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Further characterization of relief dynamics in the conditioning and generalization of avoidance: Effects of distress tolerance and intolerance of uncertainty



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ARTICLE INFO

Keywords: Avoidance Fear conditioning Generalization Relief Distress tolerance

ABSTRACT

Avoidance behaviors are central to the anxiety disorders and implicated in many other forms of psychopathology, but the reinforcing mechanism of avoidance remains largely elusive. It has been suggested that subjective relief during successful omission of threat may serve as a reinforcer and contribute to the development of excessive avoidance. Also, relatively little is known about how avoidance behaviors generalize and what the role is of relief in generalization. The purpose of this experiment was three-fold: (1) to investigate the influence of anxiety-traits on the dynamics of relief during avoidance learning, (2) to characterize the dynamics of relief during avoidance generalization, and (3) to investigate the generalization of avoidance behavior over a dimension of avoidability. In a large sample of 101 participants, two lamp colors (CS+) were first associated with an aversive electrical stimulation (US), while a third color was not (CS-). Next, clicking a button during one CS + could effectively avoid the US (CS + av), but not during the other (CS + unav). Finally, avoidance generalization was tested via button clicks during morphed colors between CS + av and CS + unav (avoidability dimension), and to morphed colors between CS + av and CS- (safety dimension). Throughout the experiment, a relief rating scale appeared whenever a lamp color was not followed by the US. Results revealed that anxiety traits (distress tolerance and intolerance of uncertainty) were associated with higher levels of avoidance and subjective relief. In addition, gradients of avoidance generalization and relief were observed over dimensions of avoidability (CS + ay \rightarrow CS + unay) and safety (CS + ay \rightarrow CS-). Together, these results suggest a role for excessive relief in the development and generalization of maladaptive avoidance.

1. Introduction

Excessive levels of fear and avoidance characterize most anxiety disorders. While fear denotes the emotional *reaction* to a signal of threat, avoidance is a defensive *action* that serves to prevent or reduce confrontation with the threat. As such, avoidance is highly adaptive in situations of real threat, but unnecessary and sometimes undesired in the absence of real threat. When they interfere with daily life activities and procurement of valued goals, these avoidance behaviors quickly become disabling. It is important, therefore, to understand the mechanism of avoidance and the factors that push adaptive into maladaptive avoidance (Krypotos Effting, Kindt, & Beckers, 2015; LeDoux, Moscarello, Sears, & Campese, 2017; Pittig, Treanor, LeBeau, & Craske, 2018)

Relief is a putative reinforcer of avoidance behaviors. Mowrer

(1951) proposed that removing oneself from a situation of possible threat produces relief from anticipatory fear, which constitutes the rewarding event that reinforces the avoidance behavior. Because anxiety patients start off with higher levels of fear, the consequential relief-from-fear after avoidance will be greater and produce stronger reinforcements that culminate in excessive avoidance. One particular problem to this relief-from-fear theory is that fear and avoidance often diverge, both in the clinic (Rachman & Hodgson, 1974) and in the laboratory (Mineka, 1979). Increases in avoidance rates are often paralleled by decreases in fear reactions to the situation of threat. This should diminish both the motivation to avoid and the reinforcement offered by relief-from-fear, but avoidance typically persists despite decreasing levels of fear (Mineka, 1979). As it became clear that fear and its relief cannot be the whole story to avoidance, interest in fear as an explanans of avoidance waned, and together with it, relief.

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The notion of relief recently regained interest, not in the form of relief-from-fear but as omission-induced relief: the relief triggered by omission of an anticipated threat. Contemporary emotion theory defines relief as the positive feeling in reaction to the absence of a negative event (Deutsch, Smith, Kordts-Freudinger, & Reichardt, 2015). Experimental studies confirmed that omissions of a signaled aversive stimulus trigger a positive feeling of relief (self-reported; Leknes, Lee, Berna, Andersson, & Tracey, 2011; Vlemincx, Meulders, & Abelson, 2017). Of note, relief was lower in these studies when the omission occurred after a safety signal, suggesting that omission-induced relief is modulated by threat expectancy. Generally speaking, high expectancy of threat produces strong relief during omissions, while low expectancy produces weak relief. We have previously proposed that in avoidance too, omissions trigger a positive feeling of relief, which may function as a reward to reinforce the avoidance behavior (Vervliet, Lange, & Milad, 2017). Specifically, omission-induced relief should be strong in early avoidance trials when threat expectancy is still high, and gradually weaken as the avoidance action becomes associated with its safety consequences and lowers the expectancy of threat.

Vervliet et al. (2017) provided the first empirical characterization of relief dynamics over the course of avoidance learning in humans. As expected, self-reported relief pleasantness was high to omissions in initial avoidance trials. But, the level of relief did not decrease over the course of avoidance learning, and the relief was also high to omissions preceded by safety signals. These observations are at odds with the hypothesis that relief is modulated by threat expectancy. Closer inspection, however, revealed large individual differences. Participants scoring high on the Distress Tolerance (DT) scale did show the hypothesized dynamics of relief (strong to omissions during initial avoidance, and weaker during later avoidance). Participants with low DT, on the other hand, displayed generally elevated levels of self-reported relief that did not decrease. Because low DT has been linked to psychopathology in general (Leyro, Zvolensky, & Bernstein, 2010), and anxiety disorders specifically (Keough, Riccardi, Timpano, Mitchell, & Schmidt, 2010), these findings suggest that anxiety-prone individuals have altered relief dynamics that may contribute to increased reinforcement of avoidance behaviors and the development of excessive avoidance. However, one limitation of the Vervliet et al. (2017) study was its small sample size (N = 24). The first objective of the current study was to replicate the avoidance-relief conditioning procedure and test the association between DT and relief in a larger sample.

The second objective was to investigate the dynamics of relief in the context of generalized avoidance. Generalization has been a topic of great interest over the last decade in the field of human fear conditioning, because many anxiety patients suffer from generalized fears and avoidance behaviors (Dymond, Dunsmoor, Vervliet, Roche, & Hermans, 2015). While fear and avoidance may be adaptive within a situation of trauma (e.g., avoiding the neighbor's garden after being bit by the neighbor's dog), fear and avoidance quickly become disabling when generalized to situations that carry little or no threat (e.g., avoiding parks because there might be dogs). In a well-validated laboratory protocol, Lissek and colleagues observed that the frequency of avoidance to a new stimulus is closely linked to the level of generalized fear to that stimulus (Van Meurs, Wiggert, Wicker, & Lissek, 2014; Hunt, Cooper, Hartnell, & Lissek, 2017). This indicates that fear generalization controls initial avoidance behaviors in a novel situation. However, whether avoidance will be maintained or even amplified in the novel situation depends on the extent to which the reinforcing consequences (relief) also generalize to that situation. We propose that differences in such relief generalization may play a role in the proliferation of avoidance.

What are the factors that could control relief in generalization? Given that relief is modulated by threat expectancy, we hypothesize strong relief with (1) a *high* level of threat expectancy (strongly generalized CS→US association), coupled with (2) a *low* level of omission expectancy (weakly generalized action→omission association). Strong

CS→US generalization will produce high expectancy of threat and motivate initial avoidance in the novel situation; weak action→omission generalization will leave the resulting omissions surprising and therefore elicit high levels of relief. Thus, we hypothesize that the dynamics of relief in generalization is not simply determined by CS→US generalization (fear), but also by action→omission generalization (safety). The second objective of this study was to characterize relief dynamics during avoidance generalization by adding a generalization test phase to the avoidance-relief conditioning protocol of Vervliet et al. (2017). We expected that relief would also follow a generalization gradient, which may be dysregulated in individuals with lower DT (cf. Vervliet et al., 2017).

The third objective of this study was to measure avoidance generalization over a dimension of avoidability. The standard generalization protocol measures gradients of fear/expectancy/avoidance over a danger-safety dimension, ranging between a conditional danger stimulus (CS+) that was previously paired with an aversive unconditional stimulus (US) and a conditional safety stimulus (CS-) that was never paired with the US (Lissek et al., 2008). This allows investigating how fear generalizes and how it influences avoidance: Close approximations to the safe stimulus (CS-) may elicit less avoidance because they elicit less fear (Van Meurs et al., 2014; Hunt et al., 2017). However, low levels of avoidance could also result from weak generalization of the action-omission association, which relates to a reduced confidence that the avoidance action will effectively produce the omission of threat in the novel situation. The standard danger→safety dimension does not allow disentangling these two different mechanisms, because both the CS-US and action-omission associations can decrease towards closer approximations of the CS- and therefore influence the level of avoidance in the same direction. Instead, we propose that studying avoidance generalization over a dimension of avoidability allows disentangling these two mechanisms more effectively.

The avoidance-relief conditioning protocol of Vervliet et al. (2017) provides an opportunity to examine action-omission generalization independently from CS-US generalization over a dimension of avoidability. This is because during the avoidance conditioning phase, the US is associated to two CS+, avoidable to one (CS + av) but not to the other (CS + unav). Arguably, this leads to the formation of an action→ omission association to CS + av and an action→no_omission association to CS + unav. We propose that creating a stimulus dimension between CS + av and CS + unav allows measuring a gradient of avoidance that is driven by the generalization of the action→omission association (from CS + av towards CS + unav), while keeping the level of threat expectancy constant (the CS-US association is equally high for both CS+). Hence, a broad gradient of avoidance from CS + av towards CS + unav would reflect strong generalization of the action→ outcome association, while a shallow gradient would reflect weak generalization. We also expect higher relief following avoidance to close approximations of CS + unav, since omissions will be more surprising after CS + unav. Therefore, in the current experiment, we measured levels of fear, avoidance and relief over a standard dangersafety dimension between CS + av and CS-, as well as an avoidable→ unavoidable dimension between CS + av and CS + unav.

Taken together, the three main objectives of the current study were (1) to replicate the avoidance-relief conditioning protocol of Vervliet et al. (2017) and test the influence of DT on self-reported relief in a larger sample, (2) to characterize the dynamics of relief in generalized avoidance, and (3) to investigate the generalization of avoidance over a novel dimension of avoidability. With regard to individual differences, we also questioned whether the previously observed effects with DT are unique to this specific trait, or whether they reflect a broader influence of general anxiety traits. Furthermore, we wondered whether the previous effects of DT truly reflect differences in tolerating distressing experiences, or differences in the experienced intensity of the distress. For these two purposes, we statistically controlled for levels of trait anxiety and the experienced intensity of the US, by including a trait anxiety

(TA) questionnaire and a rating of the perceived aversiveness of the US. As a final addition, we included intolerance of uncertainty (IU), a trait that has been found before to influence fear generalization (Morriss, Macdonald, & Van Reekum, 2016) and avoidance frequency independent of trait anxiety levels (Flores, López, Vervliet, & Cobos, 2018; but see: Morriss, Chapman, Tomlinson, & Van Reekum, 2018; Vervliet & Indekeu, 2015; Xia, Dymond, Lloyd, & Vervliet, 2017). The availability of a validated Dutch version of the IU scale (Helsen, Van den Bussche, Vlaeyen, & Goubert, 2013) also provided a point of reference for the non-validated Dutch version of the DT scale that we translated ad hoc for this experiment. Thus, we expected to observe effects of both DT and IU on relief and avoidance, independent of individual levels of trait anxiety and perceived US aversiveness.

2. Methods

2.1. Participants

A total of 14 men and 116 women participated in the study (mean age 19 years old, range 17-38). Three (female) subjects were excluded from the experiment due to problems with the recording of skin conductance. Trait anxiety questionnaires scores were retrieved from a separate collective screening session, but unfortunately, this was only successful for 101 participants. Given our primary interest in the individual differences factors, we decided to restrict all analyses to this subgroup of participants with fully collected data sets (mean age 18.33 years old, range 17-22; 10 men and 91 women). Most of the participants were undergraduate Psychology students and participated to earn course credits or financial compensation (8 EUR). Before the experiment, participants were screened via self-report and excluded for the following conditions: pregnancy, cardiovascular, pneumological, neurological or other serious medical conditions, psychiatric conditions, chronic pain near the wrists, electronic implants, or having received medical instructions to avoid stressful situations. Participants signed an informed consent and were also informed that they could decline further participation at any time during the experiment. This study was approved by the Social and Societal Ethical Committee and the Medical Ethical Committee of the University of Leuven-KU Leuven.

2.2. Stimuli and apparatus

Conditional stimuli and generalization stimuli. The pictures used as CSs depicted an office room with a desktop lamp that could be of the color yellow (580 nm), green (502 nm) or red (642 nm; CSs were adapted from Milad, Orr, Pitman, & Rauch, 2005). Yellow was always the avoidable CS+ (CSav+), red and green were counterbalanced as CS- and unavoidable CS+ (CSunav+). GSs were two colors between yellow and red (600 nm, 620 nm) and two colors between yellow and green (560 nm, 540 nm), selected based on similarity ratings from a pilot study in a different sample (N = 9). Pictures were presented on a computer screen located on eye level in front of the participant at approximately 500 mm. All trials started with 3 s presentation of the office room with the desktop lamp switched off (context-only presentations), after which the lamp lit up in one of the colors for 6 s on nonavoidance trials. On avoidance trials, availability of the avoidance response was signaled by a red button that appeared on top of the picture, 1 s after onset of the lamp color for a duration of 2 s. Following removal of the avoidance cue, the lamp color picture remained on screen for another 6 s, resulting in a total lamp color duration time of 9 s (see Fig. 1A for a depiction of an avoidance trial timeline).

Unconditional stimulus. A Digitimer DS7A constant current stimulator (Hertfordshire, UK) delivered 2 ms, 400 V electrical stimulation to the forearm of the left hand, via a pair of 11-mm Fukuda Standard AG/AGCl electrodes, filled with K–Y Jelly. A standard workup procedure was used to select an intensity (mA) of the stimulation that the participant experienced as "definitely uncomfortable, but not

painful."

Skin conductance. A Colbourn Instruments skin conductance coupler (model V71- 23, Allentown, PA) was used to measure fluctuations in skin conductance. The coupler applied a constant voltage of 0.5 V across a pair of sintered-pellet silver chloride electrodes (8 mm), attached to the hypothenar palm of the left hand. Electrodes were approximately 10 mm apart and filled with K–Y Jelly. A Labmaster DMA 12-bit analog-to-digital converter (Scientific Solutions, Solon, Ohio) digitized the recorded signal at 10 Hz throughout all experimental phases.

Relief ratings. A horizontal visual analogue scale (VAS, 10 mm) appeared on the screen 4 s after CS/GS offsets on non-US trials, along with the question "How pleasant was the relief that you felt?" and labeled "Neutral" on the left and "Very pleasant" on the right end of the scale. The scale remained on screen for 6 s, and participants could move over the scale with the computer mouse and completed their rating by clicking the left mouse button.

Retrospective ratings of US-expectancy. Explicit expectancies of US occurrence were measured retrospectively after the fear conditioning phase and after the avoidance conditioning phase on a five-point scale, with the left end of the scale labeled as "certainly no shock" and the right end "certainly shock". Retrospective ratings after the fear conditioning phase consisted of 6 questions, probing the level of US-expectancy for each of the three colors (CSs), separated for the first and the last trial ("On a scale from 1 to 5 (1 = not at all, 5 = very much), how much were you expecting to be shocked for the first/last presentation of green/yellow/red"). Retrospective ratings of the avoidance conditioning phase again consisted of 6 questions, but now separating the expectancies to each color under hypothetical conditions of clicking or not clicking the avoidance button ("On a scale from 1 to 5 (1 = not at all, 5 = very much), how much were you expecting to be shocked if you did/didn't press the button during green/yellow/red").

Post-experimental questions. Five VAS scales probed the subjective (un)pleasantness of the US, each CS, and the avoidance cue. Three additional questions asked to estimate the number of lamp colors seen during the experiment, the number of avoidance reponses, and the number of experienced shocks (not analyzed).

Trait questionnaires. The Distress Tolerance Scale (DTS) contains 15 items that measure one's perceived ability to tolerate emotional distress and is composed of 4 subscales: tolerance, appraisal, absorption, and regulation. This measure has shown good internal consistency, as well as convergent and divergent validity (Simons & Gaher, 2005). Given the lack of a validated Dutch version, we translated the items ad hoc for the purpose of the current experiment. The Intolerance of Uncertainty Scale (IU) contains 27 items that measure emotional, cognitive and behavioral reactions to ambiguous situations, implications of being uncertain, and attempts to control the future (Freeston, Rhéaume, Letarte, Dugas, & Ladouceur, 1994). The Dutch version by de Bruin, Rassin, van der Heiden, and Muris (2006) was used, which shows good reliability and validity. Trait anxiety was measured via the State-Trait Anxiety Inventory (STAI), which consists of 20 questions (Spielberger, Gorsuch, & Luschen, 1970). The Dutch version by Van der Ploeg (1982) was used, which has good reliability and validity.

2.3. Procedure

Following completion of the informed consent process, participants filled out the questionnaires and were then fitted with the electrodes and led through the work-up procedure to select a "definitely uncomfortable, but not painful" shock level. An example picture of the room and the lamp was shown, and the operation of the relief scale was explained.

The experimental design is depicted in Fig. 1B. The **fear conditioning phase** consisted of 4 CS + av and 4 CS + unav trials (always followed by the US), and 8 CS- trials (never followed by the US), separated in two blocks of 8 trials so that in each block one of the CS +

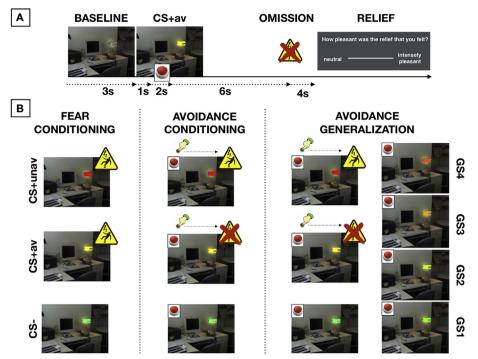


Fig. 1. Avoidance trial timeline and experimental design. 1A: All avoidance trials started with 3 s presentation of the background picture (office room), followed by a lamp color for 9 s. One second into the lamp color, a red button appeared for 2 s that signaled avoidance availability (mouse clicking). The picture of the lamp color remained on the screen for an additional 6 s, during which we measured the skin conductance response (SCR) to examine the regulation of fear by avoidance. Four seconds after picture offset, the relief rating scale appeared for 6 s. Omission SCR was measured from CS offset until onset of the relief rating (note that the 6 s delay between potential avoidance action and measurement of omission SCR minimizes movement-related confounds). 1B: During fear conditioning, the yellow and red lamp were followed by the aversive US (CS +), while the green lamp was not (CS-). During avoidance conditioning, mouse-clicking during the red button effectively canceled the aversive US at the offset of the yellow lamp (CS + av), but not the red lamp (CS + unav). These contingencies continued into the generalization phase, in which all CS were presented, and also 2 morphed color lamps between CS- and CS + av (safety dimension: GS1, GS2) and 2 morphed color lamps between CS + av and CS + unav (avoidability dimension: GS3, GS4). These GS were always presented with the red button

(avoidance cue) and never followed by the aversive US. Lamp colors of CS- and CS + unav were counterbalanced between participants. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article).

was combined with the CS- (order of the blocks was counterbalanced; trial order within each block was pseudo-random). The avoidance cue was not present in this phase, so CS + av and CS + unav were functionally similar up to this point. At the end of this phase, the experimenter entered the room to pose the retrospective US-expectancy questions. The avoidance phase started after the experimenter gave instructions about the avoidance cue (red button), the avoidance response (mouse-clicking the red button), and its function ("clicking the button may or may not cancel the shock", cf. Vervliet et al., 2017). The entire phase consisted of 2 consecutive blocks of 4 CS + av, 4 CS + unav, and 4 CS- each (trial presentations were pseudo-random in each block). The US was scheduled after each CS + av and CS + unav; clicking the mouse button during the avoidance cue effectively canceled the shock to CS + av, but not to CS + unav. At the end of this phase, the experimenter entered the room to pose the retrospective US-expectancy questions. The generalization phase consisted of 3 blocks of 7 trials (the 3 CS and 4 novel GS). The US-contingencies continued to the 3 CS (avoidable US to CS + av, unavoidable US to CS + unav, and no US to CS-). The 4 GS were never followed by the US. The avoidance cue was present on all trials. At the end of this phase, the experimenter entered the room to pose the post-experimental questions, detach the electrodes and debrief the participant. Throughout all experimental phases, intertrial intervals were 15 s on average, with a range between 12 and 18 s.

2.4. Analyses

CS-elicited skin conductance reactivity (SCR) was calculated on a trial-by-trial basis by subtracting the average skin conductance level (SCL) during 2 s prior to each CS from the peak SCL during the 6 s CS window (on avoidance trials, the 6 s window started after removal of the avoidance cue). Omission-elicited SCR was calculated on trials that contained no US, by subtracting the average SCL during 2 s prior to CS offset from the peak SCL during the 4 s post-CS window. Negative changes were scored as zero and included in all analyses. The remaining positive values were square root transformed to reduce skewness of the distribution.

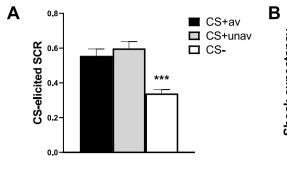
The CS-elicited SCR, omission-elicited SCR, and relief ratings were averaged per blocks of three (generalization phase) or four (fear conditioning and avoidance conditioning phases) consecutive trials per CS, and analyzed via repeated measures analyses of variance (RM-ANOVA). Greenhouser-Geisser corrections were applied when Mauchly's test of sphericity was significant. Post-hoc comparisons were Bonferroni corrected within each RM-ANOVA model to protect against inflated type I errors. Next, in order to investigate individual differences, we entered the questionnaire scores as covariate of interest into the RM-ANOVAs of avoidance conditioning and generalization (cf. Vervliet et al., 2017). We did this first for US-unpleasantness (UNP) and trait anxiety (TA), separately. Next, we added theses two questionnaires as covariates of no interest to RM-ANCOVAs that focused on the effects of DT and IU, respectively (in order to test the effects of DT and IU over and above effects of UNP and TA). Given that we only obtained TA scores from a subset of 101 participants, and that DT scores from three participants from this subset were missing due to incompleted questionnaires, we conducted all ANCOVAs (with TA, DT, IU) on the remaining subset of 98 participants, in order to increase comparability among the different analyses. For the sake of brevity, we limit our report to the individual difference analyses for the two main measures in the current study: selfreported relief and avoidance frequency (results of the individual difference analyses for post-button SCR and omission SCR can be found in Supplemental Information).

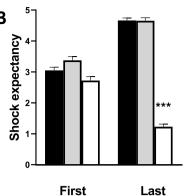
3. Results

3.1. Correlations

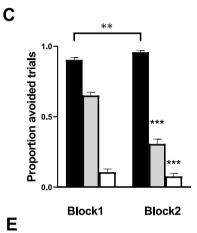
Correlational analyses revealed a moderate correlation between DT and IU, r= -.55, p< .001, N= 98, and weak correlations between DT and TA, r= -.36, p< .001, N= 98, and IU and TA, r= .31, p< .01, N= 101. There were no significant correlations between any of these traits and UNP (unpleasantness of the US), r's < .18.

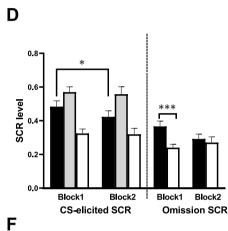
FEAR CONDITIONING

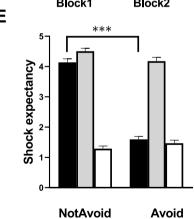


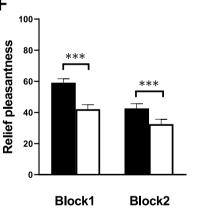


AVOIDANCE CONDITIONING









3.2. Fear conditioning phase

CS-elicited SCR. CS + av and CS + unav both elicited higher SCR than CS-, suggesting successful conditioning (Fig. 2A). This was confirmed by a main effect of Stimulus within a 3 (Stimulus) ANOVA, F(2, 200) = 35.26, p < .001, $\eta_p^2 = .26$, and post-hoc comparisons, CS + av > CS-, p < .001, CS + unav > CS-, p < .001, while CSav + and CSunav + did not differ, p = .53.

Expectancy ratings. Conditioning was successful, as CS + av and CS + unav both developed higher US-expectancies from the first to the last trial, compared to CS- (Fig. 2B). This was evidenced by a main effect of Stimulus, $F(1.58, 158.44) = 191.50, p < .001, \eta_p^2 = .66$, and a Stimulus * First/Last interaction, F(1.62, 161.63) = 157.75, $p < .001, \eta_p^2 = .61$, within the 3 (Stimulus) * 2 (First/Last) RM-ANOVA. Post-hoc analyses confirmed that US-expectancies increased

for both CS+, p's < .001, while US-expectancy decreased for CS-, p < .001. This resulted in significantly higher expectancies to the two CS + compared to the CS- for the last trial, p's < .001, while the two CS + did not differ from each other, p = 1.00.

3.3. Avoidance conditioning phase

Proportion avoided trials. Fig. 2C suggests that avoidance increased when it was effective (during CS + av), decreased when unproductive (during CS + unav), and remained low when unnecessary (during CS-). This was confirmed by a main effect of Stimulus, F(1.88, 188.23) = 502.37, p < .001, $\eta_p^2 = .83$, and a Stimulus * Block interaction, F(1.49, 149.42) = 91.76, p < .001, $\eta_p^2 = .48$, within the 3 (Stimulus) * 2 (Block) RM-ANOVA. Post-hoc comparisons further confirmed that avoidance frequency increased to CS + av, p < .01, and

decreased to CS + unav, p < .001, indicating that avoidance frequencies came under the influence of the consequences of the avoidance actions. Avoidance frequency also decreased further to CS-, p < .05.

Post-button SCR. Both CS + elicited higher post-button SCR compared to the CS- (left side of Fig. 2D), as evidenced by a main effect of Stimulus, F(2,198) = 37.07, p < .001, $\eta_p^2 = .27$, without a Stimulus * Block interaction, F < 1, within the 3 (Stimulus) * 2 (Block) RM- ANOVA. Given that we had specific predictions for a SCR decrease when the avoidance action was effective (CS + av, action—omission learning), we conducted pairwise comparisons for each CS from Block 1 to Block 2, which indeed revealed a significant decrease to CS + av, p < .05, while SCR remained high to CS + unav, p = .67, and low to CS-, p = .64.

Expectancy ratings. Participants successfully acquired the avoidance contingencies (Fig. 2E), as indicated by a main effect of Stimulus, F (1.68, 168.09) = 267.08, p < .001, η_p^2 = .73, qualified by a Stimulus * Question interaction, F(2,200) = 124.07, p < .001, η_p^2 = .55, within the 3 (Stimulus) * 2 (Question: hypothetically avoid versus hypothetically not avoid) RM-ANOVA. Post-hoc comparisons confirmed that US-expectancy was lower with versus without hypothetical avoidance during CS + av, p < .001, surprisingly also for CS + unav, p = .05, but not for CS-, p = .12. A separate 2 (Stimulus: CS + av, CS + unav) * 2 (Question: hypothetically avoid versus hypothetically not avoid) RM-ANOVA confirmed that US-expectancy decreased more to CS + av than CS + unav from hypothetical non-avoidance to hypothetical avoidance, Stimulus x Question interaction, F (1,100) = 126.99, p < .001, η_p^2 = .56.

Relief pleasantness ratings. Fig. 2F suggests that participants reported higher relief pleasantness to US omissions after CS + av than CS-, a difference that decreased over blocks. This was confirmed by a main effect of Stimulus, F(1, 100) = 97.29, p < .001, $\eta_p^2 = .49$, qualified by a Stimulus * Block interaction, F(1, 100) = 13.08, p < .001, $\eta_p^2 = .12$, within the 2 (Stimulus) * 2 (Block) RM-ANOVA. Post-hoc comparisons revealed significant decreases in ratings to both CS + av and CS- from the first to the second block, p's < .001.

Omission SCR. US omissions triggered higher SCR after CS + av compared to CS-, particularly during the first block (right side of Fig. 2E). This was evidenced by a main effect of Stimulus, F(1, 97) = 18.07, p < .001, $\eta_p^2 = .16$, and a marginally significant Stimulus * Block interaction, F(1,97) = 3.36, p = .07, $\eta_p^2 = .03$, within the 2 (Stimulus) * 2 (Block) RM-ANOVA. Post-hoc analyses confirmed CSav+ > CS- on the first block, p < .001, but not on the second, p = .33. Indeed, omission SCR decreased significantly from Block 1 to Block 2 for CSav+, p < .01, but not for CS-, p = .90. Hence, SCR was higher during initial, more surprising omissions of the US after CS + av. Finally, differential omission SCR correlated significantly with differential relief across the two blocks (CS + av minus CS-), r = .23, p < .05.

3.4. Generalization phase

Proportion avoided trials. Fig. 3A suggests highest avoidance frequency to CS + av, with falling gradients towards both CS + unav and CS-, but with higher levels of avoidance on the CS + unav dimension. This was confirmed in a Stimulus (7) RM-ANOVA, by a main effect of Stimulus, F(4.05, 404.81) = 64.92, p < .001, $\eta_p^2 = .39$, with a quadratic trend, F(1,100) = 2227.35, p < .001, eta = .70, that confirms the falling gradients on both sides, and a linear trend, F(1,100) = 87.70, p < .001, eta = .47, that confirms the higher levels of avoidance on the CS + unav dimension versus CS- dimension. Indeed, the average avoidance frequency to the two GS on the CS + unav dimension was higher compared to the two GS on the CS- dimension, paired t-test, t(100) = 4.52, p < .001.

In order to capture each gradient more specifically, we conducted two separate Stimulus (4) RM-ANOVAs from the CS + av to either side

of the dimension. On the CS- dimension, the main effect of Stimulus was significant, F(2.17, 217.03) = 146.78, p < .001, eta = .60, with both linear, F(1,100) = 636.30, p < .001, eta = .86, and quadratic trends, F(1,100) = 9.14, p < .001, eta = .08. Post-hoc comparisons revealed that all stimuli differed significantly from each other, p's < .001. On the CS + unay dimension, the main effect of Stimulus was again significant, F(2.56, 255.72) = 39.32, p < .001, eta = .28, with both linear, F(1,100) = 114.65, p < .001, eta = .53, and quadratic trends, F(1,100) = 4.52, p < .05, eta = .04. Post-hoc comparisons revealed that CS + av was higher than all other stimuli, p's < .001, but that only the first GS (G3) was higher than CS + unav, p < .001, while the second GS (G4) was neither different from CS + unay, p = .17, nor from the first GS, p = .23. In sum, the presence of both linear and quadratic trends supports the observation of generalization gradients over both dimensions, although the results of the post-hoc comparisons are more convincing for the CS- dimension than the CS + unav di-

Post-button SCR. Fig. 3B shows increasing SCR from CS- to CS + unav, with an unexpected peak on CS + av. This was confirmed by a main effect of Stimulus, F(4.41, 432.47) = 2.81, p < .05, $\eta_p^2 = .03$, with a linear trend, F(1,98) = 11.13, p < .01, eta = .10, and a marginally significant quadratic trend, F(1,98) = 3.66, p < .06, eta = .04, within a 7 (Stimulus) RM-ANOVA. Post-hoc analyses showed higher SCR to CS + av compared to CS-, p < .01, and no difference between CS + av and CS + unav, p = 1. The GS closest to CS + unav elicited also higher SCR than CS-, p < .05. The main effect and linear trend were still significant when the two CS+ were removed from the RM-ANOVA, F(3.30,322.94) = 2.80, p < .05, eta = .03, and F(1,98) = 9.06, p < .01, eta = .09, respectively.

Relief pleasantness ratings. Fig. 3C shows increasing relief pleasantness from CS- towards the GS closest to CS + unav, which was confirmed by a main effect of Stimulus, F(2.92,289.02) = 60.73, p < .001, $\eta_p^2 = .38$, with a significant linear trend, F(1,99) = 117.37, p < .001, eta = .54, and a marginally significant quadratic trend, F(1,99) = 3.04, p = .08, within the 6 (Stimulus) RM-ANOVA. Post-hoc analyses revealed that CS + av and all generalization stimuli triggered higher relief pleasantness than CS-, p's < .001. Paired sample t-tests further confirmed that the average relief rating to the two GS on the CS + unav dimension was higher compared to the CS- dimension, t = 0.001, t = 0.001.

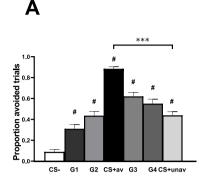
Given that we were mostly interested in the relief consequences of avoidance, an additional RM-ANOVA was conducted that included only the avoided trials. This obviously limits the number of data points (depending on individual frequencies of avoidance); therefore, average relief ratings were computed for the two generalization stimuli on either side of the CS + av, and CS- was left out of the analysis given the low level of avoidance frequency to this stimulus. This revealed a main effect of Stimulus, F(1.71, 104.45) = 31.69, p < .001, eta = .34, with a quadratic trend, F(1,61) = 35.78, p < .001, eta = .37, within a 3 (Stimulus) RM-ANOVA. The linear trend was also significant, F(1,61) = 23.95, p < .001, eta = .28, which indicates that relief ratings were higher on the CS + unav dimension compared to the CS-dimension. Post-hoc comparisons confirmed that all three Stimulus levels were significantly different from each other, p's < .001.

Omission SCR. Fig. 3D suggests an increasing level of omission SCR from CS- towards the GS closest to CS + unav, but this was not supported by a Stimulus (6) RM-ANOVA, with an absence of main effect of Stimulus, F(2.82, 279.41) = 1.18, p = .32. Also, a separate RM-ANOVA that only included avoided trials (3 Stimulus levels: averaged GS on either side of the CS + av, and CS + av), failed to reveal a main effect of Stimulus, F < 1.

3.5. Individual differences: US-unpleasantness (UNP)

Proportion avoided trials. During avoidance conditioning, higher levels of UNP were associated with higher avoidance frequency, as

GENERALIZATION



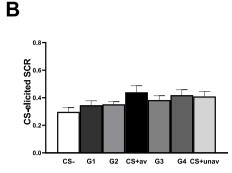
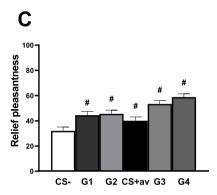
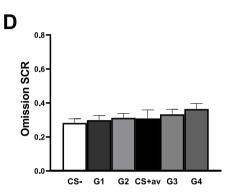


Fig. 3. Results from the generalization phase. Black bars represent CS + av, gray bars CS + unav and white bars CS-. The remaining colors represent the generalization stimuli between CS- and CS + av (GS1, GS2) and between CS + av and CS + unav (GS3, GS4). 3A: Avoidance actions were most frequent during CS + av, and more frequent during GS3 and GS4 compared to GS1 and GS2. 3B: CS-elicited SCR was lower to CS- compared to CS + av and all GS. 3E: Relief pleasantness was lower during omissions after CS- compared to CS + av and all generalization stimuli. 3D: Omission SCR results did not reveal a gradient. Errors bars represent standard errors of the mean; ***p < 0.001, # significantly higher than CS- at p < .05, ### significantly higher than CS- at p < .001. See text for further details.





indicated by a main effect of UNP, F(1,99) = 6.22, p < .05, eta = .06, and a UNP x Stimulus interaction, F(1.86,184.19) = 6.56, p < .01, eta = .06, within the UNP x Stimulus (3) x Block (2) RM-ANCOVA. Bonferroni-corrected correlations further specified that the interaction was driven by CS-, r = .39, p < .01. During avoidance generalization, UNP did not influence avoidance frequencies, as indicated by a main effect that was only marginally significant, F(1,99) = 3.89, p = 0.51, eta = .04, and no UNP x Stimulus interaction, F(3.98,394.04) = 1.13, p = .25, within the UNP x Stimulus (7) RM-ANCOVA.

Relief pleasantness. During avoidance conditioning, higher levels of UNP were associated with overall higher levels of relief pleasantness, as indicated by a main effect of UNP, F(1,99) = 6.53, p < .05, eta = .06, within the UNP x Stimulus (2) x Block (2) RM-ANCOVA. The same was true during generalization, main effect of UNP, F(1,98) = 5.03, p < .05, eta = .05, within a UNP x Stimulus (6) RM-ANCOVA.

3.6. Individual differences: trait anxiety (TA)

Avoidance frequency. During avoidance conditioning, there was no association between TA and avoidance, all Fs < 1 within the TA x Stimulus (3) x Block (2) RM-ANCOVA. The same was true during generalization, all Fs < 1 within the TA x Stimulus (7) RM-ANCOVA.

Relief pleasantness. During avoidance conditioning, TA had a stimulus-specific influence on relief pleasantness, as indicated by a TA x Stimulus interaction, F(1,99)=4.21, p<.05, eta=.04, within the TA x Stimulus (3) x Block (2) RM-ANCOVA. A follow-up correlation indicated the direction of the effect: Higher TA levels were associated with *less* differential relief pleasantness (CS + av minus CS-), r=-.20, p=.05. During avoidance generalization, TA had no effect on relief pleasantness, all Fs<1, within the US x TA x Stimulus (6) RM-ANCOVA.

3.7. Individual differences: distress tolerance (DT)

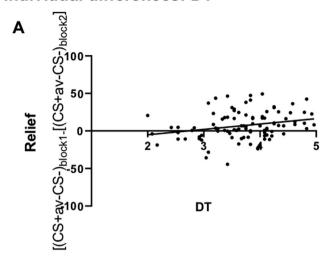
Proportion avoided trials. During avoidance conditioning, DT had a stimulus-specific influence on avoidance frequency, as indicated by a DT x Stimulus interaction, F(2,188)=4.97, p<.01, eta=.05, with a quadratic trend, F(1,94)=7.18, p<.01, eta=.07, within the UNP x TA x DT x Stimulus (3) x Block (2) RM-ANCOVA. Follow-up Bonferronicorrected partial correlations (controlling for UNP and TA) revealed that the influence of DT was most pronounced for CS + unav, r=.26, p<.05 (partial correlations for CS + unav and CS-, p's > .35). During avoidance generalization, the US x TA x DT x Stimulus (7) RM-ANCOVA did not reveal any significant effects of DT on avoidance frequency, all p's > .05.

Relief pleasantness. During avoidance conditioning, lower levels of DT were associated with higher levels of relief pleasantness, as evidenced by a main effect of DT, F(1,94) = 9.68, p < .01, eta = .09, within the UNP x TA x DT x Stim (2) x Block (2) RM-ANCOVA. The DT x Stimulus x Block interaction was also significant, F(1,94) = 4.90, p < .05, eta = .05. The direction of this effect was clarified by a follow-up partial correlation (controlling for UNP and TA): DT correlated positively with a stronger decrease of differential (CS + av minus CS-) relief from the first to the second block, r = .22, p < .05 (see Fig. 4A). Low DT levels were thus associated with more persistent relief over the course of avoidance (cf. Vervliet et al., 2017). During the generalization test, lower levels of DT were again associated with overall higher levels of relief pleasantness, as indicated by a main effect of DT, F(1,93) = 9.87, p < .01, eta = .10, within the UNP x TA x DT x Stimulus (6) RM-ANCOVA.

3.8. Individual differences: intolerance of uncertainty (IU)

Proportion avoided trials. There were no significants effects with IU during avoidance conditioning, all *F*s < 1, within the UNP x TA x IU x Stimulus (3) x Block (2) RM-ANCOVA. During generalization, on

Individual differences: DT



Individual differences: IU

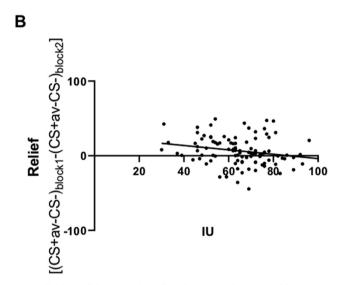


Fig. 4. Individual differences in relief dynamics during avoidance conditioning. The Y-axes display individual values of the CS * Block interaction, as calculated by subtracting the difference between CS $^{+}$ av and CS- in Block 2 from Block 1. 4A: The scatter plot visualizes the significant correlation with individual scores on the distress tolerance scale (DT). 4B: The scatter plot visualizes the significant correlation with individual scores on the Intolerance to Uncertainty scale (IU). See text for further details.

the other hand, IU was associated with overall higher avoidance frequency, as evidenced by a main effect of IU, F(1,96) = 4.50, p < .05, eta = .05, within the UNP x TA x IU x Stimulus (7) RM-ANCOVA.

Relief pleasantness. During avoidance conditioning, IU was associated with overall higher relief pleasantness, main effect of IU, F(1,96)=6.44, p<.05, eta=.06, within the UNP x TA x IU x Stimulus (2) x Block (2) RM-ANCOVA, which also revealed an IU x Stimulus x Block interaction, F(1,96)=5.78, p<.05, eta=.06. The direction of this effect was clarified by a follow-up partial correlation (controlling for UNP and TA): IU correlated negatively with the decrease of differential (CS + av minus CS-) relief from the first to the second block, r=-.24, p<.05 (see Fig. 4B). High IU levels were thus associated with more persistent relief over the course of avoidance. During

avoidance generalization, IU was again associated with generally higher levels of relief, as evidenced by a main effect of IU, F (1,95) = 6.86, p < .05, eta = .07, within an UNP x TA x IU x Stimulus (6) RM-ANCOVA.

Disentangling the influence of DT and IU on rates of avoidance during conditioning and generalization.

The analyses above suggest specificity in the influence of DT and IU over rates of avoidance: DT influenced avoidance during conditioning but not generalization, whereas IU influenced avoidance during generalization but not conditioning. We addressed this more directly by combining both factors in the RM-ANCOVAs, resulting in a UNP x TA x DT x IU x Stimulus (3) x Block (2) RM-ANCOVA for conditioning, and a UNP x TA x DT x IU x Stimulus (7) RM-ANCOVA for generalization. In line with the suggested specificity, the influence of DT over avoidance remained significant during conditioning when controlling for IU, Stimulus x Block x DT interaction, F(2,186) = 4.16, p < .05, eta = .05, and main effect of DT, F(1,93) = 4.96, p < .05, eta = .05. Likewise, the influence of IU over avoidance remained significant during generalization when controlling for DT, albeit at trend-level only, F(1,93) = 3.41, p = .068, eta = .04.

4. Discussion

Relief is a putative reinforcer of avoidance behaviors, but has received scant empirical scrutiny. Vervliet et al. (2017) proposed that dysregulated relief may play a role in the development of excessive avoidance behaviors and found elevated relief in individuals with lower levels of distress tolerance (DT). The three main objectives of the current study were (1) to replicate the avoidance-relief conditioning protocol of Vervliet et al. and test the influence of DT on subjective relief in a larger sample, (2) to characterize the dynamics of relief during generalized avoidance, and (3) to investigate the generalization of avoidance over a dimension of avoidability. Overall, we replicated the effects of DT on relief, we observed a relief gradient in generalized avoidance, and we observed an avoidance gradient over a dimension of avoidability. In general, self-reported relief was higher when omissions of threat were allegedly more surprising, and correlated with omission SCR, a physiological index of surprise (see Spoormaker et al., 2012). This confirms that relief is modulated by threat expectancy and related to the pleasant surprise when an expected aversive event is omitted. As such, relief might be an emotional correlate of the prediction error, a theoretical signal that is thought to govern associative learning including action→outcome learning in avoidance (Maia, 2010; Moutoussis, Bentall, Williams, & Dayan, 2008). Altered relief dynamics may mirror disturbances in PE processing that contribute to the development of maladaptive avoidance. We contend that routine inclusion of relief measures in clinical and laboratory studies on fear and avoidance will shed more light on the learning mechanisms involved.

With regard to the conditioning of avoidance, the current findings address a number of shortcomings in the study of Vervliet et al. (2017). First, DT was related to relief but not to avoidance frequency in Vervliet et al. (only at trend-level), which challenged the assumption that relief is implicated in the conditioning of avoidance. In the larger sample of the current study, DT was related to relief and avoidance frequency during avoidance conditioning, which supports the avoidance—relief relation. Second, the expected course of subjective relief (high during initial avoidance, low during later avoidance) was not observed in the whole sample of Vervliet et al., but only in high DT individuals. In the current study, the predicted course was evident in the whole sample, while we also replicated the altered course in lower DT individuals. Third, Vervliet et al. included DT as the only individual difference factor, which left it unclear whether the observed effects reflected a general anxiety trait or DT specifically, and whether these effects were driven by a lower tolerance for similar levels of aversive experiences, or by different levels of the aversive experience itself. For those purposes, the current study included both a measure of trait anxiety (TA) and a

measure of US aversiveness, and showed the effects of DT on relief and avoidance after controlling for these two factors. Furthermore, a similar picture emerged for intolerance of uncertainty (IU), a trait that is conceptually and empirically related to DT (Laposa, Collimore, Hawley, & Rector, 2015; MacDonald, Pawluk, Koerner, & Goodwill, 2015; Allan et al., 2015). This provides further support for an involvement of beliefs about one's inability to tolerate distress or uncertainty, rather than levels of general anxiety or US aversiveness. It is also in line with earlier studies that found IU influences on fear generalization (Morriss et al., 2016) and avoidance conditioning (Flores et al., 2018; but see Morriss et al., 2018, Vervliet & Indekeu, 2015, and Xia et al., 2017). Finally, a moderate correlation between DT and IU (r = -.55, in the range of previous reports, Laposa et al., 2015; MacDonald et al., 2015; Allan et al., 2015) provides preliminary validation of the ad hoc Dutch translation of the DT scale used in this study.

With regard to the generalization of avoidance, the results contribute to the literature in two ways. First, generalization was tested over two dimensions: (1) the standard danger→safety dimension that lies between a CS + that was followed by the aversive US and a CS- that was never followed by the US, and (2) a novel dimension of avoidability that lies between a CS + during which the US was avoidable (CS + av)and a CS+ during which the US was unavoidable (CS+ unav). We propose that these two dimensions allow disentangling the Pavlovian and operant influences over avoidance. The first dimension primarily tracks Pavlovian influences, by focusing on how the antecedent CS/GS motivates avoidance via the generalization of fear (by activating the CS→US association). The second dimension primarily tracks operant influences, by focusing on how the consequent event (omission/relief) controls avoidance (by activating the action→omission association). On this dimension, the antecedent stimulus is better conceptualized as a discriminative stimulus (SD) that signals when the avoidance response is effective (S^D: action \rightarrow omission). Conversely, S^{Δ} denotes a discriminative stimulus that signals when the avoidance response is not effective (S^{Δ} : action \rightarrow no omission). Hence, CS + av functions as S^{D} , while CS + unav functions as S^{Δ} . Whether a given GS will trigger avoidance is determined by the interaction between the generalized SD properties from the CS + av and the generalized S^{Δ} properties from the CS + unav (see Honig & Urcuioli, 1981). We propose that including these two generalization dimensions in patient studies will help disentangling Pavlovian from operant deficits in excessive avoidance generalization.

The second way in which the results contribute to the literature on avoidance generalization concerns the measurement of the rewarding consequences in the form of relief pleasantness. When generalized fear motivates avoidance in a novel situation (Hunt et al., 2017; Van Meurs et al., 2014), the consequential absence of the aversive event could trigger relief and thereby reinforce the generalized avoidance behavior further. In the current study, self-reported relief on avoided trials was significantly higher to the GS compared to the conditioned avoidance stimulus (CS + av), with the highest relief levels to the GS most proximal to CS + unav. These results provide a proof-of-principle that the rewarding consequences of avoidance (relief) may increase during generalization and thereby lead to amplified avoidance. One potential mechanism behind increased relief would be that the (operant) action→ omission association of avoidance generalizes less strongly than the (Pavlovian) CS→US fear association, which would leave the actual omissions more surprising and trigger more relief. Thus, a combination of strong CS→US fear generalization and weak action→omission generalization could constitute a vicious cycle in which generalized avoidance becomes a self-reinforcing behavior. To test this hypothesis, future studies should include a US-expectancy rating after each avoidance response, in order to track more directly the development and generalization of action→omission associations.

Interestingly, the individual differences analyses also showed specificity of DT and IU over rates of avoidance, where DT influenced avoidance only during conditioning and IU only during generalization.

This specificity could reflect the involvement of different processes in conditioning and generalization: during avoidance conditioning, the aversive US is a certain threat and avoidance will be motivated mostly by the willingness to tolerate the aversive US or not (as captured by DT). During generalization, on the other hand, the threat is uncertain, and the avoidance action may not only reduce exposure to the aversive US itself, but also to the uncertainty of US occurrence (as captured by IU; Flores et al., 2018; Morriss et al., 2016). In line with this reasoning, the avoidance conditioning procedure of Flores et al. (2018) included an atypically high level of uncertainty and a link with IU was found, whereas other studies arguably had lower levels of uncertainty and failed to observe the link with IU during conditioning (Morriss. Saldarini, Chapman, Pollard, & van Reekum, 2019; Vervliet & Indekeu. 2015; Xia et al., 2017). Thus, the level of uncertainty within a given context may be an important factor to understand the influence of individual differences in the development of clinical avoidance (it should also be noted that Flores et al., 2018, and Vervliet & Indekeu, 2015, had much larger sample sizes, which may have yielded a wider distribution of IU scores).

The current study has a number of limitations. First, the avoidance conditioning protocol does not include action selection strategies, as it focuses on one, instructed avoidance action. Also, only a single action per trial is required, which is not optimal for measuring excessive avoidance (cf. Flores et al., 2018), and there is no cost associated to the avoidance response (Krypotos, Vervliet, & Engelhard, 2018). Thus, the current results may relate only to simple, acute avoidance behaviors that carry low cost, but the protocol could easily be adjusted to investigate these factors in a controlled way (increasing the number of buttons and clicks and adding a monetary or gamified response cost). Second, the protocol did not include US-expectancy ratings that could have directly tracked the development and generalization of the action→omission association in avoidance. Third, the relief pleasantness ratings are intended to measure the emotional reaction to an expectedbut-omitted aversive US; however, we cannot fully exclude that the ratings are influenced by the decrease of fear at CS offset and/or by mere awareness that the US is unlikely. Fourth, we intermixed generalization tests across the two dimensions, which could have crossinfluenced the two gradients. Future studies may consider separating the two dimensions in distinct test blocks. Also, presenting a larger set of GS on both dimensions would be advisable to examine the gradients in greater detail. Fifth, in order to measure the relief consequences of generalized avoidance, we could only include actually avoided generalization trials (46% of all generalization trials). For instance, seventeen participants were excluded from this analysis because they never avoided during generalization stimuli. Future studies may benefit from instructing participants to always press the button during a first generalization test block, in order to investigate relief consequences in a more unbiased way and with more statistical power. Finally, the avoidability dimension went from fully avoidable (CS + av) to fully unavoidable (CS + unav), which leaves the possibility that the avoidance gradient is influenced both by learned avoidability and learned unavoidability. Future studies may opt to focus on learned avoidability only, by investigating avoidance generalization towards a Pavlovian stimulus (CS+) that has no history of unavoidability.

In summary, the current study confirmed that distress tolerance (and intolerance of uncertainty) influences self-reported relief, a putative reinforcer that could drive avoidance to maladaptive levels. Self-reported relief was consistently higher in generalized avoidance compared to conditioned avoidance (CS + av), which could constitute a self-reinforcing cycle of generalized avoidance. The study further confirmed an avoidance gradient over a danger-safety dimension and discovered a similar gradient over a dimension of avoidability. We propose that the feeling of relief during omissions tracks the prediction error signal that underlies the reinforcement of conditioned and generalized avoidance behaviors.

Funding

C. San Martín was supported by a National PhD Scholarship (Chile) awarded by CONICYT's Advanced Human Capital Training Program (CONICYT-PCHA/Doctorado Nacional/2015-21150074). B. Vervliet was supported by a Marie Curie International Outgoing Fellowship within the 7th European Community Framework Programme (PIOF-GA-2013-627743).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brat.2019.103526.

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