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Startle reflex modulation during "threat" of shock or reward

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Abstract

During threat of shock, the startle reflex is potentiated, suggesting modulation by defensive mobilization. To determine whether startle potentiation is specific to aversive anticipation, startle reflexes were measured in the context of either aversive or appetitive anticipation in a between-subject study. Participants wore a device on the wrist that could deliver electrical shock (n=49), or vibrotactile stimulation indicating monetary reward (n=48). Cues signaling "threat" or "safe" periods were presented alone, or accompaned by presentation of affective and neutral pictures on half of the trials. Results indicated that the startle reflex was significantly potentiated when anticipating either shock or reward, compared to "safe" periods, both when no picture was presented, as well as during picture viewing. The difference between threat and safety in both reflex magnitude and skin conductance changes were larger for those anticipating shock, suggesting that the aversive context was more motivationally engaging. The pattern of reflex modulation as a function of picture valence varied under threat and safety, but was identical in the shock and reward groups, consistent with a hypothesis that anticipation of either aversive or appetitive events prompts heightened perceptual vigilance, potentiating the acoustic startle reflex.

Threat of shock is a potent aversive context that elicits measurable defensive behavior, including potentiated startle reflexes, heightened skin conductance, as well as activation of neural regions mediating defense (Bradley, Moulder, & Lang, 2005; Gold, Morey, & McCarthy, 2014; Grillon, Ameli, Woods, Merikangas, & Davis; 1991). In a threat of shock paradigm, a cue signals periods in which it is possible that an aversive electric shock will be delivered, and startle blink reflexes elicited in these periods of "anticipatory anxiety" are potentiated, compared to reflexes elicited in periods safe from shock threat (Grillon et al., 1991). A number of studies, however, suggest that anticipating the upcoming presentation of an appetitive stimulus can also induce reflex potentiation, although the contexts in which this effect is found differ significantly from the threat of shock paradigm (e.g., Sabatinelli, Bradley & Lang, 2001; Skolnick & Davidson, 2002). In the current study, we directly compared startle reflexes when participants were under threat or safety, using the same paradigm whether the reinforcer was aversive (shock) or appetitive (money).

Startle modulation in the context of appetitive or aversive anticipation has been investigated in a number of paradigms that differ in numerous ways from a threat of shock design. For instance, cues have been used to signal whether an upcoming picture will be unpleasant or

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pleasant, which results in potentiation of the startle reflex during the anticipatory period in both cases (Dichter, Tomarken, & Baucom, 2002; Nitschke, Larson, Smoller, Navin, et al., 2002; Sabatinelli, Bradley, & Lang, 2001; Sege, Bradley & Lang, 2014). In a more complex design, participants first entered 6 numbers in a computerized lottery game. Depending upon the number of matches, one group received an aversive noise blast, whereas another group received money, and, in both groups, reflexes were potentiated during the pre-feedback period (Skolnick & Davidson, 2002). In a more recent conditioning study (Andreatta & Pauli, 2015), on the other hand, startle reflexes elicited in the context of a cue signaling the upcoming receipt of food (for hungry participants) were attenuated, rather than potentiated, although it differs from a threat paradigm in that each cue is reliably followed by the reinforcer.

Thus, studies investigating effects of threat of shock often present a single (Grillon et al., 1991; Grillon & Davis, 1997) or no reinforcer (e.g., Phelps, O'Connor, Gatenby, Gore, Grillon, & Davis, 2001) in the context of the threat cue, since the targeted process is one in which the aversive event is possible, but not probable. The latter paradigm, in which a cue reliably signals upcoming shock exposure, is a conditioning protocol (in which the contingency can be either instructed, as in threat of shock, or uninstructed). Studies that investigate anticipatory anxiety depart from the classical learning design primarily in the number of actual exposures to the unconditioned stimulus, which is greatly reduced or non-existent in threat studies. Because of this feature, the current study used a between, rather than within, subject design, as experience with the low reinforcement schedule in one context (e.g., electrical) provides information about the reinforcement schedule in the other context (e.g., vibrotactile).

Whereas electric shock is a potent threat for most people, the amount of money necessary to equate the two reinforcers, in terms of emotional engagement, might be prohibitive in the laboratory environment. In fact, many laboratory studies of reward use quite modest amounts of money as reinforcers (e.g. quarter, dime). In the current study, participants were told that each vibrotactile stimulation would result in receiving $20, which we hoped would be enough to motivate active anticipation. Nonetheless, we measured skin conductance activity as an index of motivational engagement during the anticipatory periods in both the shock and reward groups. Assuming that these aversive and appetitive contexts are not equivalent in terms of emotional intensity, we expected larger differences in the magnitude of conductance changes during threat of shock, compared to safety, which might be accompanied by larger differences in startle modulation for those anticipating shock as well.

The procedure is illustrated in Figure 1: one color cue (e.g. blue; "threat") signaled the possibility of receiving stimulation (electrial or vibrotactile) whereas a second cue (e.g., red; "safe") signaled that no stimulation would be received. On half of the trials, only the signaling cue was present during threat and safe periods ("blank"). On the remaining trials, a pleasant, neutral, and unpleasant scene were additionally presented, and a secondary goal of the study was to determine whether anticipating aversive or appetitive stimulation affects the pattern of reflex modulation during affective pictures. Numerous studies have confimed that, compared to neutral scenes, startle reflexes are typically potentiated when viewing unpleasant scenes and attenuated when viewing pleasant scenes (Vrana, Spence, & Lang, 1988; Bradley, Codispoti, & Lang, 2006).

Two previous studies (Dunning, DelDonno, & Hajcak, 2013; Bublatzky Guerra, Pastor, Schupp, & Vila, 2013) measured startle reflexes when participants viewed emotional scenes under threat of shock or safety. Both studies report significant main effects of threat and hedonic content, with threat enhancing reflexes overall, together with a main effect of hedonic content. However, the specific pattern of reflex modulation when viewing pleasant or unpleasant, compared to neutral, scenes was not reported, making it difficult to know whether both the reflex potentiation and attenuation found when viewing pictures are both retained under threat of shock. Moreover, Grillon & Charney (2011) reported that fearful, compared to neutral, stimuli (faces) showed startle potentiation only when viewed under threat of shock, whereas there was no difference under safety. Thus, we conducted planned comparisons to assess whether both aspects of affective modulation -- defensive potentiation and appetitive attenuation -- are retained when viewing natural scenes under threat or safety, and when the anticipated event is aversive or appetitive.

Method

Participants—Participants were 97 students recruited from General Psychology classes at the University of Florida, who received course credit for their participation. Of these, 49 participants (21 women) anticipated receiving electric shock, and 48 participants (33 women) anticipated receiving money. The study was approved by the local IRB committee and all participants gave informed consent.

Materials and Design—A diffuse light was used to signal that there was a probability that electrical (shock) or vibrotactile (money) stimulation could occur during the period when one light was on, but would not occur when another light was present. The cue lights were red and blue and were counterbalanced across threat and safe conditions over participants. All participants wore a device on the right wrist. For those threatened with shock, the device was a concentric Tursky electrode placed on the participant's inner right wrist and connected to a Grass S8800 Stimulator with an attached SIU7 Stimulus Isolation Unit (Grass Instruments, Quincy, MA). For those anticipating money, the device was a vibrotactile transducer (Engineering Acoustics, Inc. Winter Park, FL) also placed on the inner right wrist that delivered a sensation similar to a cell phone vibration, and signaled receipt of $20 following study conclusion.

The red and blue cues were projected onto a wall across from the participant (an area approximately 32 inches wide by 18 inches high) using a Kodak Ektapro 9010 slide projector. Cue lights were illuminated for 20 s, with a 2 s inter-trial interval (ITI) in which no cue light was presented (see Figure 1). On 32 "blank" trials[1], only the cue light was presented during each 20 s period, and presented 16 red and 16 blue cues. On 32 trials, 3 pictures (one pleasant, one neutral, and one unpleasant) selected from the International

[1]Startle data for participants anticipating electric shock on blank trials only were previously reported as control group data (low dental fear) in a study investigating reflex modulation in participants reporting high fear of pain (Bradley, Silakowski & Lang, 2008).

Affective Picture System[2] (IAPS; Lang, Bradley & Cuthbert, 2008) were additionally projected during red and blue cue light periods. On picture trials, the 3 pictures were presented beginning 2 s after cue onset for 4 s each, separated by a 2 s ITI. Startle probes were presented when viewing pleasant or unpleasant scenes on 12 trials overall, and on 8 trials when viewing neutral pictures.

Startle probes were 98 dB, 50 ms bursts of white noise generated by a Coulbourn S81-02 noise generator and gated by a Coulbourn S82-24 audio-mixer amplifier. Startle probes were delivered through E-A-RTONE 3A air conduction insert earphones (Aearo Company, Indianapolis, IN). One startle probe was presented during each 20 s cue period at either 4.5, 10.5, or 16.5 s following onset of the cue light (2.5 s after the onset of the first, second or third picture on trials presenting pictures).

Cues were presented in blocks of 4, with 2 threat cues (one with pictures, one blank) and 2 safe cues (one with pictures and one blank) in each block of 4. Four orders were constructed that balanced the condition in each serial position across participants. Four additional practice trials were not included in the data analysis.

Experimental stimuli were controlled and presented by VPM software (Cook, 2001) on a desktop computer and VPM software was used for physiological data acquisition and reduction.

To equate procedures in the two groups, there was no shock workup prior to the experimental session for those anticipating electric shock. In both groups, one reinforcer was delivered midway through the study in the context of a threat cue, with participants in the threat of shock group receiving electric shock stimulation (2 milliamps, 500 ms duration) and participants in the reward group receiving vibrotactile stimulation ($20.00).

Physiological Data Acquisition and Reduction

The startle reflex was recorded using two small silver/silver chloride electrodes placed over the left orbicularis oculi muscle. Raw orbicularis oculi activity was sampled at 1000 Hz from 50 ms prior to probe onset to 250 ms after probe onset. The raw signal was filtered online with a 90–250 Hz bandpass filter using a Coulbourn S75-01 bioamplifier, and integrated with a 120 ms time constant using a Coulbourn S76-01 contour-following integrator. Peak magnitude and onset latency were scored off line using VPM software (Cook, 2001). Trials with a blink onset of less than 20 ms were omitted from analysis. Raw scores were standardized and converted to T-scores to reduce inter-individual variability.

Skin conductance was sampled at 20 Hz using two large silver/silver chloride electrodes filled with 0.05-m NaCl paste that were placed adjacently over the hypothenar eminence of the left palm. A constant current (.5 v) was generated between the electrodes using a Coulbourn S71-22 coupler. Skin conductance activity was averaged into half-second bins, deviated from a 1 s baseline prior to cue onset, log-transformed, and averaged across each 20

[2]IAPS (Lang et al., 2008) pictures were pleasant: 4650, 4660, 4670, 4680, 4690, 4800, 5910, 7230, 7330, 7350, 8162, 8502; neutral: 2190, 2220, 2383, 2393, 6150, 7100, 7130, 7500; unpleasant:3530, 6250, 6260, 6350, 6370, 6510, 7380, 9301, 9480, 9600, 9620, 9622.

s trial, resulting in change scores that reflected increases (or decreases) from a pre-cue baseline.

Procedure—After completing the informed consent and the EASI temperament questionnaire[3] (Buss & Plomin, 1975), the participant was seated in the testing room and sensors for physiological recording and electric shock or vibrotactile stimulation were attached. Depending upon group assignment, participants were instructed that an electric shock or vibrotactile stimulation (indicating monetary award of $20) could be delivered through the sensor on their wrist in the presence of one light, but not in the presence of another light. Participants were queried a number of times regarding the meaning of each cue light prior to beginning the experiment.

Following all trials, a post-experimental questionnaire asked participants to rate the pleasantness of anticipating and receiving the reinforcer on a scale of 1 (unpleasant) to 7 (pleasant) Participants were then debriefed and thanked for their participation. Those in the reward group received $20.00 for the single reinforced trial. The entire procedure lasted approximately two hours.

Data Analysis—Anticipatory effects were separately assessed for blank trials and for trials in which pictures were presented. For blank trials, the ANOVA included reinforcer (shock, money) as a between subject variable and cue (safe, threat) as a repeated measure. For picture trials, the ANOVA included reinforcer (shock, money) as a between subject variable, and cue (safe, threat and hedonic content (pleasant, neutral, unpleasant) as repeated measures.

Post-experimental pleasure ratings of anticipating or receiving the reinforcer were analyzed using reinforcer (shock, money) as a between group variable. Greenhouse Geisser corrections are reported.

Results

Startle reflex

Figure 2 illustrates startle blink amplitude over all participants, and separately for those anticipating shock or reward (money). In the analysis of blank trials (i.e. no picture was presented), a main effect of cue, $F(1, 95) = 60.8$, $p < .0001$, $\eta\rho^2 = .39$, indicated that startle reflexes elicited in the context of threat were potentiated, compared to those elicited during safe periods, and this difference was found both for participants anticipating shock, $F(1, 48) = 76$, $p < .0001$, $\eta\rho^2 = .61$, and for those anticipating money, $F(1, 47) = 5.2$, $p = .02$, $\eta\rho^2 = .10$. The significant interaction of cue and reinforcer, $F(1, 95) = 21$, $p < .0001$, $\eta\rho^2 = .18$, indicated that the difference in startle magnitude between threat and safe trials was larger for those anticipating an aversive shock, compared to those anticipating money. There were no

[3]The EASI temperament questionnaire (Buss & Plomin, 1975) scores 5 temperament scales of Fear, Anxiety, Sociability, Impulsivity, and Activity. Mean scores on the 5 scales did not differ for participants in the shock and reward groups, and, in these unselected samples, there were no significant correlations between scores on any scale and startle magnitude during threat or safety, or for post-experimental ratings.

other significant effects involving aversive or appetitive anticipation in the analysis of blank trials.

When pictures were viewed under threat or safety, a main effect of cue, $F(1, 95) = 50.8$, $p < .0001$, $\eta\rho^2 = .35$, again indicated that reflexes elicited under threat were greater than those under safety, both for those anticipating shock, $F(1, 48) = 47$, $p < .0001$, $\eta\rho^2 = .50$, and for those anticipating money, $F(1, 47) = 8$, $p = .007$, $\eta\rho^2 = .15$. The difference was again larger for those anticipating shock, Cue x Reinforcer, $F(1, 95) = 13$, $p < .0001$, $\eta\rho^2 = .12$. There were no other significant effects involving aversive or appetitive anticipation in the analysis of reflexes elicited on picture trials.

A significant main effect of hedonic content, $F(2, 190) = 23.1$, $p < .0001$, $\eta\rho^2 = .20$, was accompanied by a marginal interaction of cue and content, $F(2, 190) = 3.1$, $p = .05$, $\eta\rho^2 = .03$. Although the effect of hedonic content was significant both under threat, $F(2, 190) = 14.6$, $p < .0001$, $\eta\rho^2 = .13$, and safety, $F(2,190) = 13.9$, $p < .0001$, $\eta\rho^2 = .13$, the pattern of affective modulation differed somewhat in these two contexts, as Figure 2 illustrates. During safe periods, reflexes were potentiated when viewing unpleasant, compared to neutral, scenes, $F(1, 96) = 7.3$, $p = .008$, $\eta\rho^2 = .07$, and attenuated when viewing pleasant, compared to neutral, scenes, $F(1, 96) = 6$, $p = .02$, $\eta\rho^2 = .06$, replicating previous modulatory effects found when viewing affective pictures. Reflexes elicited when viewing neutral scenes during safe trials did not differ from those elicited on safe trials that were blank, ($F < 1$).

Whether anticipating either shock or money, on the other hand, reflexes were not potentiated when viewing unpleasant, compared to neutral scenes ($F < 1$; interaction $F < 1$), as Figure 2 illustrates. Rather, reflexes elicited on unpleasant, neutral, or blank trials were similarly potentiated and did not differ in magnitude ($F's < 1$). On the other hand, startle reflexes elicited when viewing pleasant scenes under threat were significantly attenuated, whether compared to those elicited when viewing neutral scenes, $F(1, 96) = 21.7$, $p < .0001$, $\eta\rho^2 = .19$, unpleasant scenes, $F(1,96) = 21.5$, $p < .0001$, $\eta\rho^2 = .18$, or on blank trials, $F(1,96)=20.5$, $p < .0003$, $\eta\rho^2 = .18$.

Table 1 lists the raw blink magnitude for each condition, as encouraged by the SPR guidelines for startle reporting (Blumenthal et al., 2005). Although blink magnitude showed a slight increase for participants anticipating shock, compared to money, the main effect of group was not significant, and analyses of the raw blink data resulted in the same significant effects of cue, content, and the interaction of cue and reinforcer as found for the standardized scores.

Skin conductance

Figure 3 illustrates skin conductance change under threat and safety. During blank periods, skin conductance change was greater under threat, compared to safety, $F(1, 95) = 23.1$, $p < .0001$ $\eta\rho^2 = .20$, and was significant both for participants anticipating shock, $F(1, 48) = 16.2$, $p < .0001$, $\eta\rho^2 = .25$, and those anticipating money, $F(1, 47) = 8$, $p = .007$, $\eta\rho^2 = .15$. As found for the reflex data, a significant interaction of cue and reinforcer, $F(1, 95) = 6$, $p = .016$, $\eta\rho^2 = .06$, indicated that the difference was larger for participants anticipating shock, compared to money.

During picture viewing, a main effect of cue, $F(1, 95) = 28$, $p < .0001$, $\eta\rho^2 = .23$, indicated that skin conductance changes were again elevated in the context of threat, compared to safety, and this difference was found both for those anticipating shock, $F(1, 48)=21.5$, $p < .0001$, $\eta\rho^2 = .31$ and those anticipating money, $F(1, 47) = 7.2$, $p = .01$, $\eta\rho^2 = .13$. The difference was again greater for those anticipating receipt of shock, Cue x Reinforcer, $F(1, 95) = 7.2$, $p = .01$, $\eta\rho^2 = .07$.

Unlike for startle magnitude, the main effect of hedonic content, $F(2, 190) = 10.9$, $p < .0001$, $\eta\rho^2 = .10$, did not interact with reinforcer ($F < 1$), with significant simple main effects found both for those anticipating shock $F(2, 96) = 5.2$, $p = .007$, $\eta\rho^2 = .10$, and those anticipating money, $F(2, 94) = 6$, $p = .006$, $\eta\rho^2 = .11$. Both groups showed a significant quadratic relationship (quadratic shock $F(1,48) = 11.5$, $p = .001$, $\eta\rho^2 = .19$; quadratic reward $F(1, 47) = 7.5$, $p = .009$, $\eta\rho^2 = .14$), in which, compared to neutral scenes, viewing pleasant ($F(1, 96) = 10.4$, $p = .002$, $\eta\rho^2 = .10$) or unpleasant scenes ($F(1, 96) = 17.9$, **p** <.0001, $\eta\rho^2 = .16$) prompted larger skin conductance changes.

Post-experimental Pleasure Ratings (scale: 1 = unpleasant to 7 = pleasant)

Participants in the vibrotactile reward group rated the anticipation of receiving money more pleasant ($M = 5.0$; $SD =1$) than did participants anticipating shock stimulation ($M = 3.7$, $SD = 1$; $F(1,95) = 39.7$, $p <.0001$, $\eta\rho^2 = .30$), and also rated actual receipt of vibrotactile stimulation more pleasant ($M = 5.2$, $SD = 1.4$) than those receiving electric shock (M = 4; SD = 1.1 ; $F(1,95) = 21$, $p < .0001$, $\eta\rho^2 = .18$).

Discussion

Acoustic startle reflexes were enhanced when anticipating either aversive shock exposure or vibrotactile stimulation signaling monetary reward, compared to when there was no chance ("safe") of receiving either shock or money. Thus, anticipating an appetitive event modulated startle reflexes in ways similar to those found when anticipating an aversive shock. Startle potentiation was larger for those anticipating electrical, compared to vibrotactile stimulation, indicating that, not surprisingly, the two reinforcers were not equally mobilizing. Although post-experimental ratings confirmed that anticipating money was judged pleasant (and shock unpleasant), skin conductance changes confirmed that motivational intensity was higher in the aversive, compared to appetitive, context, which also varied in other critical ways. Perhaps most importantly, electrical shock is a potent primary stimulus, unconditionally producing pain (at high enough intensity) and reflexively eliciting defensive mobilization, whereas money is clearly a "second signal system" (Pavlov, 1927), acquiring its appetitive associations through learning and experience. Despite these (and other) differences, however, the data indicate that startle potentiation found during threat of shock is not specific to defensive anticipatory processing.

The startle data replicate previous studies finding that the reflexive blink is enhanced when people anticipate exposure to an aversive electric shock (e.g., Bradley et al., 2005; Bublatzky et al., 2013; Dunning et al., 2013; Grillon et al., 1991) and when anticipating appetitive stimuli in other contexts such as viewing pictures (e.g., Dichter et al., 2002; Nitschke et al., 2002; Sabatinelli et al., 2001; Sege et al., 2014) or playing computer games (Skolnick &

Davidson, 2002). The data are not consistent with a recent study in which startle reflexes were inhibited, rather than potentiated, when participants anticipated the receipt of food, although that design included more reinforced trials, the use of a primary (food) reinforcer, and the deprived state of the participant (i.e. had foregone breakfast; Andreatta & Pauli, 2015). On the other hand, a number of studies have reported attenuation of the startle reflex when participants prepare to make a motor movement (Löw, Lang, Smith & Bradley, 2008; Löw, Weymar, & Hamm, 2015; Sege, Bradley & Lang, 2014), and, because the food reinforcer in the Andreatta & Pauli (2015) study involved motor activity (selecting a snack from a jar), it is possible that reflex attenuation in that context reflects preparation for motor activity, rather than affective modulation.

In any case, the current data suggest that reflex potentiation is a general feature of anticipating emotional events, rather than being specifically stress-related,. One possibility is that both of these anticipatory contexts prompt generally heightened vigilance to external sensory events. A number of studies support the hypothesis that threat of shock facilitates initial perceptual processing. For instance, Baas, Milstein, Donlevy, & Grillon (2006) found enhanced brainstem auditory evoked potentials when participants were anticipating shock exposure, and a number of studies (e.g., Cornwell, Echiverri, Covington, & Grillon, 2008; Grillon & Davis, 1997) report enhanced prepulse inhibition during threat of shock, which is interpreted as reflecting a generalized “state of alertness” which enhances processing of the prepulse stimulus when awaiting the onset of aversive stimulation. The current data, however, indicate that it is not only aversiveness that prompts heightened vigilance, but that a vigilant processing mode is equally functional when anticipating appetitive events. This is perhaps why, unlike other fear-potentiated startle effects, diazepam fails to affect reflex potentiation during threat of shock (Baas et al., 2002; but see Grillon et al., 2006).

Studies of the orienting response also find that novel appetitive and aversive stimuli prompt similar response profiles, including heightened cardiac deceleration, skin conductance increase, and enhanced pupil diameter (Bradley, Sapigao, & Lang, 2017), which, we suggest, reflects engagement of shared processes, such as sensory intake and preparation for action, that are functional in motivationally engaging contexts (e.g., Bradley, 2009; Lang & Bradley, 2010). Vigilance, like orienting, is another process that can serve two masters, and the data are consistent with an interpretation that anticipating the imminent onset of either an appetitive or aversive event prompts heightened vigilance to external sensory events, potentiating the reflexive blink response to an incidental acoustic startle probe.

Recent fMRI studies describe both common and distinct regions that are activated during emotional anticipation. Thus, for example, anticipating the upcoming presentation of aversive or appetitive visual stimuli (e.g., pictures: Sege, Bradley, Weymar, & Lang, 2017; films: Greenberg, Carlson, Rubin, Cha, & Mujica-Parodi, 2015) activates a number of shared regions, including, among others, the thalamus, cingulate cortex, dorsolateral prefrontal cortex, and anterior insula. Anticipating pleasant pictures or films, on the other hand, uniquely activates medial prefrontal cortex, whereas threat of shock is reported to uniquely activate the intraparietal sulcus (Balderston et al., 2017). Although these data do not clearly relate to the modulatory startle circuit detailed in the animal literature (e.g., Davis, Falls, Campeau, & Kim, 1993; Lang & Davis, 2006), future brain research could help to illuminate the neural mechanisms of reflex potentation.

From a sensory perspective, some data suggest that processing is further enhanced when modality-related (in this case, tactile) stimuli are delivered during shock threat (Cornwell et al., 2008). The facilitatory effects of anticipation found in the current study are not due to modality, however, as the acoustically elicited blink reflex was potentiated when participants anticipated tactile stimulation, and acoustically elicited blinks are also potentiated when anticipating the onset of visually evocative scenes (e.g., Dichter et al., 2002; Sabatinelli et al., 2001; Sege et al., 2014). Although early studies showed that blinks elicited by acoustic probes were potentiated during anticipation when attention was specifically directed towards the acoustic modality (e.g., Bohlin & Graham, 1977; Silverstein, Graham, & Bohlin, 1981), a key feature in terms of whether anticipation shows modality-specific or general facilitation may be the extent to which the anticipated event activates fundamental appetitive and defensive systems. In studies that find modality-specificity, stimuli are typically innocuous auditory or tactile signals that elicit engagement only through task requirements (e.g., judging duration). Emotionally evocative events, on the other hand, reliably prompt sympathetic arousal and a "*natural selective attention*" that does not rely on instructions or task (Bradley, 2009) and may more broadly enhance vigilance to multiple sensory channels during anticipation.

Affective picture modulation—Emotional anticipation had large, consistent effects on affective startle modulation during picture viewing, regardless of whether shock or money was the reinforcer. In both groups, startle reflexes elicited in the context of safety replicated a pattern in which, compared to viewing neutral scenes, reflexes were attenuated when viewing pleasant scenes and potentiated when viewing aversive scenes (e.g., Vrana et al., 1988). When pictures were viewed under threat, however, subtle changes in the pattern of startle modulation were found in which the only modulatory effect, in both the shock and reward groups, was significant attenuation of the startle reflex when viewing pleasant scenes, consistent with theory that startle reflex modulation during picture processing reflects the net effects of multiple co-occurring processes (Bradley et al., 2006).

Thus, compared to safety, reflexes were potentiated during aversive and appetitive anticipation when viewing any type of picture, as well as for blank cues, but there was no evidence of further potentiation when unpleasant scenes were viewed under threat - rather, reflexes elicited in this context were equivalent to those elicited when viewing neutral (or blank) scenes, regardless of whether shock or money was the anticipated event. Based on the descriptive data presented in previous studies, this pattern seems to replicate Bublatzky et al. (2013), whereas the data presented in Dunning et al. (2013) suggest at least numerically larger blinks when viewing unpleasant, compared to neutral, scenes under threat (of shock). Neither study, however, provided inferential tests of these comparisons. Thus, the current findings can only be considered a cumulative data point regarding changes in affective startle modulation during picture viewing under threat or safety.

On the surface, the fact that attenuation of the startle reflex is only found when viewing pleasant pictures in an anticipatory context seems to support recent studies finding that threat of shock may facilitate response inhibition (e.g., Grillon et al., 2017a, 2017b). In these studies, infrequent NO-GO signals (interspersed among frequent GO signals) showed fewer errors when participants were under threat of shock (i.e., better able to inhibit responses), suggesting that stress facilitates response inhibition, which the researchers note could also be mediated by enhanced sensory processing. Whether inhibition of a voluntary motor response and the attenuation of the reflexive blink during appetitive picture viewing share a common mechanism, however, is not clear, and awaits future studies.

Despite the varying patterns of startle reflex modulation when viewing pictures under threat or safety, skin conductance was modulated by picture content similarly in both threat and safe contexts, with larger changes when viewing emotional, compared to neutral, scenes. These data suggest that it is not motivational intensity, per se, that modulates the startle reflex during anticipation, but rather, that motivational intensity acts a gain factor on processes such as perceptual vigilance that are engaged by appetitive or defensive mobilization during anticipatory processing.

Summary

Anticipating a tactile stimulus signaling either shock or reward "threat" prompts potentiation of the acoustically-elicited startle reflex, indicating that reflex potentiation during anticipatory processing is not solely a property of threat of shock. Although reflex potentiation (and electrodermal engagement) were significantly larger for those anticipating shock, both groups showed significant reflex potentation during threat, compared to safety, as well as similar patterns of affective modulation when viewing pictures under threat or safety, suggesting heightened vigilance to perceptual stimulation in both anticipatory contexts. Taken together, the data indicate that startle reflex potentiation is not restricted to a context of anticipatory anxiety or stress, but is instead a more general feature of anticipating an motivationally relevant event.

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References

Andreatta M, Pauli P. Appetitive vs. aversive conditioning in humans. Frontiers Behavioral Neuroscience. 2015; 9(128):1–8. https://doi.org/10.3389/fnbeh.2015.00128.

Baas JM, Grillon C, Bocker KB, Brack AA, Morgan CA, Kenemans LJ, Verbaten MN. Benzodiazepines have no effect on fear-potentiated startle in humans. Psychopharmacology. 2002; 161:233–247. https://doi.org/10.1007/s00213-002-1011-8. [PubMed: 12021826]

Baas JM, Milstein J, Donlevy M, Grillon C. Brainstem correlates of defensive states in humans. Biological Psychiatry. 2006; 59:588–593. https://doi.org/10.1016/j.biopsych.2005.09.009. [PubMed: 16388780]

Balderston, NL., Hale, E., Hsiung, A., Torrisi, S., Holroyd, T., Carver, FW., Coppola, R., Ernst, M., Grillon, C. Threat of shock increases excitability and connectivity of the intraparietal sulcus; eLife. 2017. p. 1-27.https://doi.org/10.7554/eLife.23608

Blumenthal T, Cuthbert BN, Filion DL, Hackley S, Lipp OV, van Boxtel A. Guidelines for human startle eyeblink electromyographic studies. Psychophysiology. 2005; 42:1–15. https://doi.org/10.1111/j.1469-8986.2005.00271.x. [PubMed: 15720576]

Bohlin M, Graham F. Cardiac deceleration and reflex blink facilitation. Psychophysiology. 1977; 14:423–430. [PubMed: 905479]

Bradley MM. Natural selective attention: Orienting and emotion. Psychophysiology. 2009; 46:1–11. https://doi.org/10.1111/j.1469-8986.2008.00702.x. [PubMed: 18778317]

Bradley MM, Codispoti M, Lang PJ. A multi-process account of affective startle modulation during affective perception. Psychophysiology. 2006; 43:486–497. https://doi.org/10.1111/j.1469-8986.2006.00412.x. [PubMed: 16965611]

Bradley MM, Codispoti M, Cuthbert BN, Lang PJ. Emotion and motivation I: Defensive and appetitive reactions in picture processing. Emotion. 2001; 1:276–298. https://doi.org/10.1037/1528-3542.1.3.276. [PubMed: 12934687]

Bradley MM, Moulder B, Lang PJ. When good things go bad: The reflex physiology of defense. Psychological Science. 2005; 16:468–473. https://doi.org/10.1111/j.0956-7976.2005.01558.x. [PubMed: 15943673]

Bradley, MM., Sapigao, R., Lang, PJ. Sympathetic ANS modulation of pupil diameter in emotional scene perception: Effects of hedonic content, brightness, and contrast. Psychophysiology. 2017. Advance online publication. https://doi.org/10.1111/psyp.12890

Bradley MM, Silakowski T, Lang PJ. Fear of pain and defensive activation. Pain. 2008; 137(1):156–163. https://doi.org/10.1016/j.pain.2007.08.027. [PubMed: 17904289]

Bublatzky F, Guerra PM, Pastor MC, Schupp HT, Vila J. Additive effects of threat-of-shock and picture valence on startle reflex modulation. PLOS ONE. 2013; 8:1–6. https://doi.org/10.1371/journal.pone.0054003.

Buss, AH., Plomin, R. A temperament theory of personality development. New York, USA: John Wiley; 1975.

Cook, EW, III. VPM Reference Manual. Birmingham, AL: Author; 2001.

Davis M, Falls WA, Campeau S, Kim M. Fear-potentiated startle: a neural and pharmacologicall analysis. Behavioral Brain Research. 1993; 20:175–198.

Dichter GS, Tomarken AJ, Baucom BR. Startle modulation before, during and after exposure to emotional stimuli. International Journal of Psychophysiology. 2002; 43(2):191–6. [PubMed: 11809522]

Dunning JP, DelDonno S, Hajcak G. The effects of contextual threat and anxiety on affective startle modulation. Biological Psychology. 2013; 94:130–135. https://doi.org/10.1016/j.biopsycho.2013.05.013. [PubMed: 23727541]

Gold AL, Morey RA, McCarthy G. Amygdala-prefrontal cortex functional connectivity during threat-induced anxiety and goal distraction. Biological Psychiatry. 2015; 77:394–403. https://doi.org/10.1016/j.biopsych.2014.03.030. [PubMed: 24882566]

Grillon C, Ameli R, Woods SW, Merikangas K, Davis M. Fear-potentiated startle in humans: effects of anticipatory anxiety on the acoustic blink reflex. Psychophysiology. 1991; 28:588–595. https://doi.org/10.1111/j.1469-8986.1991.tb01999.x. [PubMed: 1758934]

Grillon C, Baas JMP, Pine DS, Lissek S, Lawley M, Ellis V, Levine J. The benzodiazepine alprazolam dissociates contextual fear from cued fear in humans as assessed by fear-potentiated startle. Biological Psychiatry. 2006; 60:760–766. https://doi.org/10.1016/j.biopsych.2005.11.027. [PubMed: 16631127]

Grillon C, Charney D. In the face of fear: Anxiety sensitizes defensive responses to fearful faces. Psychophysiology. 2011; 48:1745–1752. https://doi.org/10.1111/j.1469-8986.2011.01268.x. [PubMed: 21824155]

Grillon C, Davis M. Effects of stress and shock anticipation on prepulse inhibition of the startle reflex. Psychophysiology. 1997; 34:511–517. [PubMed: 9299905]

Grillon C, Robinson OJ, O'Connell K, Davis A, Alvarez G, Pine DS, Ernst M. Clinical anxiety promotes excessive response inhibition. Psychological Medicine. 2017a; 47:484–494. https://doi.org/10.1017/S0033291716002555. [PubMed: 27776562]

Grillon C, Robinson OJ, Krimsky M, O'Connell K, Alvarez G, Ernst M. Anxiety-mediated facilitation of behavioral inhibition: Threat processing and defensive reactivity during a go/no-go task. Emotion. 2017b; 17:259–266. https://doi.org/10.1037/emo0000214. [PubMed: 27642657]

Greenberg T, Carlson JM, Rubin D, Cha J, Mujica-Parodi L. Anticipation of high arousal aversive and positive movie clips engages common and distinct neural substrates. Social, Cognitive, and Affective Neuroscience. 2015; 10:605–611. https://doi.org/10.1093/scan/nsu091. [PubMed: 24984958]

Lang, PJ., Bradley, MM., Cuthbert, BN. Technical Report A-8. University of Florida; Gainesville, FL: 2008. International affective pictures system (IAPS): Affective ratings of pictures and instruction manual.

Lang PJ, Bradley MM. Emotion and the motivational brain. Biological Psychology. 2010; 84:437–450. https://doi.org/10.1016/j.biopsycho.2009.10.007. [PubMed: 19879918]

Lang PJ, Davis M. Emotion, motivation, and the brain: Reflex foundations in animal and human research. Progress in Brain Research. 2006; 156:3–29. https://doi.org/10.1016/S0079-6123(06)56001-7. [PubMed: 17015072]

Lang PJ, Greenwald MK, Bradley MM, Hamm AO. Looking at pictures: Affective, facial, visceral, and behavioral reactions. Psychophysiology. 1993; 30(3):261–273. https://doi.org/10.1111/j.1469-8986.1993.tb03352.x. [PubMed: 8497555]

Löw A, Lang PJ, Smith JC, Bradley MM. Both predator and prey: emotional arousal in threat and reward. Psychological Science. 2008; 19:865–73. https://10.1111/j.1467-9280.2008.02170.x. [PubMed: 18947351]

Löw A, Weymar M, Hamm AO. When threat is near, get out of here: dynamics of defensive behavior during freezing and active avoidance. Psychological Science. 2015; 26:1706–1716. https://doi.org/10.1177/0956797615597332. [PubMed: 26408036]

Nitschke JB, Larson CL, Smoller MJ, Navin SD, Pederson AJ, Ruffalo D, Mackiewicz KL, Gray SM, Victor E, Davidson RJ. Startle potentiation in aversive anticipation: evidence for state but not trait effects. Psychophysiology. 2002; 39(2):254–258. https://doi.org/10.1017/S0048577202010156. [PubMed: 12212676]

Pavlov, IP. Conditioned reflexes, an investigation of the physiological activity of the cerebral cortex. Anrep, GV., translator. Oxford University Press; Humphrey Milford: 1927.

Phelps EA, O'Connor KJ, Gatenby JC, Gore JC, Grillon C, Davis M. Activation of left amygdala to a cognitive representation of fear. Nature Neuroscience. 2001; 4:437–441. https://doi.org/10.1038/86110. [PubMed: 11276236]

Robinson OJ, Vytal K, Cornwell BR, Grillon C. The impact of anxiety upon cognition: perspectives from human threat of shock studies. Frontiers in Human Neuroscience. 2013; 7:203. https://doi.org/10.3389/fnhum.2013.00203. [PubMed: 23730279]

Sabatinelli D, Bradley MM, Lang PJ. Affective startle modulation in anticipation and perception. Psychophysiology. 2001; 38:719–722. [PubMed: 11446586]

Sege CT, Bradley MM, Weymar M, Lang PJ. A direct comparison of appetitive and aversive anticipation: Overlapping and distinct neural activation. Behavioural Brain Research. 2017; 32:96–102. https://doi.org/10.1016/j.bbr.2017.03.005.

Sege CT, Bradley MM, Lang PJ. Startle modulation during emotional anticipation and perception. Psychophysiology. 2014; 51:977–981. https://doi.org/10.1111/psyp.12244. [PubMed: 24980898]

Silverstein LD, Graham FK, Bohlin G. Selective attention effects on the reflex blink. Psychophysiology. 1981; 18:240–247. [PubMed: 7291439]

Skolnick AI, Davidson RI. Affective modulation of eyeblink startle with reward and threat. Psychophysiology. 2002; 39(6):835–850. [PubMed: 12462511]

Vrana SR, Spence EL, Lang PJ. The startle probe response: a new measure of emotion? Journal of Abnormal Psychology. 1988; 97(4):487–491. [PubMed: 3204235]

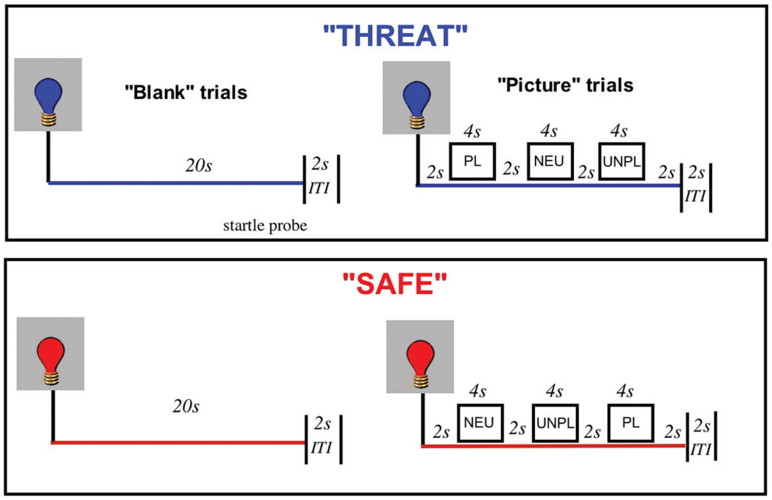

Figure 1.

A colored light cued whether there was a possibility that electrical (shock) or vibrotactile (money) stimulation could occur, with half of the trials (“blank”) presenting only the cue, and the other half of the trials (“picture”) additionally presenting one pleasant, one neutral, and one unpleasant picture in the context of the cue. One acoustic startle probe was presented on each trial.

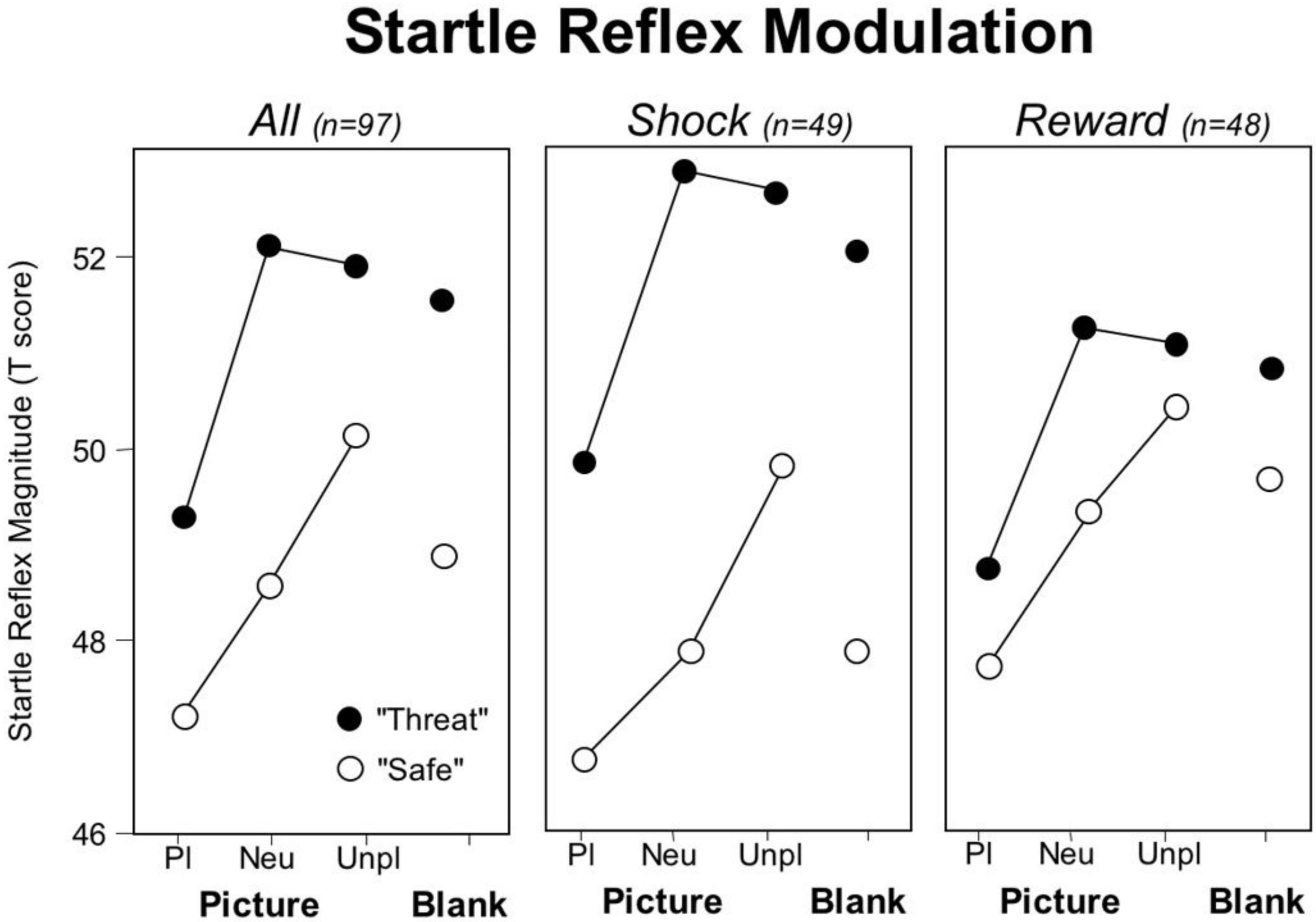

Figure 2.

Standardized startle reflex magnitude elicited in periods during which electrical or vibrotactile stimulation was possible (“threat”) or not (“safe”), averaged over participants on picture and blank trials (right panel), and separately for those anticipating electrical (middle panel) or vibrotactile (left panel) stimulation. Standard deviations (ordered: all participants, shock group, reward group) for the safe condition are: Pleasant: 3.5, 4.0, 2.9; Neutral: 3.7, 3.3, 3.9; Unpleasant: 4, 4.3, 4.2; Blank: 2, 1.8, 1.8; and for the threat condition: Pleasant: 3.6, 3.5, 3.7; Neutral: 4.7, 5.2, 4.0; Unpleasant: 3.7, 4, 3.1; Blank: 2.5, 2.5, 2.4.

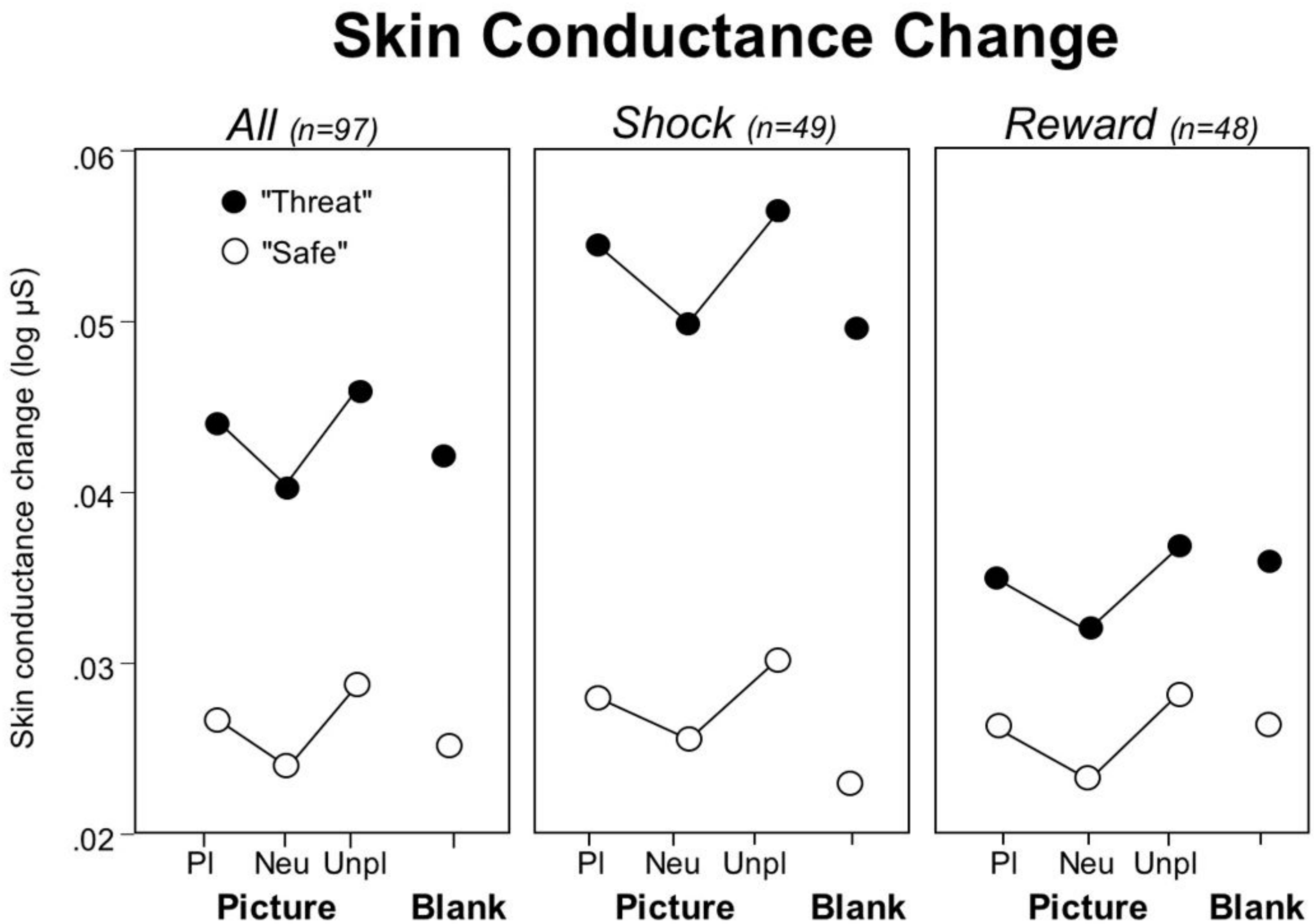

Figure 3.

Skin conductance change in periods during which electrical or vibrotactile stimulation was possible (“threat”) or not (“safe”), averaged over participants on blank and picture trials (right panel), and separately for those anticipating electrical (middle panel) or vibrotactile (left panel) stimulation. Standard deviations (ordered: all participants, shock group, reward group) for the safe condition are: Pleasant: .03, .03, .03; Neutral: .02, .02, .02; Unpleasant: .03, .03, .03; Blank: .02, .02, .02 and for the threat condition: Pleasant: .04, .04, .03; Neutral: .04, .05, .03; Unpleasant: .04, .05, .04; Blank: .04, .05, .03.

Table 1

Raw blink magnitude (SE) during anticipation (“threat”) of shock or reward and on control (“safe”) trials, separately for trials that presented emotional or neutral scenes, or did not (“blank”).

		CUE	
REINFORCER		**“Threat”**	**“Safe”**
Shock	Pleasant	5.8 (0.7)	4.6 (0.5)
	Neutral	7.0 (0.8)	5.2 (0.7)
	Unpleasant	6.8 (0.7)	5.8 (0.7)
	Blank	6.5 (0.7)	5.2 (0.6)
Reward	Pleasant	4.4 (0.5)	4.1 (0.5)
	Neutral	5.4 (0.7)	4.8 (0.6)
	Unpleasant	5.2 (0.6)	5.0 (0.6)
	Blank	5.0 (0.6)	4.8 (0.6)