The impact of induced anxiety on affective response inhibition

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Abstract

Studying the effects of experimentally induced anxiety in healthy volunteers may increase our understanding of the mechanisms underpinning anxiety disorders. Prior work has shown that experimentally induced anxiety (via threat of unpredictable shock) improves accuracy at withholding a response on the Sustained Attention to Response Task (SART), and in separate studies improves accuracy to classify fearful faces, creating an affective bias. Integrating these findings, in this study participants (N=47) at a public science engagement event were recruited to explore the effects of experimentally induced anxiety on an affective version of the SART. On the basis of previous work, we hypothesised that we would see an increased accuracy at withholding a response to affectively congruent stimuli (i.e. increased accuracy at withholding a response to fearful “no-go” distractors) under threat of shock. Replicating previous findings, threat of shock slowed reaction time. However, contrary to predictions there was no evidence to suggest an interaction between induced anxiety and stimulus valence on accuracy. Indeed Bayesian analysis provided decisive evidence in favour of the null. We suggest that valence effects could emerge after processing durations longer than those allowed by the present task.
Introduction

Anxiety can be both adaptive and maladaptive, but in both cases lead to altered cognitive performance (Robinson, Vytal, Cornwell & Grillon, 2013a). Anxiety can, for instance, promote a tendency to focus on negative experiences at the expense of positive ones; a so-called ‘negative bias’ (Robinson et al., 2013a). Whilst a bias towards threatening information can be adaptive, encouraging the adoption of behaviours that reduce risk of harm, it may also precipitate the onset of mood disorders (Kendler, Kuhn & Prescott, 2004; Kendler, Karkowski & Prescott, 1999). Indeed, negative biases in cognition are prevalent in people suffering from anxiety disorders (MacLeod & Mathews, 2012; Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg & van IJzendoorn, 2007), and Major Depressive Disorder (MDD) (Yoon, Joormann & Gotlib, 2009; Stuhrmann, Suslow & Dannlowski, 2011). One hypothesis, therefore, is that pathological anxiety is an extension of the same mechanisms that contribute to adaptive anxiety (Robinson et al., 2014a).

Inducing adaptive anxiety in healthy controls may thus enable the interaction between anxiety and cognition to be investigated, contributing to our understanding of the mechanisms that underlie maladaptive mood states. An anxious state can be induced in participants by introducing the threat of an unpredictable electric shock, a well-validated technique (Robinson, Letkiewicz, Overstreet, Ernst & Grillon, 2011), which induces a state thought to be analogous to real life anxiety (Robinson et al., 2014a). In a within-subjects design, the influence of anxiety on cognition can be investigated by comparing task performance in the same individual when they are at risk of an unpredictable electric shock and when safe from shock. This technique has previously been used to investigate the interaction between anxiety and response inhibition; the ability to withhold a response, using a Sustained Attention to Response Task (SART). In this task participants are alternately at
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risk of an unpredictable shock (threat condition) and safe from a shock (safe condition). They must respond to frequent “go” target stimuli, and withhold a response to infrequent “no-go” distractor stimuli. Threat of shock increases accuracy to “no-go” distractor stimuli (Robinson, Krimsky & Grillon, 2013b) whilst slowing down response time overall (Aylward, Roiser, & Robinson, 2015; Mkrtchian, Roiser & Robinson, 2015; Hu, Bauer, Padmala & Pessoa, 2012).

Threat of shock can also be used to instantiate a negative affective bias, with threat of shock enhancing the processing of affectively congruent stimuli (Robinson, Charney, Overstreet, Grillon, 2014b). It has been reliably reported that when under threat of unpredictable shock (and therefore experiencing a higher level of state anxiety), compared with performance in a safe condition, fearful faces are more accurately classified than happy faces. In line with this, when at risk of shock, responses to unexpected fearful faces are increased relative to unexpected happy faces (Grillon & Charney, 2011; Robinson, Overstreet, Charney, Vytal & Grillon, 2013c). Taken together these findings have led to a theory that threat of shock, and anxiety disorders, may indeed promote harm avoidant behaviour (Robinson et al., 2013b).

In summary, it has been suggested that threat of shock can both selectively enhance processing of affectively congruent stimuli and promote inhibitory control. In this study, conducted during a public scientific engagement event, we used an adapted version of the SART described above to investigate whether inhibitory effects interact with affective bias. In this new task, participants were instructed to respond to happy faces and withhold responses to fearful faces whilst they were alternately at risk of unpredictable shock and safe from shock. The nature of the event enabled us to investigate effects within a more naturalistic setting than in highly controlled laboratory conditions.
Based on results from the clinical literature, and previously discussed research investigating negative affective biases instantiated by threat of shock, we predicted that the threat of shock manipulation would induce a state of transient anxiety in participants, and we would see an increased accuracy at withholding a response to affectively congruent stimuli (i.e. increased accuracy at withholding a response to fearful “no-go” distractors) under threat of shock. In addition, as individual differences modulate the interaction between cognition and anxiety (Cools et al., 2005; Stein, Simmons, Feinstein & Paulus, 2007), state and trait measures of anxiety were recorded, allowing us to look at individual differences in vulnerability to threat of shock and task performance. Considering the nature of the event where data collection took place, blood alcohol measurements were recorded. It is known that alcohol selectively reduces anxiety, but not fear (Moberg & Curtin, 2009), so collecting this data allows for the possibility of the interaction between alcohol and anxiety on task performance to be investigated.
Methods

This study was completed as part of a public engagement event at the Royal Institution entitled ‘Questioning Reality’. It was completed in a large room, with two computers setup but event attendees were free to wander around the room and watch the testing. The overall sound levels and potential for distraction were considerably greater than a controlled testing environment but can be thought of as a naturalistic representation of an informal social event.

Participants

Forty-seven participants, (Male = 25) aged between 19 and 65 (Mean = 30.7, SD = 9.43) completed the study. All participants provided written informed consent. UCL Ethics Committee approved an amendment to existing ethics (ref: 1764/001) allowing offsite data collection. Subjects completed a screening form that verified that they had no history of neurological, psychiatric, or cardiovascular conditions. An a priori power analysis was run in G*Power (Faul, Erdfelder, Langer & Buchner, 2007). The power analysis was based on the results of the SART (Robinson et al., 2013b) that gave an effect size of 0.56 for the effect of threat of shock on response accuracy to “no-go” distractor stimuli. A post hoc matched t-test power analysis showed that with 47 participants (with alpha = 0.05, two tailed) we had 96.4% power to detect an effect of this magnitude.

Shock set up

Two electrodes were attached to the back of the participants’ wrists (on their non-dominant hand) to induce anxiety via threat of unpredictable electric shock. They were instructed to make their responses using the opposite hand. For each participant, the shock level was set to a level where it was “unpleasant but not painful” (Schmitz & Grillon, 2012). Shocks were

1 For event program, see here: http://www.rigb.org/docs/questioning_reality_floorplan_web_0.pdf
delivered using a Digitimer DS7A Constant Current Stimulator (Digitimer Ltd., Welwyn Garden City, UK).

**Affective Response Inhibition Task**

Participants completed a new task adapted from our previously used Sustained Attention to Response Task (Robinson et al., 2013b) under two different conditions; they were alternately at risk of an unpredictable shock and safe from a shock. For 3 seconds at the beginning of each block, “YOU ARE NOW SAFE FROM SHOCK!” or “YOU ARE NOW AT RISK OF SHOCK!” (order counterbalanced) appeared on the screen. When in a safe block, the background was blue (and no shocks were delivered), and when in a threat block the background was red.

Participants were required to respond to frequent “go” target stimuli by pressing the space bar as quickly as possible after presentation and to inhibit a response to infrequent “no-go” distractor stimuli by withholding a key press. 47 “go” stimuli and 5 “no-go” stimuli were randomly presented in each block. For half of the trials, happy faces were the “go” target stimuli, and fearful faces were “no-go” distractor stimuli (order counterbalanced). Halfway through the contingency changed (with explicit instructions), and happy faces became “no-go” distractor stimuli, and fearful faces became “go” target stimuli. The order of contingencies was counterbalanced across participants as well as the order of threat and safe blocks.

Face stimuli were presented for 250ms, followed by an interstimulus interval of 750ms, before presentation of the next stimulus. There were a total of four blocks (two threat and two safe blocks), with each block lasting 52 seconds (See Figure 1). Participants received, at random, either one (45th trial) or two shocks (45th and 97th trial), during the shock condition. They were informed that the shocks would be delivered at random and...
uncontrollable (i.e. they were not punished as a result of an incorrect key press). Total task duration was approximately 4 minutes and 30 seconds.

**Figure 1.** Participants were instructed to press the space bar as quickly as possible for “go” stimuli and withhold responses to infrequent “no-go” stimuli (“go” and “no-go” stimuli valence was counterbalanced). A: Participants received an unpredictable electric shock (independent of behavioural response) during the threat condition. B: Participants were not at risk of shock during the safe condition. Note: this is a schematic, the experimental task used Ekman faces (Ekman & Friesman, 1976).

**Between subject measures**

Immediately after completing the task, participants were asked to report how anxious, afraid and stressed they had felt in the safe and threat conditions. They made a response between 1 (not at all) and 10 (very much so). Thirty-two participants also completed self-report measures of State and Trait Anxiety (Spielberger, Gorsuch, Lushene, Vagg & Jacobs, 1983).

Blood alcohol concentrations were recorded by asking participants to breathe into an AlcoDigital ProPack 7000 machine. However, it should be noted that we have concerns that
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166 the breathalyser was not functioning correctly (e.g. some very high readings were gained
167 alongside self-reported claims that they had not consumed any alcohol for 20 years).

Data analysis

168 Reaction time and accuracy was analysed using two repeated-measures general linear models
169 in SPSS version 22 (IBM Crop, Armonk, NY). For all analyses, \( p = 0.05 \), was considered
170 significant. Bayesian statistics were also run for these frequentist analyses (in JASP (Love et
171 al., 2014), version 0.7), employing the default prior. Data are available for download\(^2\)
172 Performance accuracy for each condition (threat/safe) and trial type (“go” / “no-go”)
173 was calculated by dividing the number of correct trials by the total number of trials. Accuracy
174 analysis was performed on no-go trials only (“go” accuracy was 95.2 %). Response accuracy
175 on “no-go” trials was analysed using a two-way ANOVA with factors valence (happy / sad)
176 and condition (threat / safe). Reaction time analysis was performed on “go” stimuli. Prior to
177 analysis, a square root transform was applied to reaction time data as it was not normally
178 distributed. Reaction time to targets (“go” stimuli) was analysed using a two-way ANOVA
179 with factors valence (happy / sad) and condition (threat / safe). Bayesian ANOVAs were used
180 to generate log BF\(_{10}\) factors for model of interest relative to a null model (main effect of
181 subject). The ‘winning’ model BF\(_{10}\) was defined as the highest BF\(_{10}\) relative to the null. The
182 following labels were assigned to BF\(_{10}\): anecdotal (1-3), substantial (3-10), strong (10-30)
183 decisive (>100) to interpret the magnitude differences between models. (Jeffreys, 1998).
184 Post hoc analyses were run to investigate the effect of STAI anxiety scores and blood
185 alcohol concentration on performance. Pearson’s \( r \) correlations between symptom measures
186 (STAI State and Trait scores, and blood alcohol concentration) and reaction time / accuracy
187 data were run. Only \( N = 32 \) participants could be included in the secondary analysis of STAI

\(^2\) [http://dx.doi.org/10.6084/m9.figshare.1609723](http://dx.doi.org/10.6084/m9.figshare.1609723)
anxiety scores due to missing data. To determine if the correlations survived multiple comparisons a Monte Carlo resampling method (using 10,000 permutations) was performed.
Results

Threat of shock manipulation

Subjective ratings of anxiety levels were significantly higher during the threat condition relative to the safe condition ($t(46) = 5.83, p < 0.001$, Safe Mean = 3.36, SD = 2.20, Threat Mean = 5.25, SD = 2.75). Bayesian analyses confirmed a model with main effect of condition was the winning model, with a decisive magnitude difference ($BF_{10} = 2327.10$).

Reaction Time

We found a significant effect of condition ($F(1,46) = 6.55, p = 0.014, \eta^2 = 0.125$) with participants slower to respond to targets in the threat condition (Safe Mean = 322.19, SD = 62.27, Mean Threat = 311.47, SD = 73.21; see Figure 2). Participants’ reaction time was not affected by valence ($F(1,46) = 0.274, p = 0.60, \eta^2 = 0.006$) nor was there a (valence x condition) interaction ($F(1,46) = 0.03, p = 0.86, \eta^2 = 0.001$).

Bayesian analysis confirmed that a model with main effect of condition was the winning model albeit with an anecdotal $BF_{10} = 2.02$. The null model was in fact 9.26 substantially better than a model including a valence x condition interaction.
Figure 2. Participants were significantly slower to respond to targets when under threat of shock. Error bars represent SEM, $p = 0.014$.

Accuracy

We did not find a significant main effect of valence ($F_{(1,46)} = 3.22$, $p = 0.079$, $\eta^2_p = 0.065$) or condition ($F_{(1,49)} = 0.005$, $p = 0.95$, $\eta^2_p < 0.001$), nor was there a significant (valence x condition) interaction on participants’ accuracy ($F_{(1,46)} = 0.117$, $p = 0.77$, $\eta^2_p = 0.0025$).

Bayesian analysis confirmed that no models had a BF10>1 indicating no evidence of an effect of valence or threat. Indeed, a model including an interaction term between valence and threat was substantially (38.46) worse than the null enabling us to reject our hypothesis of a threat x valence interaction.

Post hoc between subject analyses:
Correlations were run to look at response accuracy and response time differences (to distractors and targets respectively) across threat conditions against STAI state and trait scores, and blood alcohol measures.

We calculated the behavioural measures by computing four variables; threat minus safe accuracy to 1) fearful faces, and 2) happy faces, and threat minus safe reaction time to 3) fearful faces and 4) happy faces. There was a significant negative association between the difference in accuracy in withholding a response to fearful faces and STAI state anxiety score ($r = -.399, p = 0.024$). The smaller the difference in accuracy at withholding a response across conditions, the higher the STAI state anxiety score. However, post hoc analyses using the “Monte Carlo” method identified that this effect did not remain after allowing for multiple comparisons ($p = 0.49$). No other significant correlations were found with any other between subject factors.

Table 1. Response accuracy and response time differences across conditions against behavioural measures

<table>
<thead>
<tr>
<th>Response accuracy and response time differences across conditions</th>
<th>STAI state</th>
<th>STAI trait</th>
<th>Blood alcohol level (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Threat minus safe accuracy to Fearful faces</td>
<td>-.399 *</td>
<td>-.190</td>
<td>.098</td>
</tr>
<tr>
<td>Threat minus safe accuracy to Happy faces</td>
<td>-.103</td>
<td>.137</td>
<td>-.016</td>
</tr>
<tr>
<td>Threat minus safe reaction time to Fearful faces</td>
<td>-.217</td>
<td>-.001</td>
<td>.090</td>
</tr>
<tr>
<td>Threat minus safe reaction time to Happy faces</td>
<td>-.082</td>
<td>.204</td>
<td>.238</td>
</tr>
</tbody>
</table>

All $p > .05$ with the exception of Threat minus safe accuracy to fearful faces * ($p = 0.024$)
Conclusion

This study demonstrates that threat of shock slows response times to target stimuli. However, there was no evidence in support of our hypothesis that threat of shock selectively increased accuracy for task congruent stimuli (i.e. that accuracy at withholding a response to fearful “no-go” distractors would increase when under threat of shock). This is further supported by our Bayesian analyses, which provided evidence in favour of the null model over a model including the interaction term.

First, we replicated a previously finding, and intuitive result, that threat of shock slows down response times for “go” responses (Aylward et al., 2015, Mkrtchian et al., 2015, Hu et al., 2012), being cautious when under threat of shock prevents impulsive and sudden responding, reducing the risk of harmful behaviour. It is also consistent with the Pavlovian account of behavioural control in which an aversive context (such as the threat of shock condition in our study) gives rise to a “pre-programmed” response, inhibition of a behavioural response (Boureau & Dayan, 2011). Taken together, the slower reaction times when under threat of shock and significantly higher ratings of self-report anxiety in this condition demonstrate that an effective change in behaviour has resulted from the threat of shock manipulation.

Secondly, we did not find evidence to support the idea of an affective bias in our study, i.e. a valence x condition interaction in response accuracy. Bayesian analysis confirmed that a null model was in fact 38.46 times better than a model including this interaction term. In threatening conditions it would be adaptive to focus on aversive information to avoid harm, so we predicted that the ability to withhold a response to fearful distractors would increase when under threat of shock. Although this has not been directly compared before, we based our predictions on previous research and observations in the
clinical populations (MacLeod & Matthews, 2012; Bar-Haim et al., 2007) and previous studies demonstrating an affective bias instantiated by threat of shock. For example, induced anxiety increases accuracy at classifying fearful faces relative to happy faces (Robinson et al., 2011, Robinson et al., 2014b). In line with this, threat of shock increased aversive prediction errors (evidenced by an increased ventral striatum response to unexpectedly fearful faces when expecting happy faces) but did not affect appetitive prediction errors (Robinson et al., 2013c).

Whilst threat of shock had an influence on reaction time and subjective ratings of anxiety between sessions, we did not see an improvement in response inhibition (i.e. improved accuracy at inhibiting a response to fearful faces under threat of shock). Why, therefore, do we not see the predicted valence effect in this study? In the present study the stimuli were presented for 250ms, whilst in a previous study (which demonstrated an affective bias) the faces were presented for 1000ms. These different presentation times across studies corresponded with different average reaction times (present study safe condition = 311.21ms, threat condition = 322.07ms, previous study safe condition = 739ms, threat condition = 741ms). Since it is thought that conscious processing of faces occurs above chance for presentations of 330ms or more (Williams et al., 2004) the motor response could have been made before the valence was detected.

In addition, a few limitations regarding the data collection environment should be considered when interpreting our results. Data was collected in a very busy room with event attendees free to wander around and watch the testing. This suggests that attention on the task might plausibly be less than it would have been in a controlled laboratory setting. This could be particularly relevant as individual differences in attentional control mechanisms interact with performance across threat and safe conditions (Grillon, Robinson, Mathur & Ernst, 2015) and prominent theories of anxiety (Derakshan & Eysenck, 2009; Eysenck, Derakshan, 2009).
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Santos & Calvo, 2009). Additionally, alcohol was widely available at the event. In order to address this potential confound and to also look at potential interactions between anxiety level, blood alcohol concentration and task performance, blood alcohol measurements were recorded. Whilst blood alcohol concentration did not correlate with any performance measure ($p > 0.05$ – see Table 1) it should be noted that the breathalyser measures may have been unreliable. Since alcohol reduces anxiety (Moberg & Curtin, 2009) and the key to investigating this affective bias in our task is comparison of performance across safe and threat (anxiety-inducing) conditions, the presence of unaccounted for alcohol-driven variance might explain our null finding.

Our sample was not generated specifically to look at individual anxiety levels and the impact of threat of shock on task performance. We found a significant negative correlation state anxiety level and task performance; the smaller the difference in accuracy at withholding a response to fearful faces across conditions, the higher the STAI state anxiety score. However this result did not remain after controlling for multiple comparisons. A more targeted, and wider sample would allow us to investigate this in future studies.

To summarise, we replicated a previously observed effect, namely that threat of shock reliably slows down reaction times for “go” responses (Aylward et al., 2015, Mkrtchian et al., 2015, Hu et al., 2012). Our data do not, however, support the hypothesis that this effect is valence specific. We did not observe an interaction between accuracy and valence in response to fearful stimuli. We hypothesise that factors such as the timing of stimulus presentation, the testing environment and presence of alcohol could have impacted our results. Nonetheless, unlike traditional controlled laboratory settings, these results can be considered a naturalistic representation of performance during a social event and demonstrate collecting data during public engagement events is possible.
Data accessibility

The data has been deposited in an external repository: figshare:
(http://dx.doi.org/10.6084/m9.figshare.1609723)

Competing interests

The authors declare no competing financial interest.

Authors’ contributions

J.A. collected and analysed the data and wrote the paper. V.V. was involved in task preparation and study design, collected the data and reviewed the manuscript. A.M, N.L & T.L collected the data and reviewed the manuscript, O.J.R conceived and designed the study, collected the data and reviewed the manuscript.

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