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Contextual fear conditioning predicts subsequent avoidance behaviour in a virtual reality environment

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Avoidance behaviour is a crucial component of fear and is importantly involved in the maintenance of anxiety disorders. Presumably, fear conditioning leads to avoidance of the feared object or context. A virtual reality contextual fear conditioning paradigm was used to investigate the association between explicit conditioning effects and subsequent avoidance behaviour. Mild electric shocks were administered in one context (anxiety context), but never in a second context (safety context). Subsequent avoidance behaviour was assessed by asking participants to choose two out of three contexts (a neutral context was added) to visit again. Participants avoided the anxiety context, but did not prefer the safety over the neutral context. Participants with substantial conditioning effects, as reflected in differential valence, arousal and anxiety ratings, avoided the anxiety context but not the safety context. In sum, we demonstrated an association between context conditioning effects on an explicit level and later avoidance behaviour.

Keywords: Contextual fear conditioning; Avoidance; Ratings; Virtual reality.

Anxiety disorders have a high prevalence of approximately 14% within 12 months (BGS98, 2000). This finding has inspired research concerning the origin and maintenance of these disorders. The most prominent aetiological model for anxiety disorders refers to learning processes. Specifically, anxiety disorders are likely to depend on fear conditioning (Field, 2006; LeDoux, 2000; Mineka & Zinbarg, 2006; Mowrer, 1953). Fear conditioning means that a distinct neutral stimulus is paired with a naturally aversive unconditioned stimulus (US). After several pairings, the neutral stimulus becomes a conditioned stimulus (CS), which evokes a specific conditioned fear response (CR). In a differential fear conditioning paradigm, one stimulus (CS+) is paired with an aversive US, while another stimulus (CS–) is never paired

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with this US. Extinction occurs if the CS+ is presented several times without the US.

Marks (1987) suggested a distinction between fear and anxiety. Fear is linked to a specific threat, whereas anxiety is a more diffuse state not related to a specific object or stimulus. Cue conditioning is regarded as a model for phasic fear: the cue becomes a valid time-bound predictor for threat because it is contingently delivered with or shortly after the CS (Grillon, 2002a). If specific cues signalling threat occurrence are lacking, the individual experiences a chronic status of anxiety because of an inability to identify periods of safety (Seligman, 1968; Seligman & Binik, 1977). Experimentally, anxiety can be modelled by contextual fear conditioning paradigms, with USs presented in absence of any specific CS. As a consequence, the context becomes associated with a US because it is the best predictor for the US. Thus, context conditioning induces a state of chronic anticipatory anxiety as the occurrence of the US is not time-bound and therefore is experienced as unpredictable (Grillon, 2008). Experimental studies have shown that unpredictable aversive events induce greater contextual anxiety and chronic expectations of these aversive events than predictable ones (Grillon, Baas, Lissek, Smith, & Milstein, 2004; Vansteenwegen, Iberico, Vervliet, Marescau, & Hermans, 2008). On a neural level, phasic fear reactions are coordinated by the amygdala, whereas sustained anxiety reactions are additionally mediated by the bed nucleus of the stria terminalis in rodents (BNST; Davis, Walker, Miles, & Grillon, 2010) and by the hippocampus in humans (Alvarez, Biggs, Chen, Pine, & Grillon, 2008; Hasler et al., 2007; Lang et al., 2009; Marschner, Kalisch, Vervliet, Vansteenwegen, & Büchel, 2008).

Differential context conditioning may serve as a model for panic disorder with agoraphobia, which is characterised by unexpected and unpredictable panic attacks and strong avoidance of places where such panic attacks are expected to occur (American Psychiatric Association, 2000). As these patients mostly are not able to identify specific cues predicting their panic attacks (which may function as a US), the attacks are perceived as unpredictable. As a result, the context where the panic attacks occurred might become associated with the panic attacks. In turn, this context (CXT+) might trigger future panic attacks, which, however, are still rather unpredictable. This might induce sustained and chronic anxiety states and lead to avoidance behaviour. By contrast, a context not associated with a panic attack may become a safety context (CXT–) and may be approached later (Gorman, Kent, Sullivan, & Coplan, 2000). In the same vein, patients with posttraumatic stress disorder (PTSD) have also experienced unpredictable threatening and traumatic events and suffer from intrusions, increased arousal and intensive avoidance behaviour of locations where the traumatic event occurred (American Psychiatric Association, 2000). Experimental studies have demonstrated that panic and PTSD patients show increased contextual anxiety but did not differ in their fear reactions to a single predictable cue (Grillon et al., 2008, 2009). Increased contextual anxiety elicited by unpredictable aversive events may be an important pathogenic marker for anxiety disorders characterised by diffuse and sustained anxiety states.

Several theories have emphasised the important role of avoidance and safety-seeking behaviour in the maintenance of anxiety disorders (Barlow, 2002; Rachman, 1984). Specifically, Mowrer's influential two-factor theory (1953) emphasised that fear leads to a strong motivation to avoid the CS+. However, if the CS+ is avoided, extinction cannot occur. This has recently been confirmed experimentally in humans. If participants were given the possibility of avoiding the CS+ during extinction training, their fear responses to the CS+ decreased less compared to participants who were not able to avoid the CS+ during extinction. Thus, the avoidance response prevented extinction learning (Lovibond, Mitchell, Minard, Brady, & Menzies, 2009).

According to Bradley and Lang (2000), a fear response has three response levels: (i) behaviour (e.g., avoidance or freezing); (ii) verbal report (e.g., valence or fear ratings); and (iii) physiological response (e.g., startle reflex, skin conductance response). Many studies have examined physiological or verbal responses to a CS in a fear conditioning paradigm. However, experimental studies examining overt avoidance behaviour to a specific cue or a context with a fear conditioning paradigm have been rare. To our knowledge, only three conditioning studies have investigated direct behavioural effects to contexts. First, Grillon (2002b) reported that participants who did not return to the experimental context after a cued fear conditioning experiment were more likely to be unaware of the contingency between the CS and US. The author assumed that participants who were unaware of the CS–US contingency would perceive the US as unpredictable, resulting in contextual conditioning and future avoidance of that context. Second, a study on adolescents observed that high fear ratings for the CS+ after a cue conditioning session predicted avoidance behaviour (i.e., adolescents did not return for the second session; Lau et al., 2008). Third, using a virtual reality paradigm, Grillon, Baas, Cornwell, and Johnson (2006) created three different contexts where the USs were either unpredictably, predictably or not administered. They found that after conditioning most participants avoided the unpredictable context (i.e., did not choose), followed by the predictable context and least avoided the safety context. The authors also reported that anxiety ratings were highest for the unpredictable context, followed by the predictable and safety context. Unfortunately, they did not go into detail about whether these explicit anxiety responses were associated with avoidance behaviour. Importantly, these previous studies did not provide a neutral context; thus, it remains unclear whether the observed effects are due to avoiding the anxiety context or approaching the safety context.

Virtual reality (VR) is a powerful tool that can be used to study fear conditioning (Alvarez, Johnson, & Grillon, 2007; Baas, Nugent, Lissek, Pine, & Grillon, 2004; Baas, van Ooijen, Goudriaan, & Kenemans, 2008) and context-dependent fear reactions in ecologically valid environments (Mühlberger, Bülthoff, Wiedemann, & Pauli, 2007; Mühlberger, Wieser, & Pauli, 2008). Additionally, it has been used successfully for therapeutic interventions (Mühlberger, Herrmann, Wiedemann, Ellgring, & Pauli, 2001; Mühlberger, Weik, Pauli, & Wiedemann, 2006).

Given the relevance of avoidance of specific contexts, especially in panic disorder and PTSD, it is crucial to understand which conditions actually lead to this overt contextual avoidance behaviour. Therefore, we conducted two differential contextual fear conditioning studies in VR with three different contexts. In both studies, one context (anxiety context, CXT+) was associated with unpredictable mildly painful electric stimuli, whereas another context (safety context, CXT–) was never paired with electric stimuli. A third context (neutral context, CXTn) served as a neutral control context, which was not seen during conditioning. Behaviour after conditioning was assessed by asking participants to choose contexts for a second visit. In the first experiment, participants were placed in front of the three contexts and were able to successively select two of these three contexts by pointing to them with a joystick. Once they pointed to one room, they were passively guided through the selected context on a prerecorded path. In the second experiment, participants' behavioural freedom was increased so that they were able to actively enter the selected contexts using a joystick. In both experiments, we assessed ratings of valence, arousal, anxiety, and contingency triggered by the contexts to demonstrate explicit conditioning effects.

Based on animal (Endres & Fendt, 2007) as well as human studies (Grillon et al., 2006), we expected that participants would avoid the anxiety context. Regarding approach behaviour towards the safety context, our expectations were less clear. On the one hand, the safety context may be preferred compared to the neutral context because it is predictive of the absence of the US. On the other hand, the safety context might become somewhat associated with the conditioning procedure, and therefore the neutral context would be preferred. Supporting the latter assumption, previous cue-conditioning studies observed that the CS– is more aversive compared to the inter-trial interval (ITI; e.g., Hamm, Greenwald, Bradley, &

Lang, 1993). Finally, we were interested in revealing determinants of overt avoidance behaviour following context conditioning. We expected participants who showed clear conditioning effects in explicit ratings to avoid the anxiety context.

EXPERIMENT 1

Materials and method

Participants

Twenty-eight volunteers (20 female) participated in this study. Seven participants were examined but had to be excluded because of several reasons: simulator sickness, regular drug consumption, current psychiatric disorder (both indicated by self-report), familiarity with conditioning procedures, technical problems during assessment, failure to identify contexts on screenshots (see below), and unawareness of the contingency between context and electric shock (one subject was excluded for each reason). The final sample consisted of 21 participants (15 female; mean age = 23.4 years, $SD = 4.2$ years). All participants gave their written informed consent. Participants were paid €8 for their participation. The study was approved by the Ethics Committee of the Medical Faculty of the University of Würzburg.

Stimuli and apparatus

Contextual stimuli. The VR environment was created with the Source Engine from Valve Corporation (Bellevue, USA). The VR environment consisted of three office rooms that were arranged around a corridor so that one room was always on the left-hand side, one in front of the participants, and one on the right-hand side. Participants were placed at the end of the corridor so that they could see the doors of all three rooms. They would begin here before entering another room. The three office rooms served as different contexts. Each context had a neutral grey floor and were the same size, but they were different in layout, window style, and view (big buildings vs. small buildings vs. mountains) and arrangement of furniture (see Figure 1). We created similar contexts (all contexts were office rooms) because we wanted to avoid initial differences in valence and arousal. Nevertheless, contexts were different enough to be clearly distinguishable.

The software CyberSession, which manipulated the VR environment during the experiment, was written in house. The virtual environment was displayed by a Z800 3D Visor head-mounted display (HMD; eMagin, Hopewell Junction, USA). The head position was monitored with an electromagnetic tracking device (Patriot, Polhemus Corp., Colchester, USA) in order to adapt the field of view to head movements and to assess head orientation.

Unconditioned stimulus. The US was an electric stimulus generated by a current stimulator (Digitimer DS7A, Digitimer Ltd, Welwyn Garden City, UK) and delivered by a surface electrode at the non-dominant inner forearm. It was triggered automatically for 200 ms and pulsed with a frequency of 50 Hz by CyberSession. The intensity of the current was individually adjusted for each participant at the person's pain threshold (see Andreatta, Mühlberger, Yarali, Gerber, & Pauli, 2010) and increased by 30% to avoid habituation. In this sample, the electric shock had a mean current of 2.0 mA ($SD = 1.0$), and participants rated its intensity with a mean of 6.3 ($SD = 1.6$) on a scale with anchors at 0 (*no feeling at all*), 4 (*just noticeable pain*), and 10 (*very strong pain*).

Procedure and design

Before the experimental session, participants were asked to complete several questionnaires: the Brief Fear of Negative Evaluation Questionnaire (BFNE; Leary, 1983; German version: Vormbrock & Neuser, 1983), the State-Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, & Edward, 1970; German version: Laux, Glanzmann, Schaffner, & Spielberger, 1981), and the Tridimensional Personality Questionnaire (TPQ; Cloninger, 1987; German version: Weyers, Krebs, & Janke, 1995).

The experiment consisted of three phases: preacquisition, acquisition, and behavioural test.

Figure 1. *Three virtual office rooms (a–c) served as different contexts. They were arranged around a corridor (d), which was used as a starting point for each phase during the experiments.*

During pre-acquisition, participants were free to navigate through all three contexts for 2 minutes using a joystick. They were told before they began that they would not receive any electric shock during this phase. During the acquisition phase, participants received 3–5 mild electric shocks in one context (anxiety context) per visit. The time between entering the anxiety context and receiving a shock was between 9 and 18 s with an average of about 13 s. The time between shocks varied between 7 and 21 s. In a second context, participants never received any electric shock (safety context). The third context was never visited during acquisition (neutral context). Participants spent approximately 60 s in each context per visit. The contexts were randomly assigned to three different conditions, counterbalanced across participants. There were two acquisition blocks: Acquisitions 1 and 2. During each block, the anxiety and safety contexts were visited three times each. Before each acquisition block, participants were told that they could receive electric shocks in this block. Participants were passively moved through the VR environment during acquisition. The paths leading through the corridor and office rooms were pre-recorded and played back. However, participants were always able to adapt their line of sight in the VR by head movements. The US was presented at different locations in the anxiety context, preventing the participants from associating specific cues within the rooms with shock administration. For the third and final phase of the experiment, the behavioural test, participants were again placed in the corridor and were able to see all three rooms (doors were left open). They were instructed that they could choose one room to visit once again by pushing the joystick towards the selected room (i.e., to the right, forward, or to the left). They were also told that they might receive electric shocks. Participants were not able to move themselves towards the rooms with the joystick, but the experimenter could follow the selection they made on his computer. The experimenter started the same pre-recorded path as used during the acquisition blocks leading through the selected context. After that, participants were again placed at the starting point in the corridor. Then they were told that they could choose another room that they wanted to visit once more. Again, the investigator started the path. Thus, participants chose two out of three contexts, and they never received any electric shock during this behavioural test. The behavioural test was similar to the acquisition blocks because we wanted the participants to anticipate electric shocks in the anxiety context as they did in the acquisition phase. Additionally, we wanted to avoid participants choosing a room with a novelty seeking or exploratory intention (e.g., to navigate freely and explore the details of the rooms).

Ratings. There were several ratings after pre-acquisition and Acquisitions 1 and 2 as measures of explicit fear conditioning. Ratings were assessed by different questions. For each question regarding the contexts, participants saw the scale and a screenshot of the context and heard the question via headphones. They were instructed that they should answer the following questions taking into account the last phase of the experiment. Participants rated the contexts regarding valence ("How positive or negative did you experience this room to be?" from 0 = *very negative* to 100 = *very positive*), arousal ("How aroused did you feel in this room?" from 0 = *not arousing at all* to 100 = *very arousing*), anxiety ("How anxious did you feel in this room?" from 0 = *no anxiety* to 100 = *extreme anxiety*) and contingency between CXT and US ("What was the possibility of receiving an electric stimulus in this room?" 0 = *unlikely* to 100 = *very likely*). Participants responded orally, and the investigator noted the answers. We expected no differences between contexts before conditioning. After each acquisition block, we first asked "Were the electric shocks predictable?" (answers: yes, no, don't know) and "In which room did you receive electric shocks?" to assess awareness of the contingency between context and electric shock. Participants who stated the correct room after the second acquisition run were labelled "aware"; subjects who did not correctly state the association between the CXT+ and the US were labelled "unaware". Only one participant was "unaware" and was excluded from further analysis (see also Baas et al., 2004). Additionally, participants rated the anxiety and safety contexts on valence, arousal, anxiety, and contingency. We expected explicit effects of fear conditioning: The anxiety context should be rated as more negative and more arousing, and participants should be more afraid in this context compared to the safety context. At the end of the experiment (after the behavioural test), we again presented the US, and participants rated the intensity on the same scales as used in the shock workup procedure. Here, we wanted to assess habituation to the US. To test whether participants could identify the VR contexts on the screenshots, we again presented these pictures at the end of the experiment and asked how the rooms were arranged around the corridor (left-hand side, middle, right-hand side) in VR. All participants except one could describe the location of the three contexts correctly. The participant who failed was excluded from further analysis.

Statistical analyses

Pre-acquisition ratings were analyzed separately with repeated-measures analyses of variance (ANOVAs) with Context (anxiety vs. safety vs. neutral) as the within-subjects factor. Conditioning ratings were analysed with repeated-measures ANOVAs with Context (anxiety vs. safety) and Block (Acquisition 1 vs. Acquisition 2) as within-subjects factors. Partial η^2 values were used as a measure of effect size. To analyse the behavioural data, chi-square tests were conducted for the order of room entries in the pre-acquisition phase, avoidance of a context (anxiety, safety, neutral) and for all possible combinations of two entry choices during the behavioural test. To test for an association between conditioning effects in ratings and avoidance behaviour, we first calculated the difference score for each rating after Acquisition 2 (CXT+ − CXT−) and divided the sample into participants who avoided the anxiety context or the safety context. Then, we performed independent *t*-tests to compare both groups on their amount of contextual fear conditioning. Additionally, we correlated the difference scores for ratings with questionnaire data to assess inter-individual differences in contextual fear conditioning and compared anxiety and safety context avoiders on their questionnaire scores using independent *t*-tests. We reported corrected degrees of freedom, if Levene's test of variance equality was significant. The significance level was set at $p \leq .05$ for all statistical tests.

Results

Pre-acquisition phase

Contexts did not differ regarding valence, arousal, and anxiety ratings (all ps $> .12$). Additionally, there was no preference for a special order of entries into the three rooms, $\chi^2(5, N = 21) = 3.27$, $p = .656$.

Behavioural test

Participants chose five different combinations of entries: neutral–safety ($n = 13$, 62%), safety–neutral ($n = 2$, 9.5%), safety–anxiety ($n = 1$, 5%), anxiety–neutral ($n = 2$, 9.5%), and neutral–anxiety ($n = 3$, 14%), revealing a significant difference in the occurrence of these choices, $\chi^2(4, N = 21) = 23.52$, $p < .001$. Additionally, there was a significant difference between the first choice: 16 participants choose the neutral context first, followed by three participants who choose the safety context and two participants who choose the anxiety context, $\chi^2(1, N = 21) = 17.43$, $p < .001$.

Chi-square tests revealed significant differences in the frequencies of the avoidance choice, $\chi^2(2, N = 21) = 14.86$, $p = .001$. The anxiety context was more frequently avoided ($n = 15$) than the safety context ($n = 5$), $\chi^2(1, N = 20) = 5.00$, $p = .025$, or the neutral context ($n = 1$), $\chi^2(1, N = 16) = 12.25$, $p < .001$.

Ratings

Valence. Analyses revealed only a significant main effect of Context, $F(1, 20) = 24.16$, $p < .001$, $\eta_p^2 = .547$, meaning that the anxiety context was rated as more negative ($M = 34.52$, $SD = 23.03$) than the safety context ($M = 71.07$, $SD = 20.87$) across both acquisition blocks.

Arousal. There were only significant main effects of Context, $F(1, 20) = 32.48$, $p < .001$, $\eta_p^2 = .619$, and Block, $F(1, 20) = 4.96$, $p = .038$, $\eta_p^2 = .199$. The anxiety context was rated as more arousing ($M = 40.00$, $SD = 22.15$) than the safety context ($M = 15.38$, $SD = 10.76$), but arousal declined from Acquisition 1 ($M = 30.83$, $SD = 16.53$) to Acquisition 2 ($M = 24.52$, $SD = 14.87$).

Anxiety. There were significant main effects of Context, $F(1, 20) = 19.73$, $p < .001$, $\eta_p^2 = .497$, and Block, $F(1, 20) = 6.14$, $p = .022$, $\eta_p^2 = .235$, but again, no significant Block × Context interaction ($p = .633$); anxiety ratings were higher for the anxiety context ($M = 27.50$, $SD = 24.90$) than for the safety context ($M = 6.67$, $SD = 6.24$) and decreased from Acquisition 1 ($M = 19.52$, $SD = 16.44$) to Acquisition 2 ($M = 14.64$, $SD = 14.08$).

Contingency. We found a significant main effect of Context, $F(1, 20) = 178.91$, $p < .001$, $\eta_p^2 = .899$, and a significant Block × Context interaction, $F(1, 20) = 5.40$, $p = .031$, $\eta_p^2 = .213$. Planned comparisons showed that in Acquisitions 1, $F(1, 20) = 60.62$, $p < .001$, $\eta_p^2 = .752$, and 2, $F(1, 20) = 401.23$, $p < .001$, $\eta_p^2 = .953$, the US–CXT contingency for the anxiety context was rated higher than for the safety context, but that this difference was greater in Acquisition 2 (anxiety context: $M = 91.90$, $SD = 18.27$; safety context: $M = 3.81$, $SD = 7.23$) compared to Acquisition 1 (anxiety context: $M = 84.52$, $SD = 24.49$; safety context: $M = 14.52$, $SD = 21.09$), $F(1, 20) = 5.40$, $p = .031$, $\eta_p^2 = .213$.

Correlations. We correlated the difference scores between anxiety and safety context (CXT+ – CXT–) after Acquisition 2 of every rating type with each other. We found that the difference scores of valence, arousal and anxiety ratings correlated highly significantly with each other (valence with arousal: $r = -.746$, $p < .001$; valence with anxiety: $r = -.643$, $p = .002$, arousal with anxiety: $r = .797$, $p < .001$). Difference scores of contingency rating correlated significantly with difference scores of arousal rating ($r = .478$, $p = .028$) and difference scores of valence rating at trend level ($r = -.395$, $p = .076$).

Association between ratings and avoidance behaviour

Because there was only one participant who avoided the neutral context, we excluded him from the association analysis and compared anxiety ($n = 15$) with safety context avoiders ($n = 5$). Anxiety context avoiders showed a greater amount of contextual fear conditioning (differences score between CXT+ and CXT– after Acquisition 2) compared to safety context avoiders in valence, $t(18) = -3.35$, $p = .004$, arousal, $t(16.04) = 4.44$, $p < .001$, and anxiety ratings, $t(17.80) = 2.71$, $p = .014$ (see Figure 2), but not in contingency ratings, $t(4.44) = 0.99$, $p = .372$ (anxiety context avoiders: $M = 91.33$, $SD = 13.56$; safety context avoiders: $M = 76.00$, $SD = 33.62$).

Questionnaires

Only harm avoidance (HA), a subscale of the TPQ, correlated significantly with differences in arousal and anxiety ratings (CXT+ – CXT–) after Acquisition 2 (arousal with HA: $r = .437$, $p = .048$; anxiety with HA: $r = .512$, $p = .018$). But we did not find any differences in STAI-State, $t(18) = -0.24$, $p = .815$, STAI-Trait, $t(18) = 0.56$, $p = .583$, BFNE, $t(18) = 1.71$, $p = .105$, or TPQ scales (all ps $> .39$), between anxiety ($n = 15$) and safety context avoiders ($n = 5$).

Discussion

In this experiment, we conducted a behavioural test with a passive choice task. We found clear evidence for avoidance behaviour after contextual fear conditioning: Fifteen out of 21 participants avoided the anxiety context. Importantly, participants did not prefer the safety context compared to a neutral context, and the most approached context was the neutral context. Additionally, we were able to establish fear conditioning in terms of valence, arousal, anxiety, and contingency ratings

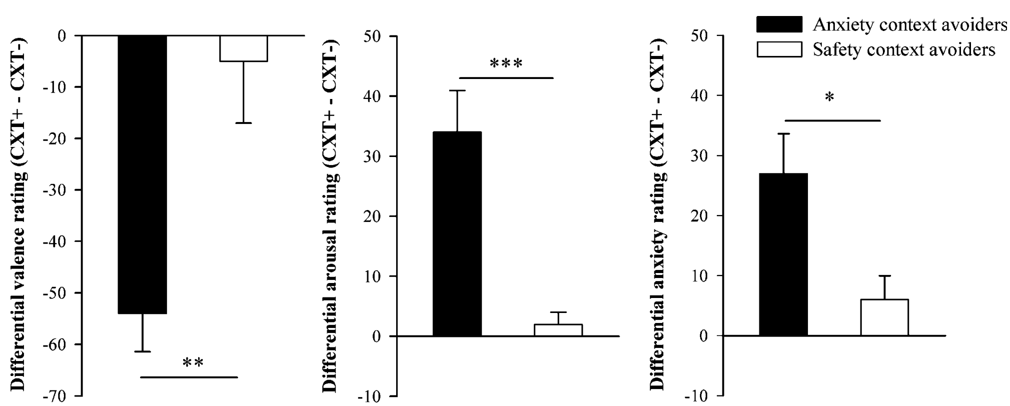

Figure 2. *Experiment 1 (passive): Mean difference scores (CXT+ – CXT–) for valence, arousal and anxiety ratings after Acquisition 2. Black bars represent participants who avoided the anxiety context (n = 15). White bars represent participants who avoided the safety context (n = 5). Error bars represent standard errors of the mean. Note that valence ratings were assessed on a scale from 0 = negative to 100 = positive. Greater negative scores for differential valence ratings indicate that CXT+ was rated as more negative than CXT–.* ***$p < .001$; **$p < .01$; *$p < .05$.

using a new VR context conditioning paradigm. Importantly, we showed a strong association between valence, arousal and anxiety ratings and behavioural avoidance, meaning that participants who avoided the anxiety context showed stronger conditioning effects on an explicit level than participants who avoided the safety context.

The advantage of using this passive choice task is that the behavioural response is much more controllable and less affected by confounding variables, which is important for establishing the reliability of a new lab measurement. However, in a next step, we further increased the ecological validity of the behavioural task by giving participants the opportunity to actively enter the contexts. This allowed us to model realistic behaviour in terms of approach and, especially, avoidance, which is displayed in many anxiety disorders.

EXPERIMENT 2

Materials and method

The second experiment was identical to the first except for the following.

Participants

Twenty-four volunteers (13 female) participated in this study. Four participants had to be excluded because of the following reasons: two because they were unable to identify contexts on screenshots (see materials and methods for Experiment 1) and two because they were unaware of the contingency between context and electric shock. The final sample consisted of 20 participants (11 female; mean age $=25.6$ years, $SD=5.6$). All participants gave written informed consent, and participants were paid €8 for participation. The study was approved by the Ethics Committee of the Medical Faculty of the University of Würzburg.

Stimuli and apparatus

Unconditioned stimulus. The electric shock had a mean current of 3.3 mA ($SD=1.6$), and participants rated its intensity as 5.1 ($SD=1.2$) on a scale with the following anchors: 0 (*no feeling at all*), 4 (*just noticeable pain*), and 10 (*very strong pain*).

Procedure and design

Compared to the first study, we changed two issues: First, we did not measure the TPQ. Second, we changed the behavioural test from a passive to an active choice. As in Experiment 1, participants were instructed that they should choose two rooms to visit once again and that they were able to actively navigate themselves toward and inside the chosen context with a joystick. After 1 minute, they were requested to leave the context. Afterwards, they were instructed to make a second choice and, again, to actively explore a second context for 1 minute. Participants were told only before the first acquisition block that they might experience electric shocks, but this instruction was not repeated before the behavioural test.

Results

Pre-acquisition phase

As in Experiment 1, the three contexts did not differ regarding valence, arousal, or anxiety in the pre-acquisition phase (all ps $>.24$). There was no preference for a specific order of entries into the three rooms, $\chi^2(5, N=20)=4.00$, $p=.995$.

Behavioural test

Participants chose three different combinations of entries: safety–neutral ($n=5$, 25%), neutral–safety ($n=8$, 40%), and neutral–anxiety ($n=7$, 35%). There was no significant difference between these choices, $\chi^2(2, N=20)=0.70$, $p=.705$. But there were significantly more participants ($n=15$) who chose the neutral context first compared to the safety context ($n=5$), $\chi^2(1, N=20)=5.00$, $p=.025$.

The analysis of the avoidance behaviour revealed that 13 participants avoided the anxiety context, whereas seven avoided the safety context, but this difference was not significant, $\chi^2(1, N=20)=1.80$, $p=.180$.

Ratings

Valence. Analyses revealed significant effects of Context, $F(1, 19) = 31.75$, $p < .001$, $\eta_p^2 = .626$, and Block × Context, $F(1, 19) = 10.16$, $p = .005$, $\eta_p^2 = .348$. Planned comparisons showed that in Acquisitions 1, $F(1, 19) = 22.30$, $p < .001$, $\eta_p^2 = .540$, and 2, $F(1, 19) = 31.32$, $p < .001$, $\eta_p^2 = .622$, the anxiety context was rated as more negative than the safety context and that this difference increased in Acquisition 2 (anxiety context: $M = 35.00$, $SD = 17.62$; safety context: $M = 70.25$, $SD = 16.10$) compared to Acquisition 1 (anxiety context: $M = 43.50$, $SD = 12.68$; safety context: $M = 64.75$, $SD = 15.17$), $F(1, 19) = 10.16$, $p = .005$, $\eta_p^2 = .348$.

Arousal. We found a significant main effect of Context, $F(1, 19) = 29.07$, $p < .001$, $\eta_p^2 = .605$, meaning that the anxiety context was rated as more arousing ($M = 33.75$, $SD = 24.83$) than the safety context ($M = 11.03$, $SD = 14.72$).

Anxiety. There was a significant main effect of Context, $F(1, 19) = 12.59$, $p = .002$, $\eta_p^2 = .399$, but no significant Block × Context interaction ($p = .646$). Anxiety ratings for the anxiety context ($M = 17.68$, $SD = 18.67$) were higher than for the safety context ($M = 6.23$, $SD = 12.87$).

Contingency. We found significant effects of Context, $F(1, 19) = 221.05$, $p < .001$, $\eta_p^2 = .921$, and Block × Context, $F(1, 19) = 5.33$, $p = .032$, $\eta_p^2 = .219$. Planned comparisons showed that in Acquisitions 1, $F(1, 19) = 43.12$, $p < .001$, $\eta_p^2 = .694$, and 2, $F(1, 19) = 1766.36$, $p < .001$, $\eta_p^2 = .989$, participants rated the contingency between context and the US higher in the anxiety context than in the safety context, and this difference increased from Acquisition 1 (anxiety context: $M = 87.50$, $SD = 26.33$; safety context: $M = 16.00$, $SD = 26.44$) to Acquisition 2 (anxiety context: $M = 98.00$, $SD = 6.96$; safety context: $M = 1.25$, $SD = 3.93$), $F(1, 19) = 5.33$, $p = .032$, $\eta_p^2 = .219$.

Correlations. We correlated the difference scores between anxiety and safety context (CXT+ – CXT–) after Acquisition 2 of every rating type with each other. We found that the difference scores of valence, arousal and anxiety ratings correlated highly significantly with each other (valence with arousal: $r = -.608$, $p = .004$; valence with anxiety: $r = -.721$, $p < .001$, arousal with anxiety: $r = .803$, $p < .001$). There were no significant correlations with the difference scores of contingency rating (all ps $> .32$).

Association between ratings and avoidance behaviour

We compared anxiety ($n = 13$) with safety context avoiders ($n = 7$) on their amount of contextual fear conditioning (differences score between CXT+ and CXT– after Acquisition 2). As in Experiment 1, anxiety context avoiders showed a greater amount of contextual fear conditioning in valence, $t(18) = -3.33$, $p = .004$, arousal, $t(16.51) = 2.58$, $p = .020$, and anxiety ratings, $t(14.04) = 3.63$, $p = .003$, than safety context avoiders (see Figure 3), but not in contingency rating, $t(18) = -1.04$, $p = .313$ (anxiety context avoiders: $M = 95.00$, $SD = 12.58$; safety context avoiders: all participants rated 100).

Questionnaires

There were no significant correlations between differences in ratings (CXT+ – CXT–) after Acquisition 2 and STAI-State, STAI-Trait, or BFNE (all ps $> .13$). Again, anxiety ($n = 13$) and safety context avoiders ($n = 7$) did not differ in STAI-State, $t(18) = -0.57$, $p = .573$, STAI-Trait, $t(18) = 0.70$, $p = .492$, and BFNE, $t(18) = 1.01$, $p = .324$.

Discussion

In this second experiment, we changed the behavioural test and conducted an active behavioural task. Virtual reality has been indicated to be an ideal tool for studying associative learning as well as anxiety disorders in humans because it allows participants to be placed in complex but experimentally controlled environments. In order to create an even more realistic situation, participants were allowed to move freely in the office rooms. Our results indicate that avoidance behaviour was

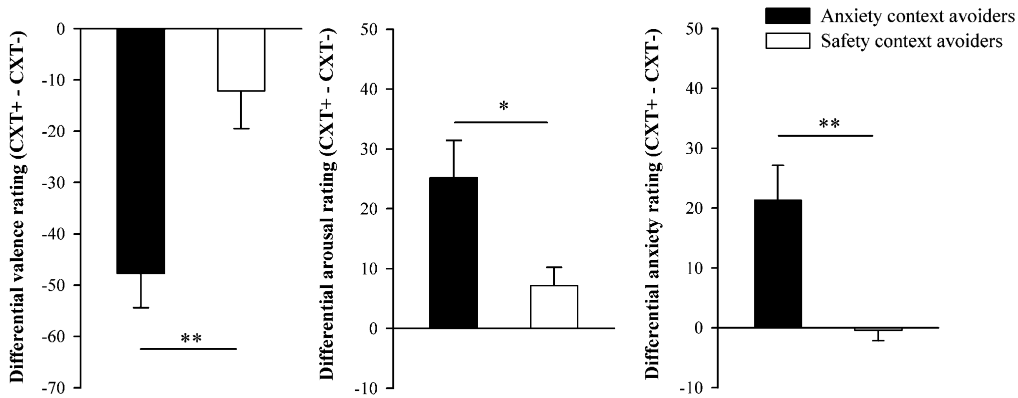

Figure 3. *Experiment 2 (active): Mean difference scores (CXT+ − CXT–) for valence, arousal and anxiety ratings after Acquisition 2. Black bars represent participants who avoided the anxiety context (n = 13). White bars represent participants who avoided the safety context (n = 7). Error bars represent standard errors of the mean. Note that valence ratings were assessed on a scale from 0 = negative to 100 = positive. Greater negative scores for differential valence ratings indicate that CXT+ was rated as more negative than CXT–. **p <.01; *p <.05.*

not as obvious as in the first experiment, but showed the same tendency: Thirteen participants avoided the anxiety context and seven participants the safety context. Importantly, we were able to replicate our findings that, first, our VR paradigm is adequate for establishing fear conditioning on an explicit level and, second, conditioning effects as reflected by explicit ratings are linked to avoidance behaviour. In detail, we found clear evidence that participants who avoided the anxiety context showed stronger conditioning effects in valence, arousal and anxiety ratings than safety context avoiders.

GENERAL DISCUSSION

In two studies using a new VR paradigm, we investigated behavioural strategies after contextual fear conditioning. Additionally, we examined fear conditioning using ratings of valence, arousal, anxiety and contingency and its relationship to past conditioning behaviour. We showed that after the contextual fear conditioning procedure, most participants avoided the context in which an unpredictable aversive US had occurred compared to a safe context. Our behavioural results replicate previous studies showing that a context associated with unpredictable threat is most frequently avoided (Grillon, 2002b; Grillon et al., 2006). Since we added a third (neutral) context, we are confident that the observed behaviour is definitely an avoidance of the anxiety context and not an approach of the safety context.

Importantly, in both studies, we found a strong relationship between past conditioning ratings and subsequent avoidance behaviour. In fact, those participants who avoided the anxiety context, showed a stronger conditioning effect in valence, arousal and anxiety ratings (indicated by a greater difference between ratings for CXT+ vs. CXT–) in Experiments 1 and 2 compared to participants who avoided the safety context. These results indicate that, in humans, experienced affect importantly determines avoidance behaviour. Thus, a context in which an aversive event occurred is avoided if this context acquired explicit negative valence, high arousal and anxiety. Conversely, a context is not avoided if it was not evaluated negatively after conditioning. These results suggest that contextual fear conditioning on an explicit level is associated with an overt avoidance of this context. Notably, this is in line with Mowrer (1953), who stated that the experience of fear acquired through classical conditioning causes avoidance behaviour, and Lau et al. (2008), who demonstrated that high fear ratings of CS+ predicted contextual avoidance behaviour. In a next step, one could additionally include a predictable context, where the US is paired with a discrete cue. It has been shown that a context where an unpredictable US occurred induced greater explicit anxiety and avoidance behaviour compared to a context where the US was predictable (Grillon et al., 2006). It would be interesting to examine whether the association between explicit ratings of the context and the later avoidance is stronger for the unpredictable context compared to the predictable context.

Additionally, investigating avoidance responses to a specific cue is also highly relevant for specific phobia. To our knowledge, there are no human studies directly comparing avoidance behaviour towards a threat cue versus a threatening context. An animal study reported enhanced avoidance to both a threat cue and a threatening context, i.e., the magnitude of avoidance behaviour did not differ between conditions (Blanchard, Yang, Li, Gervacio, & Blanchard, 2001). Based on this animal finding and clinical symptoms of strong avoidance behaviour in specific phobia, one would expect that cue conditioning also leads to avoidance of a fear cue and that cue and context conditioning do not differ in avoidance magnitude. Possibly, they might vary in avoidance duration as contextual conditioning is regarded as a model for sustained and chronic anxiety and cue condition as a model for phasic and short fear responses (Grillon, 2002a, 2008). But further studies are needed which directly compare avoidance of a cue versus a context in magnitude and duration.

Furthermore, we found an association between harm avoidance and conditioning effects in arousal and anxiety ratings. Harm avoidance is regarded as the tendency to learn to avoid punishments, non-rewards and novelty. Furthermore, subjects scoring high on harm avoidance are thought to easily acquire conditioned responses to aversive stimuli and are characterised as fearful and worried (Cloninger, 1986). Supporting this idea, we found that the higher participants scored on harm avoidance the higher was their difference between anxiety and safety context in arousal and anxiety ratings, i.e., they showed greater contextual fear conditioning effects. This result also replicates previous findings demonstrating that harm avoidance is associated with increased associative learning using an aversive but not an appetitive US (Corr, Pickering, & Gray, 1995) and increased startle responses to negative pictures (Corr, Kumari, Wilson, Checkley, & Gray, 1997). Unfortunately, we did not find significant group differences (anxiety vs. safety context avoiders) in questionnaire data, possibly due to small sample sizes. Further studies might include larger sample sizes to further elucidate inter-individual differences in avoidance behaviour.

The fact that the avoidance of the anxiety context in the active choice study was not as strong as in the passive choice study may be due to less threat of shock. In the passive task, participants expected the same path or procedure as in the acquisition phase, which could have increased context effects and reminded participants of the contingency between context and shock. Additionally, in the instructions for the passive task, we reminded participants that they might receive electric shocks. Taken together, in Experiment 1 (passive task) less procedural changes from acquisition to the behavioural test (i.e., the same path leading through the context during acquisition and behavioural test phase) and the shock instructions may have been critical to increase the expectation of receiving electric shocks in the anxiety context and to induce avoidance behaviour. Furthermore, there is evidence that different neural structures are involved in various navigation tasks. Yoshida and Ishii (2006) found that an active goal-search task required greater activation of dorsolateral prefrontal cortex, anterior cingulate cortex, and basal ganglia compared to a guided visuomotor task in which participants were instructed simply to follow a specified path. Conclusively, the involvement of different neuronal structures may also account for differences in behavioural responses.

The present studies are the first to include a neutral context as a control condition to test for inhibitory effects of the safety context. Our hypotheses regarding approach behaviour towards the safety context were less clear. On the one hand, we hypothesised that participants would prefer the safety context compared to the neutral context because they had learned that no US would occur in the safety context. On the other hand, we assumed that participants would choose the neutral context first and then the safety context because the safety context would become associated with the aversive fear conditioning procedure, whereas the neutral context was not presented during fear conditioning. In both studies we found that most participants first chose the neutral context and not the safety context, confirming our latter assumption. As mentioned above, this could be due to generalisation from the anxiety context to the safety context caused by the aversive learning process in the acquisition phases. The anxiety and safety contexts both underwent a fear-conditioning procedure, but the neutral context did not. Therefore, the safety context might still have been associated with a negative outcome and might have acquired negative properties, even if participants explicitly learned that nothing aversive happened in this context. Additionally, the neutral context may have acquired higher attractiveness because participants were less familiar with this context during the experiment. One might also consider that new contexts in video games are often associated with reward. Another explanation of the reason why we could not find an inhibitory effect of the safety context in comparison to the neutral context relates to cue conditioning studies that observed higher startle magnitudes in response to a CS– compared to the ITI, meaning that the CS– might be processed as more negative than the ITI (Hamm et al., 1993; Weike, Schupp, & Hamm, 2008). Weike et al. (2008) interpreted this finding in terms of a rapid activation of the fear system caused by both the CS+ and the CS–. The fear response elicited by the CS– has to be inhibited throughout the learning process, but this inhibition process may not be sufficient enough to result in a reduced response to the CS– compared to the ITI. Additionally, the behavioural data revealing strong approach behaviour to the neutral context in both experiments suggest that the neutral context was even experienced as more positive than the safety context. One could argue that the neutral context was not really neutral because participants experienced it as safe during the preacquisition phase. Thus, it might be speculated that the neutral context was considered as an additional safety context. Unfortunately, we did not assess ratings after the behavioural test to clarify whether the neutral context was experienced equally or as even more positive than the safety context. Future experiments could also record physiological variables (e.g., startle reflex or skin conductance) to compare the neutral context and the safety context.

Our two studies showed that the explicit negative evaluation of a context may be necessary to induce avoidance behaviour of this context. It has been shown that evaluative conditioning is not sensitive to extinction (Vansteenwegen, Crombez, Baeyens, & Eelen, 1998) and that anxiety-disorder patients even show more pronounced resistance to extinction compared to healthy controls (Michael, Blechert, Vriends, Margraf, & Wilhelm, 2007; Wessa & Flor, 2007). Therefore, chronic anticipation of aversive events and exaggerated and long-lasting negative evaluations of contexts may drive excessive avoidance behaviour in clinical anxiety. The pathway between cognitions and behaviour may be crucial and difficult to change in anxiety disorders underscoring its potential contribution to the development and maintenance of anxiety disorders. Therefore, we think that it would be of special interest to transfer our paradigm to a clinical setting. Differences between panic-disorder patients and healthy controls in context conditioning and subsequent avoidance behaviour have to be expected, although there are controversial theories about safety behaviour and safety signals in panic-disorder patients. According to Rachman (1984), panic disorder is driven by the desire to seek safety and to avoid fearful situations, leading to the hypothesis that panic-disorder patients would choose the safety context first and strongly avoid the anxiety context. By contrast, several studies have indicated that panic-disorder patients have deficits in processing safety signals (e.g., Lissek et al., 2009) indicating that panic-disorder patients might not suffer from an over-activated fear network, but rather from an altered inhibitory system, which is driven by an overgeneralisation of fear across stimuli (Lissek et al., 2009, 2010). As panic-disorder patients are thought to show strong contextual fear conditioning reflected in fear potentiated startle (Grillon et al., 2008) they might also show more pronounced evaluative conditioning, which might lead to stronger behavioural avoidance. Nevertheless, besides associative learning processes, attributional processes also play an important role in the development and maintenance of anxiety disorders (Beck, Emery, & Greenberg, 2005). Further studies should also consider attributions and unravel their contributions to the development of PTSD or panic disorder.

We have to acknowledge several limitations of our studies. We only included verbal ratings as a primary measurement of contextual fear conditioning. The participants had to respond orally and the investigator noted the answers. This might have been critical because the ratings might be influenced by demand effects. In the future, it might be better to assess ratings independently of the investigator by using technical equipment. Additionally, physiological measurements, like the fear potentiated startle, would have been useful as an implicit measure of fear (Hamm & Vaitl, 1996). In the same vein, the behavioural test might also have been influenced by demand effects because the investigator was present during this test and had to start the path leading through the selected context in Experiment 1. There are several tasks that employ reaction-time measurements resembling sensitive and implicit measures of approach and avoidance (Krieglmeyer & Deutsch, 2010). In detail, participants can push a joystick (Seibt, Neumann, Nussinson, & Strack, 2008) or move a manikin on a screen towards or away from a stimulus by button press (De Houwer, Crombez, Baeyens, & Hermans, 2001). Applied to our virtual reality paradigm, one could present different screenshots of the contexts after conditioning and assess reaction times of, for example, pushing a joystick forward or away from the CXT+ and CXT− pictures, as an index of approach and avoidance behaviour. This operationalisation might be independent of demand effects, but on the other hand ecologic validity of the behavioural measurement is decreased.

Avoidance behaviour is a crucial component of many anxiety disorders, but there have been few attempts to study overt behaviour experimentally. Our VR-based paradigm offers a reliable tool for studying behavioural responses. Taken together, our results indicate that contextual fear conditioning induces avoidance behaviour in humans and that such conditioned behavioural responses are importantly determined by the explicit evaluations of the individuals. Conclusively, our study can be regarded as preliminary evidence that successful fear conditioning on an explicit level is necessary to establish avoidance behaviour. Interestingly, exposure and prevention of avoidance is the most effective treatment component for anxiety disorders and the prevention of avoidance during exposure subsequently results in a change of the explicit evaluation of the feared object or context.

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