Elevated costly avoidance in anxiety disorders: Patients show little downregulation of acquired avoidance in face of competing rewards for approach

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Abstract

Background: Pathological avoidance is a transdiagnostic characteristic of anxiety disorders. Avoidance conditioning re-emerged as a translational model to examine mechanisms and treatment of avoidance. However, its validity for anxiety disorders remains unclear.

Methods: This study tested for altered avoidance in patients with anxiety disorders compared to matched controls ($n=40$/group) using instrumental conditioning assessing low-cost avoidance (avoiding a single aversive outcome) and costly avoidance (avoidance conflicted with gaining rewards). Autonomic arousal and threat expectancy were assessed as indicators of conditioned fear. Associations with dimensional symptom severity were examined.

Results: Patients and controls showed frequent low-cost avoidance without group differences. Controls subsequently inhibited avoidance to gain rewards, which was amplified when aversive outcomes discontinued. In contrast, patients failed to reduce avoidance when aversive and positive outcomes competed (elevated costly avoidance) and showed limited reduction when aversive outcomes discontinued (persistent costly avoidance). Interestingly, elevated costly avoidance was not linked to higher conditioned fear in patients. Moreover, individual data revealed a bimodal distribution of costly avoidance: Some patients showed persistent avoidance, others showed little to no avoidance. Persistent versus low avoiders did not differ in other task-related variables, response to gains and losses in absence of threat, socio-demographic data, or clinical characteristics.

Conclusions: Findings suggest that anxious psychopathology is associated with a deficit to inhibit avoidance in presence of competing positive outcomes. This offers novel perspectives for research on mechanisms and treatment of anxiety disorders.

Keywords

anxiety disorders, approach-avoidance conflict, fear conditioning, instrumental avoidance, panic disorder and agoraphobia, social anxiety disorder

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INTRODUCTION

Avoidance is a transdiagnostic symptom of anxiety disorders (Craske et al., 2017). Whereas adaptive avoidance prevents harm and helps coping with the threat, pathological avoidance is out of proportion to objective threat, persists, and causes serious impairments (Beesdo et al., 2007; Craske et al., 2017; Wittchen et al., 2000, 2014). Persistent pathological avoidance prevents learning that feared situations are (now) safe and thus constitutes a pathway into chronification of psychopathology (Craske et al., 2017; Lovibond et al., 2009; Pittig, 2019; Wittchen et al., 2014). Better understanding pathological avoidance may thus optimize prevention and treatment.

To this end, instrumental conditioning has re-emerged as a basic research paradigm to examine avoidance behavior (Cain, 2019; Krypotos et al., 2015; Ledoux & Daw, 2018; Pittig et al., 2020). In signaled active avoidance, animals and humans initially learn to associate a formerly neutral stimulus with an aversive unconditioned stimulus (US) and thereby acquire conditioned fear to this conditioned stimulus (CS+). Subsequently, learning of a predefined avoidance response to the CS+ (e.g., shuttling, button press) prevents the occurrence of the aversive US (i.e., US-avoidance). Given its high translational potential, avoidance conditioning represents a valuable approach for understanding anxious psychopathology and optimizing treatment.

Although some evidence suggests biased avoidance conditioning in anxious individuals, these findings are inconsistent and refer to subclinical samples (Kirlic et al., 2017; Krypotos et al., 2018; Pittig, Treanor et al., 2018; Pittig et al., 2020). Importantly, the validity of traditional avoidance conditioning for pathological avoidance has been criticized (Krypotos et al., 2018; Pittig, Treanor et al., 2018; Pittig et al., 2020). Three major criticisms are: (i) There are currently no studies examining its diagnostic validity, for example, whether clinical samples show altered responding (Krypotos et al., 2018; Pittig et al., 2020). (ii) Especially in humans, avoidance conditioning is an unambiguous paradigm that produces ceiling effects and thereby prohibits the investigation of individual differences (Krypotos et al., 2018; Pittig et al., 2020). (iii) Human avoidance conditioning typically incorporates low-cost responses, which require minimal cost and effort (i.e., there is nothing to lose when avoiding). Such avoidance is an adaptive response that arguably does not resemble pathological behavior.

In response to the criticism on low-cost avoidance, recent research established costly avoidance paradigms, in which avoidance responses are embedded in approach-avoidance conflicts. In rodents, for example, rats successfully learn to jump on a safe platform during a CS+ to avoid aversive foot-shocks but otherwise leave the platform to approach food (Bravo-Rivera et al., 2014, 2015; Martínez-Rivera et al., 2019). In human paradigms, avoidance responses are likewise in conflict with appetitive outcomes (e.g., incentives for approach; Pittig, 2019; Pittig & Dehler, 2019; Pittig et al., 2014) or inflict other costs (e.g., temporal delay, physical effort; Hunt et al., 2019; Meudlers et al., 2016; van Meurs et al., 2014; Rattel et al., 2017). Such competing outcomes strongly modulate avoidance (for an overview see Pittig et al., 2020). For example, appetitive outcomes that compete with avoidance facilitate fear-opposite responses, that is, avoidance is reduced despite high levels of fear (Pittig, 2019; Pittig & Dehler, 2019; Pittig, Hengen et al., 2018). Furthermore, costly avoidance paradigms are more ambiguous and produce larger variability in responding (Krypotos et al., 2018; Wong & Pittig, 2020).

2 | METHODS AND MATERIALS

2.1 | Participants

Forty patients and forty matched controls were included (Table 1). Twenty-two patients (55.0%) were diagnosed with primary PD/AG and eighteen with primary SAD (45.0%). Twenty-eight patients fulfilled the criteria for any PD/AG (70%) and twenty for any SAD (50%). Ten patients fulfilled the criteria for comorbid depression (25%). Eighteen patients fulfilled the criteria of a single diagnosis (45.0%), sixteen for two (40.0%), five for three (12.5%), and one patient for four diagnoses (2.5%). Control participants did not fulfill the criteria for any disorder and were recruited to match patients on age (±3 years) and sex. More details on recruitment and in-/exclusion criteria are provided in the Supporting Information Materials.

2.2 | General procedures

The local ethics committee approved all procedures (GZEK2018-20). DSM-5 diagnoses were determined using a standardized interview conducted by licensed psychotherapists (Mini-DIPS; Margraf et al., 2017). On a separate day, all participants completed dimensional measures for anxiety (PROMIS, Wahl et al., 2011; DSM-Cross-D, Lebeau et al., 2012; STAI-State anxiety version, Laux et al., 1981) and depression (depression scale of DASS-21-G; Nilges & Essau, 2015) as well as the single-cue conditioning paradigm. Patients were offered cognitive-behavioral treatment at the institute’s outpatient clinic afterwards. More details on diagnostic instruments are given in the Supporting Information Materials.
2.3 Single-Cue fear and US-avoidance learning paradigm

The paradigm was adapted from a previous study (Pittig, 2019). It included seven consecutive phases (Table 2). In each trial, a purple hexagon was presented for 8 s as CS. US expectancy ratings (0%–100%) and SCRs to the CS served as cognitive and autonomic indicators of fear learning (Pittig & Dehler, 2019; see Supporting Information Materials for SCR and US expectancy assessment). CS outcomes and the availability of avoidance responses varied across phases. After the paradigm, participants were asked to imagine continuing the paradigm and rate their motivation to avoid the US, to approach the rewards, and the intensity of approach-avoidance conflict (0–100).

### 2.3.1 Fear and low-cost avoidance acquisition

The first four phases aimed to establish fear and low-cost US-avoidance to the CS. During CS habituation (Phase 1; four trials), the CS was presented in absence of any outcomes. During fear acquisition (Phase 2; eight trials), the CS was followed by an aversive US in every trial. The US was an electrical stimulation to the nondominant forearm individually calibrated to be "causing discomfort, but not pain." Patients and controls did not differ in self-reported discomfort or objective intensity of the US (Table 1).

### 2.3.2 Costly avoidance

Before the next phase, participants were instructed that they may win rewards based on their decision to avoid or not during the subsequent trials, that three trials will be randomly selected, and that they will be paid the amount gained in these trials (Pittig, 2019). In the Reward-US phase (Phase 5; eight trials), the aversive US was...
again omitted when the avoidance button was pressed but delivered when the nonavoidance button was pressed. Additionally, each CS was now associated with a fixed reward of 0.10€ [Pittig, 2019], which was presented following nonavoidance responses (€g, “Gained reward: 0.10€” displayed as green text) but missed following avoidance responses (“Missed reward: 0.10€” in red text). These contingencies were used to establish costly avoidance: Participants could either decide to avoid the US at the cost of the reward or approach the reward and tolerate the aversive US.

Test II (Phase 6: two trials) was identical to Test I, but rewards were continued as in the previous phase. Test II examined whether participants show comparable fear responses irrespective of potential differences in avoidance in the previous phase.

### 2.3.3 Persistence of costly avoidance after removing the aversive US

The Reward-NoUS phase (Phase 7) was similar to the Reward-US phase with three important differences: First, no more USs were delivered, which was not instructed. Second, the competing rewards incrementally increased from trial to trial (€i, average increase of 0.04€ per trial in randomized step size of 0.03€, 0.04€, or 0.05€) to provide increasing incentives for nonavoidance. Third, the number of trials varied based on participants’ responses: The phase ended either after eight nonavoidance responses or after a total of 30 trials (to keep the maximum duration reasonable). The individual number of avoidance responses served as an indicator of persistent costly avoidance in absence of the US. As a secondary outcome, we aimed to analyze fear extinction during the eight nonavoidance trials.

### 2.4 Controlling for affective responses to monetary gains and losses in absence of threat

As costly avoidance incorporated missing rewards, differences between patients and controls might be confounded by general differences in responsiveness to monetary gains or losses. We therefore assessed affective responses to winning or losing small amounts of money in absence of threat. Importantly, patients and controls did not differ (see Supporting Information Materials).

### 2.5 Statistical analysis

Main analyses compared the frequency of avoidance and the level of conditioned fear (US expectancy, SCRs) between patients and controls. Change of avoidance frequency between phases was analyzed by planned 2 × 2 repeated measure analysis of variances (ANOVAs; Group × Phase). Moreover, the total amount of avoidance responses in the Reward-NoUS phase as an indicator of persistent costly avoidance was compared between groups. For conditioned fear, SCRs and US expectancy ratings from two consecutive trials were averaged to reduce noise (Pittig, 2019). These analyses were conducted within each phase using pairwise tests or repeated measure ANOVAs (Group × Trial), because different trajectories were expected per phase. Greenhouse–Geisser correction was applied when necessary. Pairwise and follow-up analyses were conducted with t tests or nonparametric U or W tests. The association between dimensional anxiety symptoms (PROMIS) and US-avoidance in the different phases was calculated with robust winsorized correlation coefficients (Field & Wilcox, 2017; trim = 0.2; Mair & Wilcox, 2020). Analyses were also performed within a Bayesian framework for which Bayes factor was used (Doorn et al., 2019; Krypotos et al., 2017). BF10 is reported for comparing the probability of the data coming from the H1 compared to the H0 and BF01 for the reversed comparison (for details see Supporting Information Materials).

### 3 RESULTS

#### 3.1 Fear acquisition

Frequency of US-avoidance and level of fear responses are shown in Figure 1. Both groups showed a decrease in US expectancy and SCRs during CS habituation followed by an increase during fear acquisition training, indicating successful fear acquisition, with an overall higher level of US expectancy but not SCRs in patients (see Supporting Information Materials).

#### 3.2 No differences in low-cost avoidance between patients and healthy individuals

During US-avoidance training, both groups showed frequent avoidance. Importantly, there were no differences between patients (M = 0.75, SD = 0.31) and controls (M = 0.72, SD = 0.28), U = 717.5, p = .416, r = .10, BF01 = 3.97. For US expectancies, there was a significant reduction across trials, F(2.51, 196.06) = 3.16, p = .033, ηp2 = 0.008, BF10 = 1.28. No effect involving group reached significance, F < 1.99, ps > .127, ηp2 < 0.005, BF01 > 1.97. For SCRs, no main or interaction effect was significant, F < 2.49, ps > .075, ηp2 < 0.012, BF01 > 2.64. During Test I, US expectancy and SCRs increased, but no group differences were found, US expectancy: U = 722.5, p = .457, r = .10, BF01 = 2.91, SCRs: t(74) = 0.01, p = .992, d < 0.01, BF01 = 4.21. Summarized, patients and controls did not differ in low-cost avoidance or conditioned fear.

#### 3.3 Elevated costly avoidance in patients with anxiety disorders

During the Reward-US phase, patients (M = 0.74, SD = 0.33) showed more frequent avoidance compared to controls (M = 0.54, SD = 0.34), U = 529.5, p = .008, r = .34, BF10 = 5.21. This difference resulted from a
reduction of avoidance responses compared to the previous phase in controls but not patients, interaction: \(F(1, 78) = 8.38, p = .005, \eta^2 = 0.018, \text{BF}_{10} = 7.60; \) follow-up for patients: \(W = 116.5, p = .673, r = .11, \text{BF}_{01} = 5.58; \) follow-up for controls: \(W = 370.5, p = .004, r = .60, \text{BF}_{10} = 24.38.\)

For US expectancies, there was no significant main or interaction effect, \(F_s < 1.38, p_s > .251, \eta_s^2 < 0.004, \text{BF}_{01} > 2.43.\) For SCRs, there was a significant decrease across trials, \(F(3, 74) = 3.01, p = .031, \eta^2 = 0.017, \text{BF}_{10} = 1.35, \) but no other significant effect, \(F_s < 0.38, p_s > .663, \eta_s^2 < 0.002, \text{BF}_{01} > 3.86.\)

During Test II, US expectancy and SCRs increased, but no group differences were found. US expectancy: \(U = 865.5, p = .517, r = .08, \text{BF}_{01} = 4.05,\) SCRs: \(t(74) = 0.73, p = .466, d = 0.17, \text{BF}_{01} = 3.34.\)

Summarized, patients showed elevated costly avoidance. These group differences emerged because controls, but not patients, showed reduced avoidance when incentives for nonavoidance were introduced. There were no differences in conditioned fear.

### 3.4 More persistent costly avoidance in patients with anxiety disorders

During the first eight trials of the Reward-NoUS phase, patients \((M = 0.63, SD = 0.42)\) showed substantially more frequent avoidance compared to controls \((M = 0.28, SD = 0.36),\) \(U = 446.0, p < .001, r = .44, \text{BF}_{10} = 134.29.\) Both groups showed a reduction compared to the previous phase. This reduction was stronger in controls compared to patients, interaction Group and trials: \(F(1, 78) = 6.94, p = .010, \eta^2 = 0.008, \text{BF}_{10} = 3.80; \) follow-up for patients: \(W = 183.0, p = .004, r = .74, \text{BF}_{10} = 13.29; \) follow-up for controls: \(W = 479.5, p < .001, r = .93, \text{BF}_{10} > 1000.\)

US expectancies significantly decreased, \(F(1.75, 136.21) = 5.42, p = .008, \eta^2 = 0.019, \text{BF}_{10} = 14.93.\) Moreover, controls indicated higher US expectancy compared to patients, \(F(1, 78) = 4.01, p = .049, \eta^2 = 0.034, \text{BF}_{01} = 1.47.\) There was no significant interaction, \(F(1.75, 136.21) = 0.94, p = .381, \eta^2 = 0.003, \text{BF}_{04} = 9.41.\) For SCRs, there was a significant interaction of Group × Trials, \(F(3, 222) = 3.44, p = .021, \eta^2 = 0.019, \text{BF}_{10} = 3.09.\) Follow-up analyses indicated a significant reduction in controls and no change in patients. Controls: \(F(3, 111) = 3.28, p = .024, \eta^2 = 0.081, \text{BF}_{10} = 1.56; \) Patients: \(F(3, 111) = 1.79, p = .153, \eta^2 = 0.046, \text{BF}_{04} = 3.50.\) This resulted in lower SCRs in controls compared to patients at the end of the phase (Trials 39–40): \(t(74) = 2.17, p = .033, d = 0.50, \text{BF}_{10} = 1.76, \) all other trials: \(ts < 1.17, ps > .247, ds < 0.26, \text{BF}_{01} > 2.34.\)

Moreover, patients \((M = 14.15, SD = 12.87)\) compared to controls \((M = 4.55, SD = 8.33)\) clearly showed more overall avoidance responses during the whole phase, \(U = 426.0, p < .001, r = .47, \text{BF}_{10} = 144.46.\) Interestingly, individual data illustrated a bimodal distribution within patients (see histogram of avoidance responses in Figure 2, right). While some patients rarely avoided, others persistently avoided during most trials. Due to persistent avoidance, 18 patients and four controls did not fulfill the criterion of eight nonavoidance trials.

![Image](image_url)
In sum, patients with anxiety disorders showed more persistent costly avoidance in the absence of threat. Stronger reduction of avoidance in controls enabled fear extinction, as, for example, indicated by lower levels of autonomic arousal despite less frequent avoidance.

### 3.5 Association with dimensional anxiety symptoms

In the whole sample, no significant association was found between anxiety symptoms and frequency of avoidance with only the US as outcome, $r(78) = .11$, $p = .350$ (Figure 3, top). Mimicking the group effects, higher anxiety symptoms were associated with more costly avoidance during the Reward-US phase, $r(78) = .35$, $p = .002$ (Figure 3, middle), and the Reward-NoUS phase, $r(78) = .43$, $p < .001$ (Figure 3, bottom). Within the patient sample, there was, however, no significant associations between anxiety symptoms and frequency of avoidance (US-avoidance: $r = .13$, $p = .428$; Reward-US: $r = .14$, $p = .390$; Reward-NoUS: $r = .20$, $p = .231$).

### 3.6 Post-hoc comparison of persistent versus low avoiders in patients

Given the bimodal distribution of avoidance responses in the last phase, we performed post-hoc exploratory analyses to compare persistent avoiders ($\geq 15$ avoidance responses, $n = 18$) with low avoiders ($<15$ avoidance responses, $n = 22$). Persistent and low avoiders did not differ in task-related variables (US intensity, US unpleasantness, state anxiety), affective response to gains and losses in absence of threat, sociodemographic data (age, sex), or clinical characteristics (comorbidities, depression, primary disorder distribution; see Supporting Information Materials). Due to reduced avoidance, low avoiders showed higher threat expectancy, but not SCR, during phases in which avoidance was available (i.e., US-avoidance acquisition, Reward-US, Reward-NoUS, Figure 4 and Supporting Information Materials). Interestingly, subgroups did not differ in threat expectancy ratings or SCRs during phases in which avoidance was unavailable (i.e., CS habituation, fear acquisition, Test I & II). These findings indicate that subsequent reduction of avoidance in low avoiders was not linked to lower levels of conditioned fear.

### 3.7 Additional analyses

Additional analyses compared self-reported motivation to avoid the US, motivation to approach the rewards, and approach-avoidance conflict after the paradigm and the rate of extinction during the eight nonavoidance trials in the Reward-NoUS phase (see Supporting Information Materials). Patients compared to controls reported a lower motivation to approach the rewards, a slightly higher motivation to avoid the aversive US, and lower approach-avoidance conflict.
FIGURE 3  Scatterplots for the association of anxiety symptoms and relative frequency of avoidance during unconditioned stimulus (US)-avoidance acquisition (top), Reward-US (middle), and Reward-NoUS phase (bottom). Dots represent raw data from each participant with shape/color indicating primary diagnosis. Correlation coefficients ($r$) represent robust winsorized correlations (trim = 0.2) with 95% CI. CI, confidence interval; None, matched healthy controls; PD/AG, panic disorder and agoraphobia; SAD, social anxiety disorder

FIGURE 4  Post-hoc comparison of unconditioned stimulus (US) expectancy (top) and skin conductance responses (SCRs; bottom) for persistent and low avoiders within the patient sample across phases (±SEM), averaged for two consecutive trials
conflict. For fear extinction in the Reward-NoUS phase, US expectancy and SCRs declined across trials, without effects involving group. Thus, those patients and controls who did not persistently avoid displayed comparable fear extinction.

4 | DISCUSSION

This study demonstrates elevated and more persistent costly avoidance, but not low-cost avoidance, in patients with anxiety disorders. No differences to matched controls were found regarding instrumental avoidance to a single aversive US. As contingencies for avoiding versus not avoiding the single US were simple, both patients and controls frequently avoided (although some exploration of the nonavoidance response remained, see also Cameron et al., 2016; Dymond et al., 2012; Pittig, 2019; Pittig & Dehler, 2019). These findings support the view that low-cost avoidance is an adaptive response, which does not link to pathological avoidance in anxiety disorders (Krypotos et al., 2018; Pittig et al., 2020). Patients, however, showed elevated avoidance in a mixed-outcome approach-avoidance conflict, that is, when avoidance of aversive outcomes conflicted with gaining appetitive outcomes. This elevated costly avoidance in patients persisted when the aversive outcome discontinued. These findings relate to clinical phenomena of pathological avoidance persisting in absence of objective threat despite causing impairments. The present findings thus demonstrate the diagnostically valid costly avoidance for anxious psychopathology.

Elevated costly avoidance in patients was associated with a lack of avoidance reduction in mixed-outcome approach-avoidance conflicts. Although aversive outcomes still occurred, healthy individuals showed an immediate reduction of avoidance in favor of obtaining positive outcomes. The immediate reduction suggests that contingencies of competing rewards were easily acquired. This reduction was further enhanced when aversive outcomes discontinued. These results replicate previous findings that healthy individuals show strong avoidance when threat is prominent, but inhibit acquired avoidance when the value of competing positive outcomes increases (Aupperle et al., 2011; Pittig, 2019; Pittig & Dehler, 2019; Sierra-Mercado et al., 2015; Talmi & Pine, 2012). In contrast, patients did not show this reduction of avoidance when aversive and competing positive outcomes were present and showed limited reduction of avoidance when aversive outcomes discontinued. The present study did not address group differences in the reduction of low-cost avoidance when aversive outcomes became absent. Using the same paradigm in a previous study, even healthy individuals did not show a reduction of such low-cost avoidance when the aversive outcome discontinued (Pittig, 2019), rendering less reduction of low-cost avoidance in patients unlikely. Thus, anxious psychopathology is associated with a distinct deficit to down-regulate avoidance in the presence of competing positive outcomes.

There may be different explanations for the differences in costly avoidance. For example, patients might have deficits in instrumental learning. However, threat and reward contingencies were simple and quickly acquired and groups did not differ in low-cost avoidance. It thus seems more likely that differences were not caused by differences in instrumental learning, but by differences in the decision processes integrating threat and reward information during approach-avoidance conflict. In this regard, patients may have more strongly weighted threat information. The subjective and objective intensity of the aversive US did not differ between patients and controls. Interestingly, elevated costly avoidance in patients was not linked to higher levels of fear. Patients initially showed elevated threat expectancies, but not autonomic arousal, during CS habituation and fear acquisition (see also Lissek et al., 2005). However, patients did not show elevated low-cost avoidance during subsequent avoidance acquisition, suggesting that elevated threat expectancies did not produce stronger avoidance. Importantly, patients and controls showed similar levels of conditioned fear when avoidance became unavailable (i.e., during Test I). These findings indicate that the subsequent reduction of avoidance in controls during approach-avoidance conflict (during Reward-US phase) was not caused by lower levels of conditioned fear, but rather a stronger impact of competing positive outcomes. This supports recent findings that competing positive outcomes trigger fear-opposite actions in healthy controls (Pittig, 2019; Pittig & Dehler, 2019). The reduction of avoidance in controls initiated fear extinction learning as indicated by a reduction of autonomic arousal during the last phase.

In contrast, patients showed deficits in performing fear-opposite actions: Despite similar levels of conditioned fear, incentives for approach had a limited effect on the reduction of avoidance in patients. This limited reduction in patients cannot be explained by a lower responses to rewards in general. No differences in self-reported affective responses to gaining rewards in absence of threat were found between patients and controls. General reward responses also did not differ between low and persistent avoiding patients. It is thus more likely that there is a tendency in patients to discount rewards more strongly when these rewards were in conflict with threat. Tentative support for such smaller impact of reward during conflict decisions in patients comes from lower self-reported motivation to approach these rewards when imagining to continue the task. These results support our preliminary finding that high compared to low trait anxious individuals tend to weight reward information less strongly in approach-avoidance conflicts (see Pittig & Scherbaum, 2020). Yet, future research is needed to disentangle the impact of threat versus reward information. Nevertheless, our findings suggest that it may be useful to expand the focus of anxiety disorder treatments. In addition to decreasing fear responsiveness, interventions may aim to strengthen fear-opposite actions by targeting reward responsiveness during approach-avoidance conflict (Crake et al., 2018; Pittig et al., 2020).

Interestingly, not all patients showed elevated costly avoidance. Individual data revealed a bimodal distribution of avoidance responses in the final phase: While some patients showed a pattern of rigid, persistent avoidance, others showed little to no avoidance. Post-hoc analyses did not reveal differences between persistent versus low avoiders in task-related factors (US intensity, US unpleasantness, and state anxiety), affective response to gains and
losses in absence of threat, sociodemographic data (age, biological sex), and clinical characteristics (distribution of primary disorders, comorbidities, depression). Interestingly, low and persistent avoiders showed similar levels of conditioned fear during fear acquisition and test phases. Again, differences in avoidance could thus not be explained by differences in fear learning. It may therefore be possible that the ability to inhibit avoidance responses despite fear is a unique behavioral marker of some patients but not others. Given that these findings were based on post-hoc analyses, replication in larger sample sizes including additional moderators is warranted.

The robust findings on differences between patients and matched controls in costly avoidance and its persistence offer novel perspectives for research on the mechanisms of anxious psychopathology and its treatment. For example, neuroimaging research may target the interaction between negative and positive valence systems to better understand the role of competing rewards in threat avoidance. Moreover, this study was limited to patients with PD/A and SAD. While descriptive data did not suggest a difference between these primary disorders, inclusion of other anxiety disorders is required as evidence for elevated costly avoidance as a transdiagnostic feature of anxiety disorders. Specifically, patients that are better characterized by anxious apprehension than anxious arousal (Nitschke et al., 1999), such as individuals with generalized anxiety disorder, might differ in costly avoidance. In the present study, we focus on responses to a conditioned fear stimulus (CS+), which was associated with an actual threat during the first phases, but not at the end. Our paradigm thus models clinical avoidance for cases in which fear and avoidance to specific stimuli or situations were developed as response to actual aversive outcomes (e.g., social rejection, actual harm). As other learning pathways exist (Rachman, 1976, 1977), future research may extend to cases in which no objective harm was experienced, for example, by investigating costly avoidance to a conditioned safety stimulus (CS–). Moreover, the present paradigm used simple contingencies for avoidance and approach and thus does not exclude differences in instrumental learning between patients and controls for more complex instrumental contingencies (e.g., Mkrtchian et al., 2017). Finally, the predictive role of individual differences in elevated costly avoidance for treatment should be investigated. For example, it seems likely that persistent compared to low avoiders respond differently to behavioral treatments such as exposure therapy.

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DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION
Additional Supporting Information may be found online in the supporting information tab for this article.

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