or humiliate you? or

   Act in a way that made you afraid that you might be physically hurt?

   ○ Yes ○ No

2. Did a parent or other adult in the household often or very often… Push, grab, slap, or throw something at you? or Ever hit you so hard that you had marks or were injured?

   ○ Yes ○ No

3. Did an adult or person at least 5 years older than you ever…

   Touch or fondle you or have you touch their body in a sexual way? or

   Attempt or actually have oral or anal intercourse with you?

   ○ Yes ○ No

4. Did you often or very often feel that …

   No one in your family loved you or thought you were important or special? or

   Your family didn't look out for each other, feel close to each other, or support each other?

   ○ Yes ○ No

5. Did you often or very often feel that …

   You didn't have enough to eat, had to wear dirty clothes, and had no one to protect you? or

   Your parents were too drunk or high to take care of you or take you to the doctor if you needed it?

   ○ Yes ○ No

6. Was a biological parent ever lost to you through divorced, abandonment, or other reason?

   ○ Yes ○ No

7. Was your mother or stepmother:

   Often or very often pushed, grabbed, slapped, or had something thrown at her? or

   Sometimes, often, or very often kicked, bitten, hit with a fist, or hit with something hard?

   or Ever repeatedly hit over at least a few minutes or threatened with a gun or knife?

   ◯ YeS ◯ No

8. Did you live with anyone who was a problem drinker or alcoholic or who used street drugs?

   ◯ Yes ◯ No

9. Was a household member depressed or mentally ill? or

   Did a household member attempt suicide?

   ◯ Yes ◯ No

10. Did a household member go to prison?

    ◯ Yes ◯ No

Appendix B

Intolerance of uncertainty scale (IUS) 12 item short form

You will find below a series of statements which describe how people may react to the uncertainties of life. Please use the scale below to describe to what extent each item is characteristic of you. Please circle a number (1 to 5) that describes you best.

1. Unforeseen events upset me greatly.
2. It frustrates me not having all the information I need.
3. One should always look ahead so as to avoid surprises.
4. A small, unforeseen event can spoil everything, even with the best of planning.
5. I always want to know what the future has in store for me.
6. I can’t stand being taken by surprise.
7. I should be able to organize everything in advance.
8. Uncertainty keeps me from living a full life.
9. When it's time to act, uncertainty paralyses me.
10. When I am uncertain, I can’t function very well.
11. The smallest doubt can stop me from acting.
12. I must get away from all uncertain situations.

Appendix C

Cluster analysis plots

Figure C1

Dendrogram obtained with Ward's method and squared Euclidean distance

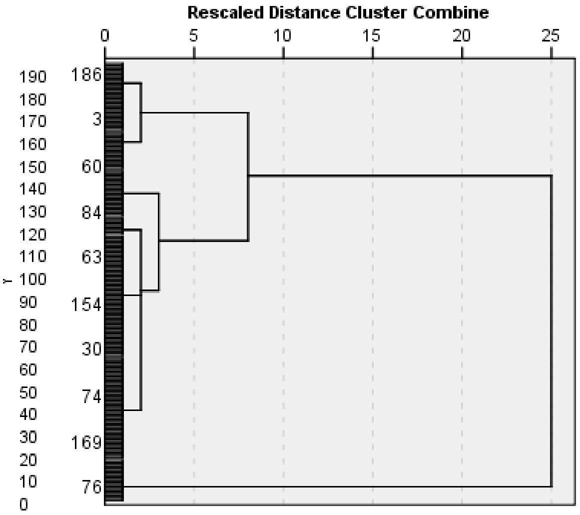

Figure C2

Scree plot obtained with k-means

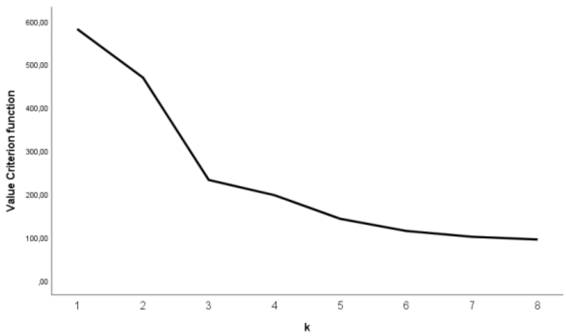

Figure C3

Silhouette obtained with k-means

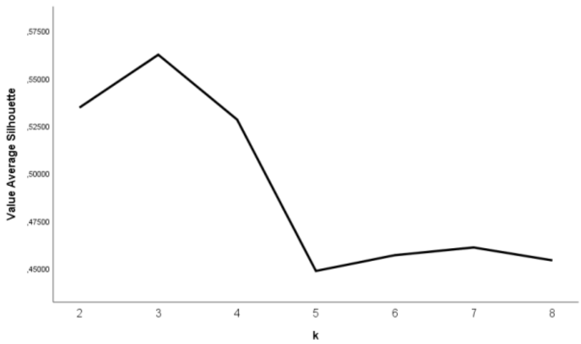

Table C1

Values of Ward's criterion function for each clustering solution

Method	Ward's method			k-means		
number of clusters	2	3	4	2	3	4
values of criterion function	339.8	253.7	204.9	469.6	232.6	197.4

Table C2

Rand and Adjusted Rand Index

comparison	Rand Index	Adjusted Rand Index
EUC_WARD_2 and kmeans_2	0.691	<0.1
EUC_WARD_3 and kmeans_3	0.764	0.532
EUC_WARD_4 and kmeans_4	0.798	0.599