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Intolerance of uncertainty as a vulnerability factor for excessive and inflexible avoidance behavior

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Abstract

Recent studies have shown that avoidance behavior may become excessive and inflexible (i.e., detached from its incentive value and resistant to extinction). On the other hand, prospective intolerance of uncertainty (P-IU) has been defined as a factor leading to excessive responding in uncertain situations. Thus, uncertain avoidance situations may be taken as a relevant scenario to examine the role of intolerance of uncertainty as a factor that facilitates excessive and inflexible avoidance behavior. In our experiment, we tested the hypothesis that P-IU is associated with excessive and inflexible avoidance in an outcome devaluation paradigm. Specifically, healthy participants learned in a free-operant discriminative task to avoid an aversive sound, and were tested in extinction to measure the sensitivity of avoidance responses to the devaluation of the sound aversiveness. The results showed that an increase in P-IU was positively associated to an increase in insensitivity to the devaluation. Moreover, P-IU was also related to an increase in the frequency of avoidance responses during the instrumental learning phase, and to resistance to extinction. Interestingly, these associations involving P-IU were still significant when trait anxiety was controlled for. The pattern of results suggests that P-IU may be a vulnerability factor for excessive and inflexible avoidance, which, in turn, has been found to be associated with several mental disorders.

Keywords: avoidance, intolerance of uncertainty, outcome devaluation, generalization of avoidance behavior, resistance to extinction.

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Excessive engagement in active avoidance behavior has been related to different forms of anxiety disorders such as obsessive compulsive disorder (Endrass, Kloft, Kaufmann et al., 2011; Gillan, Morein-Zamir, Urcelay et al., 2014), social anxiety disorder (Stevens, Peters, Abraham et al., 2014), generalized anxiety disorder (Mahoney, Hobbs, Newby et al., 2016), or post-traumatic stress disorder (Thompson & Waltz, 2010), to name a few. In many cases, avoidance behavior is thought to play a role in the maintenance of anxiety disorders by preventing the patient from experiencing a lack of correlation between the feared stimulus and the ensuing aversive consequences that the avoidance behavior is meant to eliminate (Barlow, 2002; Bouton, Mineka, & Barlow, 2001; Krypotos, Effting, Kindt et al., 2015; Lovibond, 2006; Mineka & Zinbarg, 2006). Recent studies have demonstrated that avoidance responses can become insensitive to changes in the incentive value of their consequences (Gillan et al., 2014). In general, being able to adjust behavior to changes in the incentive value of the outcome may be regarded as a primary requirement for adaptive behavior to changing environments. However, avoidance behavior may become detached from its incentive value and may be performed even though its consequences may be counterproductive in the long run. For example, we all learn that keeping some distance from a threatening dog is a valuable behavior as it reduces the likelihood of being attacked. However, if this behavior becomes insensitive to changes in the incentive value of its consequences, we may end up fearing any dog or avoiding any place or situation related to dogs, which may be quite disruptive. Nevertheless, insensitivity to changes in the incentive value is not the only form of inflexible or excessive avoidance. Unproductive high avoidance response rates, generalization of avoidance response to safety cues (Lommen, Engelhard, & van den Hout, 2010; Van Meurs, Wiggert, Wicker et al., 2014), and resistance to extinction (Vervliet & Indekeu, 2015; Xia, Dymond, Lloyd et al., 2017) are other examples.

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Given the implication of excessive avoidance in psychopathology, the study of individual differences in the sensitivity of avoidance behavior to changes in its incentive value, in the rate of avoidance, and resistance to extinction may serve to explore potential vulnerabilities to suffer from the above mentioned disorders. In this sense, laboratory work may play an important role in bridging the gap between psychopathology and the underlying processes behind individual differences in excessive avoidance (Robbins, Gillan, Smith et al., 2012). For example, Gillan and colleagues (Gillan et al., 2014; Gillan, Apergis-Schoute, Morein-Zamir et al., 2015) have pioneered the experimental study of individual differences in the sensitivity of avoidance behavior to changes in outcome value. Specifically, Gillan et al. (2014) found that OCD patients showed reduced sensitivity to outcome devaluation under overtraining conditions compared with healthy controls. These results can be interpreted as showing OCD patients' inflexible avoidance behavior in the sense that avoidance responses were still made despite knowing that the aversive outcome was no longer dispensed.

The study of vulnerabilities to mental disorders involving excessive and inflexible avoidance behavior may also benefit from focusing not just on clinical populations but on personality traits in healthy people that are considered transdiagnostic factors playing an etiological role in the development of several mental disorders such as generalized anxiety, social anxiety, and obsessive compulsive disorder. This approach may allow us to trace mental disorders involving excessive avoidance one step back to their origin, improving our knowledge of the cognitive processing styles and neurocognitive candidate endophenotypes playing a role in their development and/or maintenance (Robbins et al., 2012; Menzies, Achard, Chamberlain et al., 2007; Glahn, Almasy, Barguil et al., 2010). Additionally, this research strategy may lead us to identify populations at risk of developing these mental disorders, and may provide insights to improve their prevention and treatment efficacy. The objective of the present study was to evaluate the relationship between Intolerance of

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Uncertainty (IU) and the ease of developing excessive and inflexible avoidance behavior as shown by the insensitivity of avoidance behavior to outcome devaluation, an undue avoidance response rate, and resistance to extinction.

One reason for studying the relationship between IU and excessive avoidance is that uncertainty is commonly present in those situations in which an avoidance response is acquired. The hand washing compulsion by some OCD patients provides a clear illustration. Touching a door handle may make someone feel uncertain about the possibility of being seriously contaminated, no matter how unlikely this event may be. On the other hand, washing hands may not be 100% effective to get rid of germs. Of note, reduced effectiveness does not necessarily lower the engagement in the avoidance behavior, as was recently shown in an avoidance conditioning experiment in healthy individuals (Xia et al., 2017). Under such levels of uncertainty, individuals scoring high in IU may be especially prone to engage in excessive avoidance behavior trying to turn the uncertain situation into a more predictable one and to enhance the perception of control. This excessive avoidance behavior may include unproductive high response rates, insensitivity to outcome devaluation, and resistance to extinction. Despite their attempt to reduce the exposure to uncertainty by engaging in excessive avoidance, high IU people may typically remain anxious and still perceiving uncertainty, which would lead them to continue responding excessively to associated cues.

IU has been linked to compulsive behavior in the clinical domain in areas as diverse as problematic alcohol use (Kraemer, McLei, & O'Bryan,, 2014), hoarding (Oglesby, Medley, Norr et al., 2013) or checking behavior in OCD (Jensen & Heimberg, 2015) to name a few. Interestingly, these behaviors become problematic as their frequency increase, leading to aversive and undesired consequences. However, the potential role of IU in the development of excessive and inflexible avoidance behavior is yet to be evaluated. Traditionally, IU has been linked to worry (Buhr & Dugas, 2006; Dugas, Freeston, &

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Ladouceur, 1997) and anxiety (Carleton, 2012; for results related to inflexible behavior and trait anxiety, see Vervliet & Indekeu, 2015 or Browning, Behrens, Jocham et al., 2015 showing inflexible responses in a reversal learning paradigm) though more recently it has been acknowledged as a more transdiagnostic dispositional factor involved in various mental disorders, including depression, different forms of anxiety disorders, addictions or OCD (Birrel, Meares, Wilkinson et al., 2011). Dugas, Gosselin, and Ladouceur (2001) defined IU as “the excessive tendency of an individual to consider it unacceptable that a negative event may occur, however small the probability of its occurrence” (p. 552).

However, there is evidence showing that IU cannot be considered a unified construct. For example, Birrell and cols. (2011), using factor analysis technique on 9 previous studies on IU has distinguished two different underlying factors as measured by the IU scale (IUS; Freeston, Rheaume, Letarte et al, 1994): A cognitive or prospective (P-IU) and an inhibitory factor (I-IU). Whereas the former has been defined as the “desire for predictability and an active engagement in seeking certainty”, the latter has been defined as the “paralysis of cognition and action in the face of uncertainty” (Birrell et al., 2011; p. 1198). Moreover, these factors have been found to be associated in opposite directions with the processing of uncertain errors (Jackson, Nelson, & Hajcak, 2016) and with the processing of reward in uncertain contexts (Nelson, Kessel, Jackson et al., 2016).

According to how P-IU has been characterized, participants scoring high in such factor should feel distress about uncertain aversive events. Consequently, these participants should be highly motivated to engage in avoidance responses to enhance their perception of control and to reduce uncertainty as much as possible. Thus, high P-IU participants should engage in high response rates in the presence of stimuli signaling a probable upcoming aversive event. Additionally, these participants should be more prone to show insensitivity to outcome devaluation compared with low P-IU participants. This increased insensitivity may

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be a consequence of the high frequency of avoidance responses or a consequence of a greater tendency to reduce uncertainty. These forms of excessive avoidance may prevent learners from perceiving changes in cue-outcome contingencies. Therefore, high P-IU participants' avoidance responses should be more resistant to extinction compared with low P-IU. To test these hypotheses, we used a discriminated free-operant avoidance learning task that was designed to assess participants' response frequency, sensitivity to changes in outcome value, and resistance to extinction in an uncertain environment (see Figure 1). According to the arguments stated above, we hypothesized that increases in P-IU should be associated with an increase in avoidance response frequency, an increase in insensitivity to outcome devaluation, and an increase in resistance to extinction of avoidance behavior

Method

Participants and apparatus. One hundred and fifty-six undergraduate students (122 females, mean age 19 year-old) from the Faculty of Psychology at the University of Málaga (Spain) volunteered to take part in the experiment in exchange for course credits. Half of them were randomly assigned to a *devaluation* group (n=78) and the other half to a *control* group (n=78; see below for details).

Each participant performed the task in a semi-isolated cubicle using an IBM-compatible PC. Each computer was equipped with home-built software programmed in E-Prime ® 2.0 (Psychology Software Tools, USA) and head-phones (Sennheiser®HD-201 model). Participants' responses were registered through a standard QWERTY keyboard and the PC mouse.

Materials. Although our study focused on intolerance of uncertainty, all participants also completed a state-trait anxiety questionnaire, as both state and trait anxiety have been frequently related to intolerance of uncertainty. Specifically, we used the Spanish adaptations of the Intolerance of Uncertainty Scale: IUS (Freeston, Rheaume, Letarte et al., 1994;

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adaptation: González Rodríguez, Cubas León, Rovella et al., 2006), and the State-Trait Anxiety Inventory: STAI (Spielberg, Gorsuch, & Lushene, 1982; adaptation: Seisdedos, 1990). All participants gave written informed consent before completing the questionnaires.

The IUS (internal consistency of .91 and test-retest reliability of .78; Dugas et al., 1997) is a 27-item self-report measure that assesses the degree to which individuals find uncertainty to be distressing and undesirable. The IUS includes two subscales known as Prospective Intolerance of Uncertainty (11-items) and Inhibitory Intolerance of Uncertainty (16-items). Items are rated on a five point Likert scale ranging from 1 (not at all characteristic of me) to 5 (extremely characteristic of me).

The STAI (internal consistency ranged from .86 to .95 and test-retest reliability coefficients ranged from .65 to .75; Spielberger, Gorsuch, & Lushene, 1982; 1983) is a 40-item self-evaluation questionnaire that assesses the degree to which individuals suffer trait or state anxiety. Therefore, the STAI includes two subscales known as Trait Anxiety (20 items) and State Anxiety (20 items). Items are rated on a four point Likert scale ranging from 0 (nothing in the Trait subscale, hardly ever in the State subscale) to 3 (a lot in the Trait subscale, almost always in the State subscale).

Stimuli and design. Two different black–and-white fractal images serving as conditioned stimuli (CS_A and CS_B) were used to signal a US consisting of an aversive sound that could be presented either to the left or the right ear, which were assigned to either US1 or US2 according to a counterbalance procedure. An additional black-and-white fractal image (CS_C) was used as a safety signal preceding the absence of any noise (see Figure 1). All fractals had an approximate size of 9 x 8 cm and appeared in the center of the screen. The background of the screen was always white. The aversive sound was a 3-second beep of 44100 Hz. For the control group, a low-volume (27 ± 3 dB) and a high-volume (97 ± 3 dB) version of this sound were used as US1 and US2, respectively. For the devaluation group, the

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high-volume sound played the role of both USs until the devaluation phase, in which the intensity of US1 was lowered down to 27 ± 3 dB. The control group was included to ensure that the different sound intensities were motivationally different and led to different avoidance response frequencies in the presence of CS_A compared with CS_B. Additionally, the control group allowed us to detect possible differences in the sensitivity to the intensity of the USs as a function of IUS, independent from the devaluation procedure.

>>> Insert Figure 1 about here <<<

Procedure. One week before the experiment all participants completed the two questionnaires. The avoidance task was divided into four phases: A Pavlovian learning phase, an instrumental learning phase, a devaluation phase, and a test phase. All participants started by wearing the headphones provided, and reading the instructions concerning the first phase. The instructions told participants that some fractal images could signal an upcoming aversive sound that could be presented either to the left or to the right ear. Specifically, participants were told that the left-ear sound could follow one of the images, whereas the right-ear sound could follow the other image. Further, participants were told that there was a safety image which was not followed by any sound. On each trial, a fixation cross appeared in the center of the screen for 2 seconds. After that, one of the three images (i.e., CS_A, CS_B and CS_C) was displayed at the center of the screen for 20 seconds. Participants were presented with US1 in five out of ten CS_A trials, and with US2 in five out of ten CS_B trials. The onset of the noise was programmed according to a variable interval schedule of 10 seconds (from the onset of the CS) that followed a rectangle distribution with amplitude of 4 seconds. That is, the aversive noise could appear randomly at Second 8, 9, 10, or 11 from the onset of the CS namely, the middle part of the 20-s CS time window. The time window for the onset of the noise was independent from its duration (3 seconds). Consequently, there were two sources of uncertainty regarding the occurrence of the US: a) The non-deterministic occurrence of the

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US given the excitatory CSs, b) the unpredictability of the exact moment in which the US was delivered.

Overall, the Pavlovian training phase comprised five trial blocks each one including 2 CS_A trials (only one reinforced), 2 CS_B trials (only one reinforced), and 2 CS_C non-reinforced trials. The order of trials was randomized on a block and participant basis. Therefore, each type of trial (CS_A, CS_B, CS_C) was presented ten times along this phase.

After each phase, participants gave contingency ratings concerning the different CS-US relationships programmed. The question *To what extent do you think that this image was followed by the noise through your left/right ear?*, which could be read at the upper center of the screen, prompted these judgments. The rating scale went from 0 (*Very sure that this image was not followed by the noise through this ear*) to 9 (*Very sure that this image was followed by the noise through this ear*) and appeared at the bottom center of the screen. Participants used the computer keyboard to provide their responses. As there were three conditioned stimuli (CS_A, CS_B and CS_C) and two USs (left/right-ear noise) participants had to rate a total of six contingency relationships. Participants were allowed to confirm/modify each judgment before assessing the next CS-US relationship. Then, participants were asked to judge the aversiveness of the sound: *To what extent is the noise aversive for you?* Participants from the devaluation group only had to judge the high-volume sound (no low-volume sound was presented until the devaluation phase), and participants from the control group had to judge also the low-volume sound. Again, responses were given on a 0 (*Non aversive at all*) to 9 (*Extremely aversive*) rating scale.

After the Pavlovian phase, participants read the instructions of the instrumental learning phase. Participants were told that this phase was identical to the previous phase except that they could now avoid the sound by pressing one of two possible keys within one second before its onset whenever it was programmed to occur. To avoid the presentation of

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the noise to the right or to the left ear, participants had to press 'P' or 'Q' on the computer keyboard, respectively. Consistently with a discriminated free-operant learning procedure, participants could respond as many times as they wish along the trial. Nevertheless, they were also informed that responding was just an option they had if they wanted to avoid the sound. No immediate feedback was provided regarding the consequences of individual responses. Consequently, participants could only be completely certain that they had effectively avoided the aversive sound after the offset of the CS. This way, the instrumental learning phase not only had an important component of aversion, but, also, a high level of uncertainty regarding both the occurrence of the US and the consequences of individual responses.

As in the Pavlovian learning phase, this phase comprised five training blocks each one including 2 CS_A trials (only one reinforced, unless successfully avoided), 2 CS_B trials (only one reinforced, unless successfully avoided), and 2 non reinforced CS_C trials. Trial order was randomized on a block and participant basis. After completing this phase, contingency judgments were required as described above. The only exception was that judgments were now prompted by the sentence: *To what extent do you think that this image would be followed by the noise through your left/right ear if no key were pressed?*

After the instrumental learning phase, participants in the devaluation group went through a devaluation phase in which the sound volume associated to CS_A was substantially reduced. Firstly, the non-devalued noise was reminded and participants had to judge its aversiveness as described above. Then, the devalued noise (through the other ear, 27 ± 3 dB; counterbalanced across participants) was presented, and participants also had to judge its aversiveness. Written instructions guaranteed that the volume of the devalued noise would be held at a low volume until the end of the task. The control group went through the same procedure except for the fact that no change was made to the volume of any of the sounds presented.

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The effects of the devaluation procedure were assessed through a test phase. Instructions informed our participants that the same stimuli would be presented, and also that they could avoid the sound, as in the previous phase. However, no US was actually presented during this phase. If avoidance behavior were sensitive to the new motivational values programmed, participants should respond less to the CS that signaled the devalued noise (CS_A) than to the CS that signaled the non devalued noise (CS_B). Alternatively, if avoidance becomes detached from the reinforcer value, the difference between responses to CS_A and to CS_B should tend to disappear. The use of extinction (i.e., the withholding of the USs) for testing purposes ensures that devaluation effects are exclusively due to the updating of the value of the US rather than to the exposure to the devalued outcome contingent upon instrumental responses during this last phase. Additionally, the use of an extinction procedure allowed us to assess participants' resistance to extinction of avoidance behavior.

The test phase included four blocks, each one comprising one CS_A, one CS_B, and one CS_C trial. The order of trials was randomized on a block and participant basis.

After the test phase, contingency judgments were also required as it has already been described for the instrumental learning phase. Additionally, participants were also asked to make an additional judgment to assess how much they trusted the devaluation instructions provided. We refer to these judgments as instruction adherence judgments. For this, participants could read *To what extent do you think that the noise presented to your left/right ear was of a high or low volume during the last part of the task in case it appeared?* Ratings were made on a rating scale from 0 (*extremely low*), to 9 (*extremely high*).

Results

The data from 21 participants were excluded from the analyses as no responses were registered to cues CS_A and CS_B in the first two trial blocks of the test phase. Thus, no devaluation effect could be computed from those participants' responses (see below for

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details about the computation of this devaluation effect). Most of these participants did neither respond to CS_A and CS_B in the last trial blocks of the previous avoidance acquisition phase. As a consequence, the data from 135 participants were analyzed (68 from the devaluation group).

All the statistical analyses were performed using IBM SPSS versions 15.0 and 23.0 (IBM Corp., 2006 and 2015). In all the analyses of variance (ANOVAs) the sphericity was tested and the degrees of freedom were corrected using Greenhouse-Geisser's epsilon whenever necessary. The effect size statistics reported are partial eta squared (η^2) for the ANOVAs and Cohen's *d* in the case of the *t*-tests (Cohen, 1988).

Avoidance responses

Instrumental learning phase

Avoidance responses during the instrumental learning phase were analyzed to test if participants acquired a good level of discrimination between the different CSs, and to discard significant differences between responses to CS_A and CS_B in the devaluation group that could obscure the interpretation of possible devaluation effects. Figure 2 (Panels A and C) shows participants' mean response frequency as a function of group, CS and trial block. We conducted a mixed ANOVA, which included two within-subject factors, Cue (CS_A *vs*. CS_B *vs*. CS_C) and Block (1 to 5) and one between-subject factor, Group (Devaluation *vs*. Control), on participants' correct avoidance responses. The analysis yielded a significant effect of Cue, $F(1.42, 188.83) = 65.99$, $MSE = 2753.25$; $p < .001$; $\eta^2 =.33$, a significant effect of Block, $F(2.12, 281.82) = 11.26$, $MSE = 551.90$; $p < .001$; $\eta^2 =.08$, a significant interaction of Cue x Block, $F(5.40, 718.43) = 4.06$, $MSE = 163.48$; $p = .001$; $\eta^2 =.03$, and a significant interaction of Cue x Group, $F(1.42, 188.83) = 7.85$, $MSE = 2753.25$; $p = .002$; $\eta^2 =.56$. All remaining effects were not significant (other F's < .81). A visual inspection of Figure 2 (Panels A and C) clearly reveals that the Cue x Block interaction was due to the fact that responses to the

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safety signal, CS_C, remained relatively constant across trials whereas responses to the other two cues increased across trials. It also reveals that the Cue x Group interaction is explained as a result of participants in the devaluation group responding similarly to CS_A and CS_B, whereas, in the control group, participants' response frequency on CS_A trials falls at an intermediate point between CS_C and CS_B trials. This latter interpretation was confirmed by *post hoc t*-tests analyses in the Control group, yielding significant differences for all pairwise comparisons (M_{CSA}=19.05, M_{CSB}=36.47, M_{CSC}=6.90; t_{CSAB}=6.29, p <.001, Cohen's d = 4.10; t_{CSAC}=3.61, p = .001, Cohen's d = 4.40; t_{CSBC}=7.08, p <.001, Cohen's d = 8.63), and in the Devaluation group, yielding no differences between responses to CS_A and CS_B (M_{CSA}=35.03, M_{CSB}=33.96, M_{CSC}=9.61; t_{CSAB}= 1.01, p = .316, Cohen's d = 0.28; t_{CSAC}=6.32, p < .001, Cohen's d = 8.36; t_{CSBC}=6.14, p <.001, Cohen's d = 9.61) (see Figure 2). Note that the Bonferroni correction method for multiple *t-tests* would lead to adopt here a significance level of p < .016. Thus, as expected, the response frequency to CS_A and CS_B was similar in the Devaluation group, and higher to CS_B than to CS_A in the Control group, proving that different sound intensities led to different avoidance response frequencies.

>>> Insert Figure 2 about here <<<

Test phase

As shown in Figure 2 (Panel B), the devaluation procedure was clearly effective, as participants in the devaluation group responded to CS_A less frequently than to CS_B. Moreover, the difference between response frequency in CS_B trials and CS_A trials in the devaluation group seems to be of a similar magnitude to that found in the control group. To confirm these impressions, we conducted a mixed 3 (Cue: CS_A *vs*. CS_B *vs*. CS_C) x 4 (Block) x 2 (Group: Devaluation *vs*. Control) ANOVA on participants' correct avoidance responses, which yielded a significant effect of Cue, F(1.77, 235.06) = 69.41, MSE = 2156.11; p < .001; η^2 =.34, a significant effect of Block, F(2.13, 283.14) = 10.41, MSE = 221.12; p < .001; η^2

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=.07, and a significant Cue x Block interaction, $F(3.97, 528.42) = 7.61$, $MSE = 179.74$; $p = .001$; $\eta^2 = .05$. No effect involving the Group factor was significant (all *F*'s values < 1.66). A visual inspection of Figure 2 (Panels B and D) reveals that the Cue x Block interaction was due to a more pronounced decrease in responding across trials (i.e., extinction) to CS_B compared with CS_A and CS_C, which is likely to be a consequence of participants having noticed the absence of the aversive reinforcer during test. *Post hoc t-tests* revealed significant differences in all pairwise comparisons involving CS_A, CS_B and CS_C in the Devaluation ($t_{CSAB}=4.40$, $p <.001$, Cohen's $d = 3.00$; $t_{CSAC}=3.72$, $p <.001$, Cohen's $d = 12.64$; $t_{CSBC}=6.33$, $p <.001$, Cohen's $d = 6.55$) and in the Control ($t_{CSAB}=6.03$, $p <.001$, Cohen's $d = 6.41$; $t_{CSAC}=4.20$, $p <.001$, Cohen's $d = 11.32$; $t_{CSBC}=8.23$, $p <.001$, Cohen's $d = 12.46$) groups. Note that these statistical differences are still significant even when an $\alpha = .016$ significance criterion is adopted after the Bonferroni correction method for multiple *t-tests*.

Some readers may have expected differences between groups regarding the devaluation effect. However, we did not have strong reasons to expect such differences. The main reason to include the control group was to test for a possible association between P-IU and a general insensitivity of response frequency to differences in outcome value. The results of this analysis are reported in the next section.

Relationship between P-IU and sensitivity to outcome devaluation

A sensitivity-to-devaluation ratio (SR) was computed to evaluate how sensitive participants' performance was to the reduction in the sound volume made in the Devaluation group. A sensitive performance would entail less avoidance responses to CS_A than to CS_B after the devaluation of the aversiveness of the sound signaled by CS_A. Note, however, that response frequencies to the different CSs tended to converge across the test phase, surely due to the use of an extinction procedure (see the results described in the previous section). Therefore, the sensitivity to devaluation was calculated from participants' responses in the

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first two trial blocks, as responses in these blocks were less affected by the extinction schedule. Specifically, the sensitivity-to-devaluation ratio (SR) was calculated as the *Response frequency to the signal of the devalued noise* (CS_A) */ [Response frequency to the signal of the devalued noise* (CS_A) *+ Response frequency to the signal of the non-devalued noise* (CS_B)*]*. Ratio values well below .5 would mean a high sensitivity to the devaluation procedure in the sense that responses to the cue associated to the devalued sound were substantially lower than those associated to the cue signaling the still aversive sound. Ratio values near .5 would indicate that the participant was rather insensitive to the devaluation procedure, responding to CS_A and CS_B with similar frequency. An interesting advantage of calculating the sensitivity to devaluation with this ratio measure is that it counteracts the effect of the response-frequency baseline on the size of the differences between responses to CS_A and CS_B.

We hypothesized above several ways in which individual differences in IU, specifically in P-IU, may relate to insensitivity to outcome devaluation. Consistent with these hypotheses, increases in P-IU scores should be associated to increases in SR. Our statistical analysis will focus on the results found in the Devaluation group during the test phase. All the correlation and regression analyses conducted in this article used the nonparametric bootstrap method relying on 5000 samplings with replacement (Efron & Tibshirani, 1993), which is a robust and appropriate method when the normality assumption of residuals is violated. Bias-corrected and accelerated (BCa) bootstrap 95% confidence intervals (CIs) are reported in square brackets. Decisions regarding hypothesis testing were based on whether the interval included the zero value or not: The null hypothesis was rejected if the zero value fell out of the CI, and it was accepted otherwise. In all cases, non-standardized beta coefficients will be reported.

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First, we conducted a bivariate Pearson correlation analysis including SR, P-IU, and trait anxiety (TA). The analysis yielded the significant correlation between SR and P-IU, r = .375 [.147, .564], between SR and TA, r = .260 [.031, .463], and between P-IU and TA, r = .632 [.472, .763]. Given the significant correlations found, we conducted a hierarchical regression analyses to assess the association between P-IU and SR controlling for TA. The I-IU factor was discarded from the analysis because it did not significantly correlate with SR, r = .148 [-.126, .389]. In the first step, we only entered the P-IU factor and, in the second step, TA scores were added as an extra factor. As expected, we found that the P-IU factor significantly predicted SR scores, b = 0.013 [0.005, 0.020] (see Figure 3). In the second step, the P-IU factor was still significant when controlling for TA, b = 0.012 [0.002, 0.020]. However, TA scores ceased to be predictive of the SR when controlling for P-IU, b = 0.001 [-0.005, 0.007]. Therefore, the predictive relationship between P-IU and SR was not explained by the association between TA and SR.

>>> Insert Figure 3 about here <<<

Similar analyses were conducted within the Control group to discard that the association between P-IU and SR was due to a general insensitivity to differences in the reinforcer values. However, we did not find any correlation between P-IU and SR, r = -.096 [-.344, .187]. As expected, though, P-IU and trait anxiety were significantly correlated in the Control group, r = .294 [.043, .535].

Relationship between P-IU and avoidance frequency

We also examined the relationship between P-IU and the overall frequency of correct avoidance responses during the avoidance acquisition stage within the Devaluation group. For this, the absolute frequency of correct avoidance responses to the three CSs throughout the five blocks of the avoidance acquisition phase was calculated. Then, a bivariate Pearson correlation analysis was conducted including avoidance frequency (AF), P-IU, and TA,

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which yielded the significant correlations between AF and P-IU, r = .412 [.156, .592], and between AF and TA, r = .375 [.142, .563]. An identical hierarchical regression analysis to that described in the previous section was made on the frequency of avoidance responses. In the first step, we found that P-IU predicted significantly AF, b = 21.88 [8.271, 34.569]. In the second step, neither P-IU, b = 15.47 [-0.930, 29.042], nor TA, b = 6.36 [-3.088, 15.801], predicted significantly AF.

As these results do not allow us to disentangle the variance explained by P-IU from the variance explained by TA, we decided to analyze more deeply the mediational role of TA in the relationship between P-IU and AF. This analysis was performed using PROCESS, version 2.16.3 (Hayes, 2013), which yielded a non-significant indirect effect of P-IU on AF through TA, b = 6.410, BCa CI 95% [-3.284, 16.986].

Relationship between P-IU and extinction

The analysis of the resistance to extinction is also of special interest to assess excessive and inflexible avoidance. We calculated a resistance-to-extinction ratio (i.e., RE) as [*Response frequency to* CS_A + CS_B *during the last block of the test phase (Block 4)*] / [*Response frequency to* CS_A + CS_B *in block 4 + Response frequency to* CS_A + CS_B *during the first block of the test phase (Block 1)*], in the Devaluation group. In this case, a high ratio means high resistance to extinction, giving us an idea about how persistent avoidance responses were throughout the test phase, whereas a low ratio means strongly extinguished. We started by conducting a bivariate Pearson correlation analysis focusing on the correlation between RE and P-IU, and between RE and TA. This analysis yielded the significant correlation between RE and P-IU, r = .266 [.089, .430], and a nonsignificant correlation between RE and TA, r = .190 [-.068, .431]. We conducted a hierarchical regression analyses to assess the association between P-IU and RE controlling for TA. In the first step, we only entered P-IU as the independent variable and, in the second step, TA scores were added as an

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extra factor. As expected, we found that the P-IU factor significantly predicted RE scores in the first model, *b* = 0.009 [0.004, 0.015] (see Figure 3). However, the second model was rejected as it did not significantly increase R^2 over the first model, R^2 *Change* = .001; $F(1, 65) = 0.055$; $p = .815$. Consequently, we did not find evidence that TA mediated the relationship between P-IU and RE.

Additional exploratory analyses

<u>The role of avoidance frequency in the relationship between P-IU and insensitivity to outcome devaluation</u>

To go deeper into the mechanisms underlying the relationship between P-IU and the sensitivity ratio (SR), we decided to explore the role of avoidance frequency in this relationship. One possible explanation for the association between P-IU and SR is that it has been mediated by avoidance responses so that high P-IU participants tended to respond more frequently overall (i.e., to all cues), affecting, then, SR scores in the final test. For this, we started by conducting a Pearson correlation analysis between SR and AF, which yielded the significant correlation between these variables, *r* = .379 [.150, .560]. Then we conducted a stepwise regression analysis with SR as the dependent variable and P-IU as the independent variable in the first step. Adding AF in the second step yielded a significant predictive relationship between P-IU and SR, *b* = 0.009 [0.001, 0.016], and between AF and SR, $b = 2 \times 10^{-4}$ [4×10^{-5}, 3×10^{-4}]. Consequently, P-IU significantly predicted sensitivity to outcome devaluation even when controlling for avoidance response frequency. However, this result does not completely discard a possible meditational role of AF in the relationship between P-IU and SR. Therefore, we decided to conduct a mediational analysis to test for this hypothesis. As in a previous section, this analysis was also performed using PROCESS. This analysis yielded a significant indirect effect of P-IU on SR through avoidance frequency, *b* = 0.004, BCa CI 95% [0.001, 0.009] (see Figure 4). Consequently, our results suggest that P-IU

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and SR may be associated through two different mechanisms. One of them would involve avoidance frequency as a mediating variable whereas the other would not depend on such variable. We will return to the implications of this mediational role of AF in the relationship between P-IU and SR in the General Discussion section.

>>> Insert Figure 4 about here <<<

Exploring the role of the insensitivity to outcome devaluation in the relationship between P-IU and resistance to extinction

One possible explanation of the association between P-IU and RE is that low P-IU participants may have had more chances to detect the absence of the devalued US during the extinction test phase as a result of their lower tendency to respond in CS_A trials compared with high P-IU participants. Once low P-IU participants detected the absence of the US in CS_A trials, they may have also posited the absence of the US in CS_B trials, leading them to a general decrease in avoidance response. According to this, SR should play a mediational role in the relationship between P-IU and RE. To test this mediational hypothesis, we first conducted a Pearson correlation analyses of the relationship between RE and the sensitivity ratio (SR), which yielded a significant correlation, $r = .442$ [.193, .684]. Then, we conducted a hierarchical regression analysis including RE as the dependent variable, and P-IU and SR as the independent variables. In the second step, the analysis yielded a significant association between RE and SR, $b = 0.41$ [0.138, 0.674], and a nonsignificant association between RE and P-IU, $b = 0.004$ [-0.002, 0.010]. These results clearly suggest that SR mediated the association between P-IU and RE, which is consistent with the idea that insensitivity to devaluation prevents people from perceiving that the CS is no longer followed by the US. To corroborate this hypothesis, we conducted a mediational analysis, again performed using PROCESS. This analysis yielded a significant indirect effect of P-IU on RE through insensitivity to outcome devaluation, $b = 0.005$, BCa CI 95% [0.002, 0.011].

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The relationship between P-IU and generalization of avoidance responses to the safety signal

Some studies have demonstrated that anxiety and uncertainty may lead to the persistence of previously learned responses and decreases the ability to inhibit defensive responses toward safety signals (Grupe & Nitschke, 2013; Haaker, Golkar, Hermans et al., 2014). Therefore, the analysis of the frequency of avoidance responses to the safety signal, CS_C, is of special interest to assess excessive and inflexible avoidance. Note that this cue had never been paired with the aversive noise and, thus, avoidance responses to this cue can hardly be regarded as having any objective value. We started with a bivariate Pearson correlation analysis between the sum of avoidance responses to CS_C throughout the acquisition phase ($SumCS_C$), P-IU and TA. The analysis yielded a significant correlation between $SumCS_C$ and P-IU, $r = .406$ [.154, .581], but not between $SumCS_C$ and TA, $r = .261$ [-.058, .466]. Again, we conducted a hierarchical regression analyses to assess the association between P-IU and $SumCS_C$ controlling for TA. In the first step, we only entered P-IU as the independent variable and, in the second step, TA scores were added as an extra factor. As expected, we found that the P-IU factor significantly predicted $SumCS_C$ scores, $b = 9.20$ [2.120, 17.327] (see Figure 3). Interestingly, this relationship remained almost unaffected when controlling for TA, $b = 9.08$ [2.652, 16.597]. Conversely, TA was not associated to $SumCS_C$ after controlling for P-IU, $b = 0.12$ [-3.202, 3.995].

Assessing the role of possible confounding factors

Further analyses suggested that the association between P-IU and excessive and inflexible avoidance was not due to an association between P-IU and differences in contingency learning accuracy regarding CS_A and CS_B, differences in the perception of US aversiveness, differences in adherence to the devaluation instructions, or differences in contingency learning accuracy regarding CS_C (see Table 1). To assess contingency learning accuracy, an accuracy score was calculated for each cue-reinforcer relationship. Remember

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that participants had to make two CS-US ratings for each CS: One to judge the relationship between the CS and its associated US, and the other to estimate the relationship between the CS and alternative US. Thus, the accuracy scores regarding CS_A and CS_B were simply the difference between these two ratings. Therefore, high and low scores revealed high and low accuracy, respectively. As CS_C was not associated to any US, an average score between the two ratings was computed to calculate the accuracy score. In this case, high and low scores revealed low and high accuracy, respectively. To assess instructions adherence, an instruction score was calculated as the difference between volume-expectancy ratings for the nondevalued sound and for the devalued sound. Remember that participants had to estimate the extent to which the noise was high or low in case it had occurred during the test phase.

>>> Insert Table 1 about here <<<

General discussion

The aim of the present study was to test the hypothesis that high P-IU is associated with excessive and inflexible avoidance behavior as evidenced through higher insensitivity of avoidance response to outcome devaluation, higher avoidance response rate, and higher resistance to extinction compared with low P-IU. For this purpose, participants in a devaluation condition learnt to avoid two aversive USs consisting of an unpleasant sound, either presented to the left or to the right ear, through an operant discriminated procedure in which each US was signaled by a specific CS (CS_A and CS_B). Participants' responses to each CS were measured in an extinction phase after devaluating the aversiveness of the US signaled by CS_A. As expected, the regression analyses confirmed a significant association between P-IU and insensitivity to devaluation as well as a significant association between P-IU and the frequency with which participants responded to the CSs during the avoidance learning phase. Specifically, an increase in P-IU scores was associated with an increase in insensitivity to the outcome devaluation and with an increase in the frequency of avoidance

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responses to the CSs during the avoidance learning phase. Interestingly, the association between P-IU and insensitivity to outcome devaluation was significant even when controlling for trait anxiety. The association between P-IU and insensitivity to outcome devaluation did not seem to be due to high P-IU individuals being, in general, less able to discriminate between (or to adjust to) different outcome values as indicated by a non-significant correlation found between insensitivity to different outcome values and P-IU in a control group who was trained with different outcome values since the beginning of the avoidance learning phase. Additionally, individual differences in learning performance (as measured through CS-US contingency ratings), in US aversiveness ratings, or in adherence to instructions do not seem to have played any role in the association between P-IU and excessive and inflexible avoidance, as none of the referred variables correlated significantly with P-IU. Finally, regression analyses showed a significant association between P-IU and resistance to extinction of the avoidance response during the test phase. Specifically, an increase in P-IU was associated with an increase in resistance to extinction (RE). Exploratory regression and mediational analyses showed that this association between P-IU and RE was significantly mediated by the sensitivity to outcome devaluation ratio (SR). Additional exploratory analyses also showed a significant association between P-IU and generalization to a safety signal. Specifically, an increase in P-IU was associated with an increase in response frequency in CS_C trials. This latter result is consistent with previous studies showing similar results with different related personality traits (with trait anxiety, see Vervliet & Indekeu, 2015, with neuroticism, see Lommen et al., 2010, with experiential avoidance, see van Meurs, Wiggert, Wicker et al., 2014; see also Morris et al., 2015; 2016 for results showing more generalization of conditioned fear to safety cues in high IU participants).

The most relevant contribution of our study is that it is the first time, as far as we know, that an association between P-IU and excessive and inflexible avoidance in healthy

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participants is detected through an experimental approach. In general, the higher the participants scored in P-IU, the greater their tendency to engage in unnecessary active avoidance responses as evidenced through: a) Undue avoidance responses to avoid aversive outcomes during the avoidance learning phase, b) more difficulties to adjust avoidance frequency to changes in outcome value, and c) more persistence of avoidance responses during extinction trials. In this sense, high P-IU participants seemed to behave less optimally compared with low P-IU participants.

Therefore, our results showed that people scoring high in P-IU are more insensitive to outcome devaluation, respond more in general and are more resistant to extinction. These results are relevant for at least two reasons. One of them is that they provide support for a role of P-IU either in the development or in the maintenance of anxiety disorders associated with excessive avoidance. High P-IU may lead people not only to consider uncertain aversive situations intolerable but also to engage in excessive avoidance to reduce uncertainty and/or enhance the perception of control. This mechanism may well explain the development of excessive avoidance behavior in OCD sufferers, and could also be extended to explain the development and maintenance of excessive worry in generalized anxiety disorder and panic disorder, rumination in major depression, or "mind reading" or "fortune telling" in social phobia. It has been suggested that, in all these cases, excessive thinking would serve an avoidance function by reducing uncertainty, which would lead, in turn, to a reduction in anxiety (Boswell, Thompson-Hollands et al., 2013). This idea is consistent with the positive correlation between IU and each of these mental disorders (OCD: Toffolo, van den Hout, Engelhard et al., 2014; Generalized anxiety disorder: Carleton, 2012; Panic disorder: Gorka, Lieberman, Nelson et al., 2014; Social phobia: Hope, Heimberg, & Turk, 2010). These considerations suggest that recovery from the referred mental disorders could be significantly improved by taking IU as a crucial target for treatment.

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The other reason that speaks to the relevance of our study is that it suggests that healthy people scoring high in P-IU could be more vulnerable to anxiety disorders associated with either excessive behavioral avoidance or with excessive worry or thinking. Thus, IU could be a decisive construct to identify people at risk of developing anxiety disorders. High IU individuals could then be a target population for the design of prevention programs aimed at the reduction of IU in order to prevent different anxiety disorders.

Insensitivity to outcome devaluation and habitual vs goal-directed avoidance

Outcome devaluation experiments have been commonly conducted to study the acquisition or expression of habits (Dickinson, 1985; Tricomi, Balleine, & O'Doherty, 2009; Wood & Rünger, 2016). An effect of outcome devaluation on learners' instrumental responses may be interpreted as indicating that behavior is controlled by a goal-directed system (see Gillan, Kosinski, Whelan et al., 2016, for the implications of a deficient goal-directed control of behavior in different forms of psychiatric symptoms beyond compulsivity). The absence or the drastic reduction of this effect could be interpreted as evidence of habitual behavior. From a general perspective, our results are in line with previous findings showing outcome devaluation effects in avoidance learning preparations both in humans (Gillan et al., 2014) and in non-human animals (Fernando, Urcelay, Mar et al., 2014). Although there are very few studies assessing outcome devaluation effects in avoidance preparations, all of them suggest that, at least in some circumstances, avoidance behavior may be goal-directed. This is consistent with the idea that avoidance and reward-based learning share some mechanisms. This idea is supported by recent findings showing that habitual avoidance is associated with activity in brain areas similar to those involved in habitual rewarded behaviors (Gillan et al., 2015).

Focusing, however, on our results showing an association between P-IU and insensitivity to outcome devaluation, there are different possible interpretations. Following

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the more common interpretation of outcome devaluation effects, one of them is that an increase in P-IU is associated to an increase in avoidance habit acquisition or expression. An interesting result supporting this view is that avoidance frequency during the avoidance acquisition phase was shown to play a mediational role in the relationship between P-IU and insensitivity to outcome devaluation. The role of response frequency in outcome devaluation lends some support to the habit interpretation. In fact, it is already known the relationship between the number of response repetitions (overtraining) and the insensitivity to devaluation (Adams, 1982; Tricomi et al., 2009). However, this interpretation has two important difficulties. On the one hand, the direct association between P-IU and insensitivity to outcome devaluation was significant even when the meditational variable response frequency was included in the regression analysis. On the other hand, a significant mediational role of response frequency does not discard other alternative explanations based on goal-directed behavior. For instance, the uncertainty inherent in the procedure used in our task may have made high P-IU participants more prone to respond regardless of the outcome value as a strategy to reduce uncertainty about the occurrence of the aversive outcome. The results found in the control group do not discard this possibility because the control condition may have been perceived as less uncertain. One reason is that the use of USs with different outcome values in the control condition may have eased discrimination learning throughout the different acquisition phases compared with the devaluation condition, leading to an enhanced perception of control in the control group compared with the devaluation group. We propose that future research would need to discriminate between these hypotheses and to determine whether the greater insensitivity to outcome devaluation in higher P-IU participants is related to more habitual avoidance or is a goal-directed strategy to reduce uncertainty.

Limitations of our study

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Our experimental approach has proved useful to detect individual differences regarding different dependent measures of excessive avoidance that have been shown to correlate with each other such as avoidance response rate, sensitivity to outcome devaluation, generalization of avoidance responses to safety signals, and resistance of avoidance responses to extinction. One concern, however, is to what extent such individual differences may have been promoted by the use of a low-cost response. Some avoidance responses in daily life are low-cost responses that are easy to do and take little time such as some checking responses in OCD people or some ticks. But there are also many examples of high-cost responses such as complex and long compulsive chains of ritualistic responses or just avoidance responses that, when made repetitively, interfere with actions for reaching individual goals. Excessive avoidance in our task may have been promoted by the use of a low-cost avoidance response that has few consequences, if any, when made repetitively. It would be interesting to assess whether our results can be generalized to high-cost avoidance responses or to responses that interfere with goal achievement. The effect of response cost could be explored by incorporating a monetary or point loss per avoidance response. On the other hand, the effect of interference with goal achievement could be investigated by using approach-avoidance conflict scenarios. For example, participants could earn money or points by making an alternative response incompatible with the avoidance response. This way, investing time in avoidance responses would entail the loss of opportunities to engage in responding to earn positive rewards.

Another limitation is that the IU scale used in our study may not be well suited to detect domain-specific intolerance of uncertainty and there is recent evidence (Jensen & Heimberg, 2015) showing that IU may actually be more domain-specific than normally assumed. Thus, some people may tolerate uncertainty regarding negative social judgment but may not tolerate uncertainty regarding moderate pain. Conversely, some others may tolerate

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uncertainty regarding moderate pain but may not tolerate uncertainty regarding negative social judgment. According to this, some of the participants who scored high in P-IU could have tolerated uncertainty regarding the aversive noise quite well. As a consequence, the association found between P-IU and inflexible avoidance in our study may have been underestimated. A better correlation might have been found if, instead of an aversive noise, a specific aversive stimulus tailored for each participant had been used.

Finally, it would also be necessary to assess the role of desire for control in the association between P-IU and excessive avoidance. As stated throughout the article, one possible mechanism explaining this association is based on the idea that situations characterized by uncertainty and aversiveness may lead to a high increase in the need for control in high P-IU participants. The mere feeling of control (whether real or not) of uncertain aversive events may reduce uncertainty in high P-IU participants. Future studies should include additional measures of this desire for control such as the Desirability of Control Scale (Burger & Cooper, 1979) to assess the role of this personality trait.

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Table 1.

Correlations and 95% CIs between P-IU and contingency judgment accuracy regarding CS_A and CS_B (ContAB), contingency judgment accuracy regarding CS_C (ContC), US aversiveness (Aversiv), and adherence to instructions (Instruc).

	ContAB	ContC	Aversiv	Instruc.
P-IU	.105 [-.156, .347]	.239 [-.079, .524]	-.098 [-.341, .123]	.179 [-.062, .392]

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Figure 1.

Design and phases of the avoidance task, and images used as conditioned stimuli (CS). CS_A-CS_C refer to the different CSs used across the different phases of the task. Numbers represent the different trials of each type that were presented in each phase (see main text for further details).

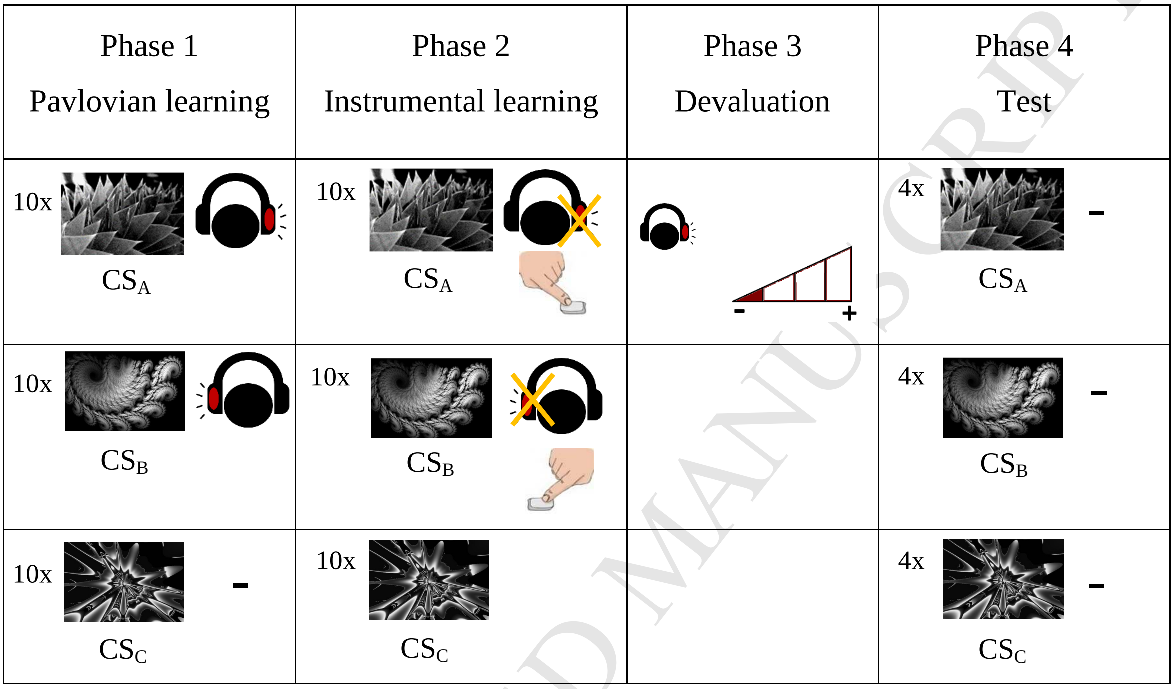

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Figure 2.

Means of correct response frequency in each Block of trials to CS_A, CS_B *and* CS_C *in the Instrumental (Panels A and C) and Test phases (Panels B and D), in both, the Devaluation and Control groups. Error bars are standard error of the means.*

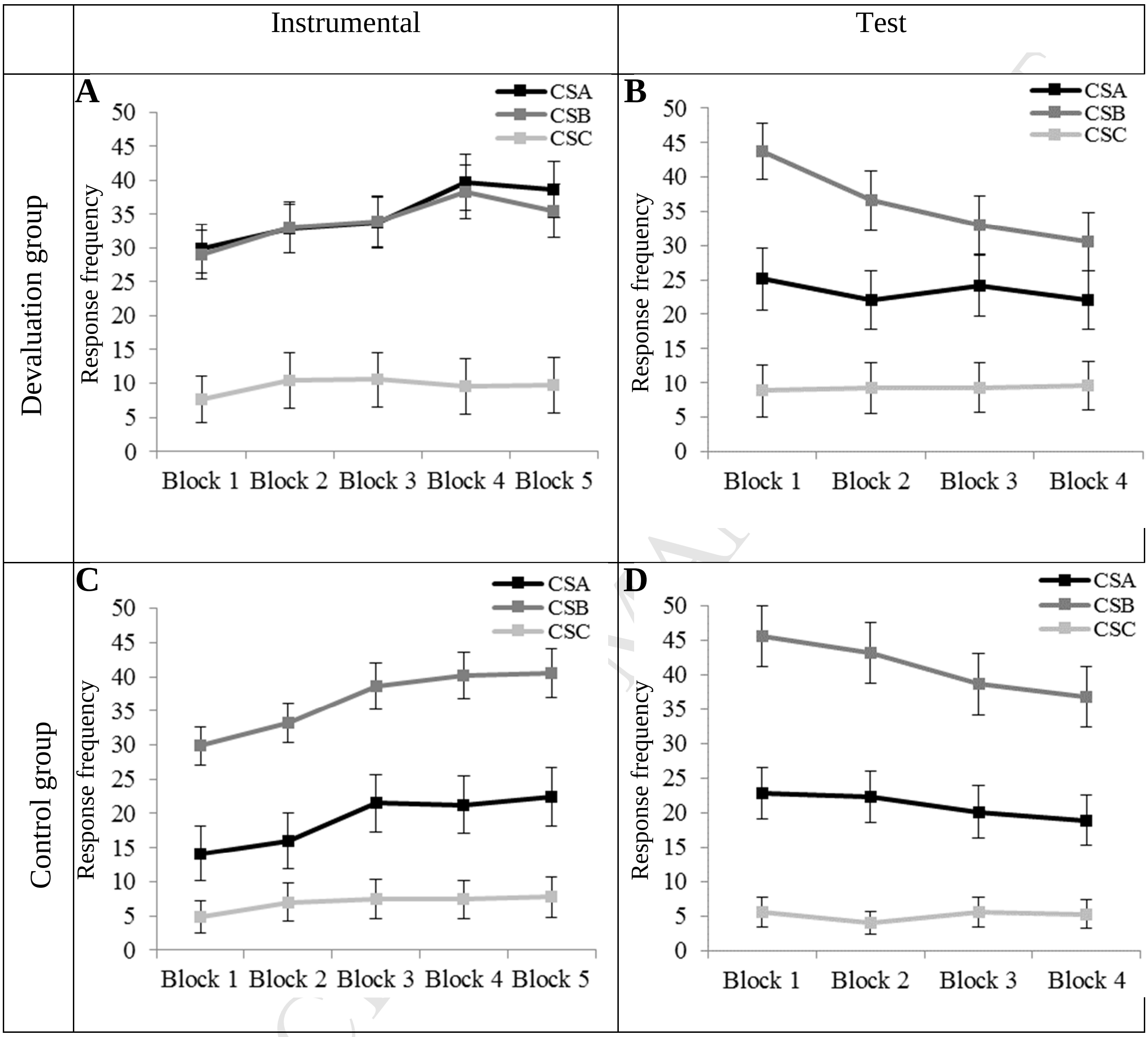

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Figure 3.

Relationship between prospective intolerance of uncertainty (IU) and ***(A)*** *devaluation (calculated as sensitivity-to-devaluation ratio, SR),* ***(B)*** *avoidance frequency during the instrumental phase (calculated as correct response frequency to* CS_A, CS_B *and* CS_C *collapsed),* ***(C)*** *avoidance frequency to the safety cue during the instrumental learning phase (calculated as response frequency to* CS_C*) and* ***(D)*** *extinction (calculated as resistance-to-extinction ratio), in the experimental group.*

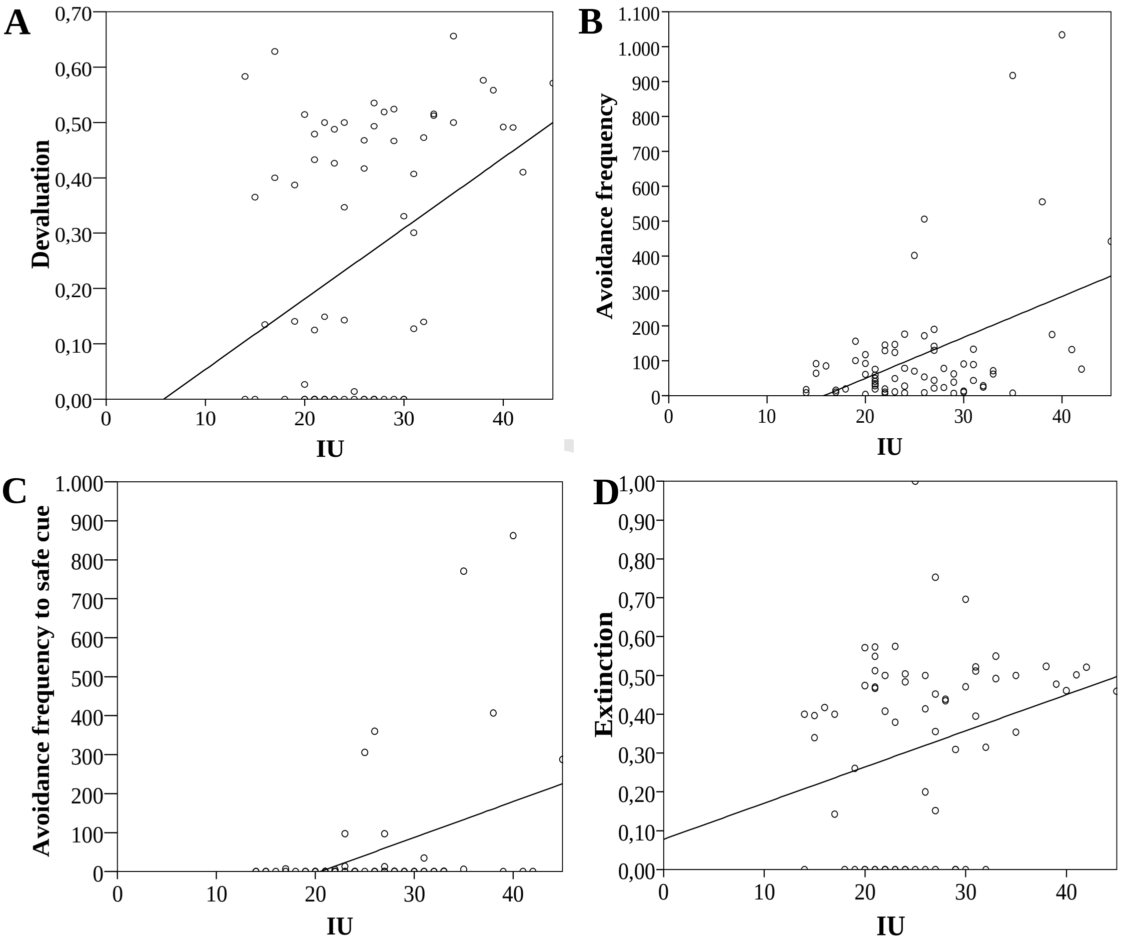

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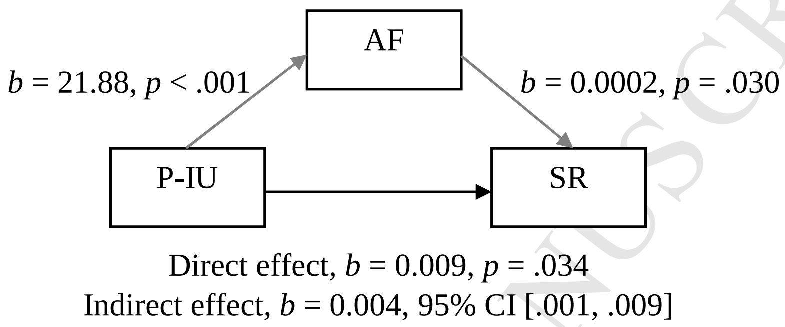
Figure 4.

Model of prospective intolerance of uncertainty (P-IU) as a predictor of sensitivity to devaluation (calculated as sensitivity-to-devaluation ratio, SR), mediated by avoidance frequency during the instrumental phase (calculated as the summed response frequency to CS_A, CS_B *and* CS_C, *AF). The confidence interval for the indirect effect is a bias corrected and accelerated bootstrap based on 5000 samples.*



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Research highlights

► Avoidance behavior may become habitual as a consequence of excessive responding.

► Prospective intolerance of uncertainty has been defined as a factor leading to excessive responding in uncertain situations.

► Prospective intolerance of uncertainty is associated to excessive avoidance and inflexible behavior in an outcome devaluation paradigm.

► Avoidance responding persisted in participants with higher prospective intolerance of uncertainty.

► Prospective intolerance of uncertainty is a vulnerability factor for excessive avoidance and inflexible behaviors-related disorders.

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