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Exploring the effect of loneliness on fear: Implications for the effect of COVID-19-induced social disconnection on anxiety

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ABSTRACT

The consequences of the COVID-19 pandemic have resulted in many disruptions to daily life, including an abrupt increase in social disconnection. As measures were put in place to combat the spread of COVID-19, people across the globe began living in states of limited social contact, fostering feelings of social isolation and loneliness. Previous literature suggests that these increases in social disconnection can have profound effects on both physical and mental health, perhaps especially in the case of fear disorders. The combination of feeling disconnected from others and the high level of daily threat experienced due to COVID-19 created conditions under which dysfunctional and persistent fears were especially likely to develop. Building on current understanding of the harmful effects of social disconnection on well-being in general as well as specific implications for fear, here we present findings from three preliminary investigations that are the first to directly examine the effects of loneliness on how fears are learned and maintained. The Results of this work show that loneliness impairs the process by which fears are extinguished, which is central to both the regulation of fear and treatment of fear disorders, and provide insight into potential avenues to mitigate such effects.

1. Introduction

Starting in early 2020, worldwide events catapulted people across the globe into a state of social disconnection. Due to the measures and precautions taken to combat COVID-19, many were forced to begin living in conditions of limited physical and emotional social contact, fostering increases in objective social isolation as well as subjective social isolation (also known as loneliness), both of which contribute to feelings of social disconnection. While the impact of this extreme shift can only be speculated, findings in animals and humans suggest that these increases in social disconnection may have severe effects on both physical and mental health and that the stress and trauma of these conditions may extend even after restrictions are lifted. Therefore, it is crucial to take a closer look at the impact of social distancing measures both to catalogue the consequences as they occur and to identify potential methods to mitigate their long-term effects. Here, we will first give an overview of the research on the effects of social disconnection on health and well-being and then discuss three preliminary investigations which provide some insight into the effects that being disconnected can have on long-term trauma and fear.

A large body of research has demonstrated the harmful consequences of feeling socially disconnected. In addition to emotional distress, individuals who report having poor quality social bonds or experiencing high levels of loneliness are at increased risk of suffering a multitude of negative mental and physical health outcomes ranging from depression (Cacioppo, Hughes, Waite, Hawkley, & Thisted, 2006), to cardiovascular disease (Hawkley & Cacioppo, 2013), and even mortality (Holt-Lunstad, Smith, Baker, Harris, & Stephenson, 2015). It is thought that these negative health outcomes may stem, in part, from the fact that loneliness and social isolation can trigger a heightened vigilance for threats. Although this heightened threat vigilance is adaptive in that it prepares an animal to defend itself in the absence of social support and group protection, it also increases fear and stress, ultimately leading to harmful wear-and-tear on the body and mind (Cacioppo, Hawkley, & Berntson, 2003).

While this increase in emotional and physiological stress can have ill effects on general bodily systems and mental health, it is notable that the increased threat-vigilance induced by social disconnection may have ill effects on fear systems in particular (Cacioppo, Hughes, et al., 2006; Cacioppo et al., 2003; Hawkley & Cacioppo, 2013). Specifically, by amplifying fear and stress, loneliness and social isolation may augment the processes by which individuals learn about threats and threatening

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cues in their environment. Understanding the effects of social isolation on fear learning is acutely important in light of the COVID-19 pandemic, during which individuals have not only been at higher risk for being social disconnected, but also have been faced with new, daily threats to their health and well-being, possibly creating the perfect conditions for the development of extreme fears and trauma.

Evidence that social disconnection impacts the ways in which threats are learned about and responded to can be found in animal research, which has demonstrated that socially isolated animals exhibit exaggerated threat-responding, increased anxious behavior, and persistent fears. In particular, socially isolated animals exhibit augmented fear learning and delayed fear extinction compared to their non-isolated counterparts (Lukkes, Mokin, Scholl, & Forster, 2009; Naert, Callaerts-Vegh, & D'Hooge, 2011; Zelikowsky et al., 2018) as well as persistent fear responding that continues even after a threat is removed from their immediate environment (Zelikowsky et al., 2018).

Notably, social isolation is also a risk factor for the development of trauma. In a preclinical model of post-traumatic stress disorder in which animals who undergo an applied trauma (e.g., many unsignaled shocks in a short period of time) display PTSD-like effects (e.g., maladaptive fear learning: rapid, augmented fear learning that is extremely resistant to extinction: Rau, DeCola, & Fanselow, 2005; Long & Fanselow, 2012; Rajbhandari, Gonzalez, & Fanselow, 2018), animals who are pair-housed following the procedure exhibit a decreased tendency toward such PTSD-like effects (Zelikowsky & Fanselow, in prep; Berardi et al., 2014). In addition, social isolation plays a central role in bringing about PTSD-like effects in other preclinical models, either via social isolation alone (Borghans & Homberg, 2015; total social isolation:; Pibiri, Nelson, Guidotti, Costa, & Pinna, 2008; social instability caused by daily housing-partner changes:; Zoladz, Conrad, Fleshner, & Diamond, 2008) or in combination with other, unpredictable stressors (Algamal et al., 2021). Altogether, these effects suggest that social isolation may cause lasting changes to the fear learning system than can contribute to the development of dysfunctional fears or trauma-related behaviors.

Investigations of the effects of social disconnection in humans provides some insight into whether these effects translate from animal research. Specifically, poorer quality social bonds or self-reported loneliness are associated with both symptom occurrence and increased symptom progression in individuals who suffer from fear disorders such as anxiety (Hawkley & Cacioppo, 2010; Chou, Liang, & Sareen, 2011; Cacioppo, Cacioppo, Cole, Capitanio, & Goossens, 2015; Cacioppo, Grippo, London, Goossens, & Cacioppo, 2015; Cacioppo, Hughes, et al., 2006) and PTSD (Charuvastra & Cloitre, 2008; Freedman, Gilad, Ankri, Roziner, & Shalev, 2015; Kaniasty & Norris, 2008; Solomon, Dekel, & Mikulincer, 2008; Solomon, Waysmun, & Mikulincer, 1990), suggesting that these experiences of social disconnection, like social isolation in animals, may increase risk for dysfunctional fears and trauma. In addition to the discomfort and distress caused by these disorders, the effect of being socially disconnected has potentially life-threatening implications, as both loneliness and the occurrence of PTSD symptomology has been shown to be connected to suicidal ideation in active duty soldiers (Griffith, 2015) and combat veterans (Fanning & Pietrzak, 2013), suggesting that the contribution of loneliness to PTSD symptomology may increase thoughts of suicide.

Importantly, the impact of social bonds may not only influence the pathogenesis of fear disorders, but also their treatment. For example, higher quality social bonds and high levels of perceived social support are associated with greater reductions of symptoms following behavioral therapies for those with PTSD (Price, Gros, Strachan, Ruggiero, & Acierno, 2013; Price et al., 2018; Thrasher, Power, Morant, Marks, & Dalgeish, 2010) or anxiety (Dour et al., 2014; Lindfors, Ojanen, Jääskeläinen, & Knekt, 2014). In combination with the findings from the animal literature, this link between social disconnection and fear-disorder symptoms, both their occurrence and response to treatment, provides further evidence that feeling disconnected from others may impact the very systems by which fears are learned about and maintained.

However, no work to date has directly explored the effects of social disconnection on fear learning in humans. Thus, here we present three preliminary investigations from our group that suggest that feeling socially disconnected (e.g., lonely) impacts the fear learning process and leads to persistent fear. Importantly, we also present data suggesting methods to mitigate these effects. Although these investigations are preliminary, and thus do not have the necessary power to draw strong conclusions, the consistency of Results across all three studies provide an important starting place for a discussion of the effect of social disconnection on fear learning processes and long-term fear-symptoms. In the context of current world events, it is important to understand the potential impacts of COVID-19-induced social disconnection on how we learn about the daily threats we are faced with and how to approach the long-term fall-out of this altered learning moving forward.

1.1. Preliminary investigations

In a series of three separate preliminary investigations using Pavlovian fear conditioning methods in humans, we found evidence that individuals who report high levels of loneliness exhibit poorer extinction of fear. Interestingly, we also found that these effects are mitigated when extinction is conducted in the presence of social support reminders (*Studies 1 & 2)* or physically warm objects (*Study 3*).

2. Methods

2.1. Overview of experimental methods

All three preliminary investigations used data from separate studies, but all studies used similar methods. Differences across studies include whether a follow-up session to assess fear reinstatement was conducted and the types of stimuli used. These study-specific differences will be noted below as we discuss each distinct study.

Participants. All participants were recruited from the University of California, Los Angeles (UCLA). Participants were all over the age of 18, with no history of any mental health disorder diagnosis, and were compensated with either course credit or monetary payment. All participants provided informed consent and all study procedures were approved by the UCLA Institutional Review Board. Please see below for study-specific participant information.

Telephone Screening. Participants first completed a telephone screening during which it was assessed whether they were 18 years of age with no history of any diagnosed mental health disorder and/or were currently taking any mental-health-related medication.

Skin Conductance Response (SCR) Screening. Based on current recommendations (Lonsdorf et al., 2017), participants determined to be eligible following the telephone screening were asked to come into the lab to complete an in person screening to determine whether the experimental equipment could detect their SCR. SCR, an index of physiological arousal used in human fear conditioning experiments to assess conditional fear responding, was assessed by placing electrodes on the medial phalanges of the palmar side of the fore and middle fingers of participants' left hands and then instructing participants to take deep, evenly spaced breaths. This will activate the sympathetic nervous system and lead to consequent increases SCR, which was monitored by an experimenter to determine if these changes in SCR could be detected using the experimental equipment. Only participants whose SCR could be detected by the equipment were allowed to continue their participation in the experiment (this procedure has been used in earlier work from this group: Hornstein, Fanselow, & Eisenberger, 2016; Hornstein & Eisenberger, 2017; Hornstein, Haltom, Shirole, & Eisenberger, 2018; Hornstein, Fanselow, & Eisenberger, 2021; and other groups: Olsson et al., 2005; Phelps, Delgado, Nearing, & LeDoux, 2004; Schiller et al., 2010). All SCR was measured using a BioPac MP100 system with EDA

Isotonic Gel Electrodes, and data were collected and analyzed using AcqKnowledge 3.9 software (BioPac Systems, Inc., Aero Camino Goleta, CA, 93117).

Loneliness Assessment. For all studies, loneliness was assessed by placing participants into a 'high' or 'low' lonely group using scores from the UCLA Loneliness Scale v3 (Russell, 1996; collected during the SCR Screening Session), a self-report measure which assesses participants' perceptions of their relationships and the accessibility of close social bonds. High or low loneliness was assessed using cut-offs from previous work (Cole et al., 2015), and individuals were considered to be high lonely if their score was greater than or equal to 41 or low lonely if their score was less than 41.

Experimental Procedures. At the start of the experimental session, participants underwent a shock calibration procedure to determine the individual level of shock to be applied for that participant during the experiment. During the procedure, a 200 ms shock was applied via a shock electrode bar that was placed on participants' right wrists, with shocks beginning at 30 V and increasing in 5-V increments. Participants were instructed to alert the experimenter when the shock became "extremely uncomfortable, but not yet painful," and this level of shock was used throughout the experiment (a work-up procedure used by this group: Hornstein et al., 2016; Hornstein & Eisenberger, 2017; Hornstein et al., 2018; Hornstein et al., 2021; and other groups: Olsson et al., 2005; Phelps et al., 2004; Schiller et al., 2010). Average voltage used was 50.02 for *Study 1*, 47.03 for *Study 2*, and 51.33 V for *Study 3*). All shocks were delivered via a bar lead electrode placed on the right wrist, and was triggered from a SD9 Pulse Stimulator from Grass Technologies (Natus Neurology, Inc. – Grass Products, Middleton, WI, 53562).

Following the shock calibration procedures, participants underwent the experimental procedures. First, during a **Habituation** stage, participants viewed four presentations each of three neutral cues that would later be used as conditional stimuli (*Studies 1 & 3*: images of neutral objects; *Study 2:* colored shapes). All presentations here, and throughout the rest of the experimental procedures, were 6 s long followed by a 10 s long inter-trial-interval, and were made via E-Prime Professional 2.0. All presentations made during this stage were in the absence of shock, and SCR from this stage was used to assess whether there were any differences in responding to the neutral cues themselves that could account for later differences in SCR. We found that there was no significant differences in SCR to any of the neutral images during this stage in any of the three studies (p's > 0.05), indicating that any differences in SCR that occurred in later stages was due to learning that occurred during those stages.

Next, during an **Acquisition** stage, participants viewed four presentations each of the three neutral cues, two of which were consistently paired with a co-terminating 200 ms electric shock (CS + s) and one of which was never paired with shock (CS-). These repeated pairings were designed to generate learning that the CS + s predict shock, producing a conditional fear response, and that the CS- does not predict shock, producing no conditional fear response. The assignment of each neutral cue as a CS + or CS- was counterbalanced across participants. This was followed by an **Extinction** stage, during which participants saw 6 non-reinforced (no shock) presentations each of all cues, with the CS + s each co-presented with an added stimulus (please see below for study-specific added stimuli) and the CS- was presented alone, enabling us to assess whether conditional fear responding was reduced after CS + s were repeatedly presented in the absence of shock and in the presence of different types of stimuli. The added stimulus/CS + pairings were counterbalanced across participants. Directly following this was a **Test** stage, during which we evaluated the strength of fear extinction by examining whether fear that had been extinguished previously, returned when the added stimuli were removed and the CS + s were once again presented on their own four times each, and in the absence of shock (return of fear). Finally, 24-h post-extinction there was a **Fear Reinstatement** stage (*Studies 1 & 2* only), during which the strength of fear extinction was evaluated using a fear reinstatement procedure (Rescorla & Heth, 1975). Participants first received 3 unsignaled 200 ms shocks and then viewed 3 non-reinforced presentations of each CS+ and the CS-. This test brings the aversiveness of shock to awareness and creates the conditions under which return of the conditional fear response is likely to occur (fear reinstatement). At no point in the procedures were participants informed of which images would be paired with shock (CS + s) or not paired with shock (CS-s), but were simply informed to "pay attention to which images are paired with shock during the procedures."

2.2. Data analyses

Data exclusion and analysis were similar for all three studies, so here we will describe these strategies.

Data Exclusion. In all studies, we first ensured that participants had acquired conditional fear responses to each CS+ during the acquisition stage by evaluating whether SCR for both CS + s was greater than SCR for the CS- for each participant (using SCR from the final 50% of the trials of the acquisition stage). If a participant did not have greater SCR for both CS + s compared to the CS-, their data was excluded from analysis. This acquisition of fear was necessary in order for us to evaluate the strength of fear extinction as well as the impact of the added stimuli on fear extinction. Please see below for study-specific exclusion based on this criterion.

Additionally, participants were assessed for being low responders. Specifically, if participants did not exhibit an SCR response on at least 25% of the trials during the acquisition stage (during which they knew to expect shock and did experience shock), they were excluded from further analysis. This was done because it could not be determined if these low responders were not exhibiting SCR because they did not acquire conditional fear or because of other factors (e.g., the equipment did not adequately pick up their responses or the shock was not aversive enough to bring about fear learning). Please see below for study-specific exclusion based on this criterion.

Data Pre-Processing. Data were pre-processed using AcqKnowledge 3.9 software. All data were pre-processed using a low-pass filter and smoothed, to reduce noise, and then were evaluated using a peak-to-peak analysis for each trial. Specifically, the first peak that occurred between .5s and 4.5s after an image was presented was measured as the response to that image, with peak-to-peak amplitude being measured in micro-siemens (μS). These procedures were determined based on current SCR analysis recommendations (see: Figner & Murphy, 2011; Lonsdorf et al., 2017). Finally, here we used the standard procedure of applying a square-root transformation to all SCR measurements (the use of which was decided a priori and has been applied in previous work by this group: Hornstein et al., 2016; Hornstein & Eisenberger, 2017; Hornstein et al., 2018; Hornstein et al., 2021). This is done to account for skew that is typically present in SCR data due to zero-response trials (trials on which no peak-to-peak measurement is detected or peak-to-peak measurements occur that are too low in magnitude to be interpreted as a response, please see further description below) (Figner & Murphy, 2011; Lonsdorf et al., 2017).

Trials were considered to be zero-response trials or were excluded from analysis under the following conditions. First, if there was no peak (no rise in SCR) within the .5s–4.5s window following the beginning of the image presentation, the trial was scored as a zero-response trial, as responses outside this window cannot definitively be attributed to the image being presented. Additionally, if measured peak-to-peak amplitude did not meet a 0.02 μS threshold, the trial was scored as a zero-response trial, as amplitudes this low cannot be definitively distinguished from noise. Lastly, if participants moved during a trial, as recorded by the experimenter during the experimental procedures, the trial was excluded from data analysis, as SCR during that trial could be due to either conditional fear responding or the movement itself. These SCR inclusion criteria were based on inclusion criteria from previous human fear conditioning work by this group (Hornstein et al., 2016; Hornstein & Eisenberger, 2017; Hornstein et al., 2018; Hornstein et al.,

2021) and others (Olsson et al., 2005; Phelps et al., 2004; Schiller et al., 2010).

Statistical Methods. In order to assess the strength of fear extinction, we evaluated whether previously extinguished conditional fears returned under the conditions most likely to bring about this return for each study: either during fear reinstatement (*Studies 1 & 2*) or a test designed to assess return of fear (*Study 3*). Using the first trial of the relevant stage for each study—the first presentation of each CS + or CS- during this stage, before any further fear extinction or learning was able to occur—we compared mean SCR in response to each CS + to that of the CS- within participants. If mean SCR for a CS+ was marginally or significantly higher than that of a CS-, this was interpreted to mean that a fear response was present and that fear extinction was not retained over time. Although the low sample sizes in these preliminary investigations limits the ability to reach significance or fully interpret these Results, it is notable that even with these small sample sizes, the trend of the results across studies is remarkably consistent.

Additionally, we conducted 2 × 2 mixed ANOVAs comparing the effect of loneliness group (high lonely, low lonely) and pairing condition (social support, safety signal: mean SCR difference scores (CS + - CS-) were used during this test to evaluate conditional fear responses to account for differences in baseline SCR across participants) in order to assess any interaction of loneliness group on learning. Because of the low sample sizes in these preliminary investigations, regardless of whether this ANOVA was significant, we conducted post-hoc tests targeted at examining differences in learning across groups, across conditions, and across groups within conditions. All marginal or significant Results are reported below.

We also conducted an investigation of the effects of loneliness as a continuous variable on fear extinction. To do this, we assessed the relationship between scores on the UCLA Loneliness Scale (v3) and conditional fear responding at either fear reinstatement (*Studies 1 & 2*) or test (*Study 3*). These analyses revealed no significant Results (p's > 0.1), perhaps due to the low sample sizes in these studies. Although loneliness scores were normally distributed in each study, there may have been insufficient numbers of conditional fear responses across the range of loneliness scores to adequately evaluate the effects of loneliness as a continuous variable.

2.3. Study 1

Using data from a study designed to assess whether the presence of images of social support figures during fear extinction leads to enhanced retention of fear extinction (indicated by reduced fear reinstatement: Hornstein et al., 2018), we investigated whether high and low lonely individuals showed different patterns of extinction by examining fear reinstatement.

Participants. Data from 30 participants was included in final data analyses (mean age = 20.2; 22 females; 36.7% Hispanic/Latinx; 33.3% Asian/Asian American; 26.7% Caucasian; and 3.3% African American). Sixty-three participants were enrolled, but a total of 33 participants who passed the telephone and SCR screening were excluded from final data analysis, 13 due to technical failure (no SCR was recorded), 10 were low responders, 8 did not acquire conditional fear to both CS + s, and 2 dropped out. After evaluating the loneliness assessment, participants were sorted into high or low lonely groups ($n_{\text{High Lonely}} = 13$, $n_{\text{Low Lonely}} = 17$) for further analysis.

Methods. All methods for this study are as described above in the overview, with the following specification. During the extinction stage, each CS+ was paired with either an image of a social support figure (social support paired condition: image provided by the participant) or an image of a stranger (stranger paired control condition: image selected so that stranger was gender, age, and ethnicity matched to social support figure image provided). The social support figures in the social support images were selected by participants as individuals who "provided them the most support on daily basis" and were rated as highly supportive on a scale of 1 (not at all supportive) - 10 (extremely supportive) (mean social support rating = 8.77).

It should be noted that while it may seem unlikely that high lonely participants would have a strong social support figure, loneliness occurs because of the disparity between one's desired level of social connection and one's perceived level of social connection (Weiss, 1973; Cacioppo et al., 2003)—thus, lonely individuals are not necessarily devoid of *any* close social bonds, but instead do not perceive the bonds they do have to be satisfactory. Therefore, individuals who score high in loneliness are still likely to be able to identify one close social support figure (as was found with the participants here and in *Study 2*).

Results. Here, to investigate the effects of loneliness on fear learning, we focused on SCR from the stranger paired control condition, which would not be expected to influence fear learning outcomes based on our previous work (Hornstein et al., 2016; Hornstein et al., 2018). To assess the retention of fear extinction, we evaluated SCR from the fear reinstatement stage and found that marginal conditional fear responding occurred in the stranger paired control condition (t (12) = 1.940, p = .076, Cohen's $d = 0.54$) in the high lonely group, suggesting fear reinstatement occurred in this group, but not in the low lonely group (t (16) = 1.469, p = .161, Cohen's $d = 0.36$), suggesting no fear reinstatement occurred in this group.

While the findings from the social support paired condition of this study cannot provide further insight into the effects of loneliness itself on fear learning, they do provide insight into whether social support, which has been shown to reduce fear acquisition (Hornstein & Eisenberger, 2017; Toumbelekis, Liddell, & Bryant, 2018) and improve fear extinction in those who are not specifically lonely (Hornstein et al., 2016; Hornstein et al., 2018; Toumbelekis, Liddell, & Bryant, 2021), is similarly able to improve fear extinction in those who are lonely. Thus, we next examined the effects of the social support paired condition in order to understand whether social support might ameliorate the effect of loneliness on fear learning. Interestingly, no significant or marginal conditional fear responding was detected in either group in the social support paired condition (high lonely t (12) = 0.933, p = .369, Cohen's $d = 0.26$; low lonely t (16) = 0.696, p = .497, Cohen's $d = 0.17$: see Fig. 1), suggesting that fear reinstatement did not occur in either group and that reminders of social support improved extinction in the high

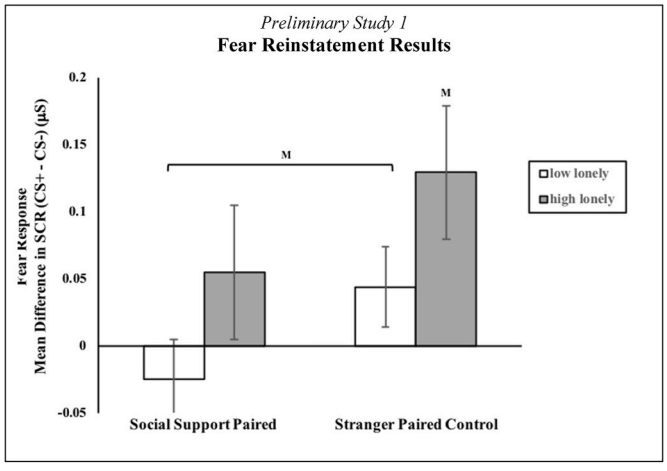

Fig. 1. Results from the fear reinstatement stage of *Study 1*. All SCR measurements are presented post-square-root-transformation and are reported in micro-siemens (μS). All error bars indicate standard error. "M" indicates a marginally significant difference score or comparison (p < .1). Results show that for high lonely individuals, fear reinstatement occurred in the stranger paired control condition, but not in the social support figure paired condition. No fear reinstatement occurred for low lonely individuals in either condition. Additionally, conditional fear responding was marginally lower in the social support paired condition compared to the stranger condition in low lonely individuals.

lonely group, leading their levels of fear reinstatement to mirror those in the low lonely group.

Finally, we examined whether there was an interaction of pairing condition (social support paired or stranger paired) and loneliness group (high or low lonely) on fear learning. We found a marginal effect of pairing condition (F (1, 28) = 3.662, p = .066, η_p^2 = 0.116, Cohen's f = 0.36), such that there was higher conditional fear responding in the stranger condition, but no interaction (F (1,28) = 0.006, p = .941, η_p^2 = 0.00, Cohen's f = 0.01), suggesting that both loneliness groups benefitted similarly from the social support paired condition.

2.4. Study 2

Using data from a study designed to directly compare the effects of the presence of images of social support figures vs. learned safety signals (colored shapes previously trained to be associated with the absence of shock) on fear extinction (Hornstein, Craske, Fanselow, & Eisenberger, *in prep*), we examined whether high and low lonely individuals exhibited different patterns of fear extinction by examining fear reinstatement.

Participants. Data from 32 participants was included in final data analyses (mean age = 20.5; 26 females; 50% Asian/Asian American; 34.4% Caucasian; 33.3%; and 9.4% Hispanic/Latinx). Sixty-two participants were enrolled, but a total of 30 participants who passed the telephone and SCR screening were excluded from final data analysis, 11 did not acquire conditional fear to both CS + s, 8 were low responders, 2 did not acquire safety learning to the pre-trained safety stimulus, and 2 were dropped due to technical failure (no SCR was recorded), and 7 dropped out. After evaluating the loneliness assessment, participants were sorted into high or low lonely groups ($n_{\text{High Lonely}} = 15$, $n_{\text{Low Lonely}} = 17$) for further analysis.

Methods. All methods for this study are described above in the overview, with the following specification. During the extinction stage, each CS+ was paired with either an image of a social support figure (social support paired condition: as described above, mean social support rating = 9.22) or a learned safety signal (safety signal paired condition: a colored-shape cue pre-trained earlier in the experimental session to signal the absence of shock when present).

Results. To investigate the effects of loneliness on fear learning, we examined SCR from the safety signal paired control condition. We found that a significant conditional fear response was measured in the safety signal paired condition in the high lonely group (t (14) = 3.413, p = .004, Cohen's d = 0.88), suggesting that fear reinstatement occurred in this group, but not in the low lonely group (t (16) = 0.465, p = .648, Cohen's d = 0.11), suggesting no fear reinstatement occurred in this group.

Additionally, as in *Study 1*, we investigated whether social support influences fear extinction outcomes in those who are lonely, as it does in those who are not specifically lonely (Hornstein et al., 2016; Hornstein et al., 2018; Toumbelekis et al., 2021). Mirroring the findings from *Study 1*, there was no significant or marginal conditional fear responding in either group in the social support paired condition (high lonely t (14) = 0.365, p = .720, Cohen's d = 0.09; low lonely t (16) = 0.051, p = .960, Cohen's d = 0.01: see Fig. 2), suggesting that fear reinstatement did not occur in either group and that once again the presence of the social support figure image mitigated the effects of loneliness on fear extinction.

Further investigations examined whether there was an interaction of pairing condition and loneliness group on fear learning, with a 2 × 2 mixed ANOVA (pairing condition x loneliness group) revealing a significant effect of pairing condition (F (1,30) = 5.752, p = 023, η_p^2 = 0.161, Cohen's f = 0.44), such that there was higher conditional fear responding in the safety signal condition, and a marginally significant interaction (F (1,30) = 3.445, p = .073, η_p^2 = 0.103, Cohen's f = 0.34). Post-hoc paired-samples t-tests revealed that in the high lonely group, there was significantly lower conditional fear responding in the social support paired condition compared to the safety signal paired condition (t (14) = 2.852, p = .013, Cohen's d = 0.74), indicating that no fear reinstatement occurred and that social support enhanced extinction in high lonely individuals. However, there was no difference across pairing conditions in the low lonely group (t (16) = 0.405, p = .691, Cohen's d = 0.10) or across loneliness groups in either pairing condition (stranger condition t (28) = 1.267, p = .216, Cohen's d = 0.45; social support condition t (28) = 1.216, p = .234, Cohen's d = 0.44), suggesting that, among those in the high lonely group, social support normalized extinction outcomes to be similar to those in the low lonely group.

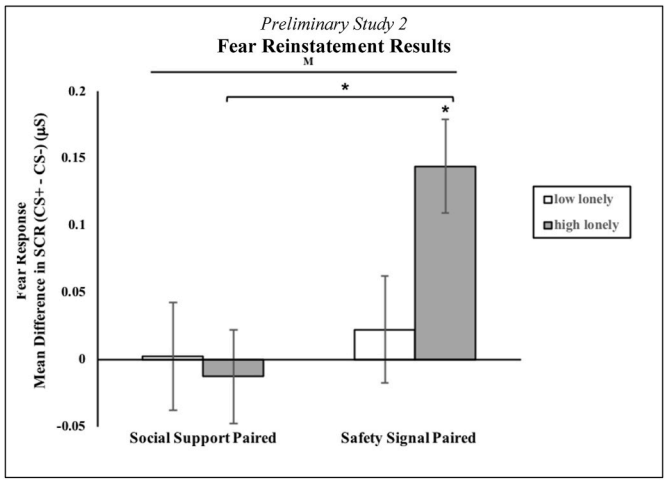

Fig. 2. Results from the fear reinstatement stage of *Study 2*. All error bars indicate standard error. All SCR measurements are presented post-square-root-transformation and are reported in micro-siemens (μS). Asterisks indicates a significant difference score, interaction, or comparison ($p < .05$) and "M" indicates a marginally significant difference score or comparison ($p < .1$). As with *Study 1*, results show that for high lonely individuals, fear reinstatement occurred in the stranger paired control condition, but not in the social support figure paired condition and no fear reinstatement occurred for low lonely individuals in either condition. Additionally, there was a marginally significant interaction of pairing condition by loneliness group, with high lonely individuals showing marginally higher conditional fear responding in the safety signal paired condition compared to low lonely individuals in the safety signal paired condition. Finally, in high lonely individuals, conditional fear responding in the safety signal paired condition was significantly higher than in the social support paired condition, indicating less fear reinstatement in this condition.

Altogether, these Results are consistent with *Study 1*, showing higher levels of fear reinstatement in high lonely individuals, suggesting that extinction learning is not retained over time for lonely individuals, and that these effects are reduced when extinction is conducted in the presence of social support cues.

2.5. Study 3

Using data from a study designed to examine whether physical warmth, which has been shown to share overlap with experiences social connection on both the behavioral and neural level (Inagaki & Eisenberger, 2013), has the same effects on fear learning as images of social support figures (retarding the acquisition of new fears, inhibiting the conditional fear response, and enhancing fear extinction: Hornstein et al., 2021), we investigated whether high and low lonely individuals showed different patterns of fear extinction by examining return-of-fear during the test stage.

Participants. Data from 30 participants was included in final data analyses (mean age = 20.6; 22 females; 47% Caucasian; 27% Asian/Asian American; 23% Hispanic/Latinx; 3% African/African American). Forty-five participants were enrolled, but a total of 15 participants who passed the telephone and SCR screening were excluded from final data

analysis, 9 did not acquire conditional fear to both CS + s, 2 were low responders, 2 dropped out, and 2 were dropped due to technical failure (no SCR was recorded). After evaluating the loneliness assessment, participants were sorted into high or low lonely groups ($n_{High\ Lonely} = 13$, $n_{Low\ Lonely} = 17$) for further analysis.

Methods. All methods for this study are described above in the overview, with the following specifications. During the extinction stage, each CS+ was paired with a tactile stimulus that was placed in the participant's right hand as the CS + came on the screen: either a physically warm object (warmth paired condition: an activated, one-time-use warm pack) or a neutral object (neutral object paired control condition: a rubber ball roughly the same weight as the warm pack).

Results. In order to investigate the effects of loneliness on fear extinction, here we examined SCR from the neutral object paired control condition, which was expected to have no impact on extinction processes due to the neutral and non-valenced characteristics of the rubber ball. In line with *Studies 1 & 2*, in the neutral object paired control condition, we found significant conditional fear responding in the high lonely group (: $t(12) = 2.685$, $p = .02$, Cohen's $d = 0.74$), suggesting that return of fear occurred in this group, and none in the low lonely group ($t(16) = 1.041$, $p = .313$, Cohen's $d = 0.25$), suggesting that no return of fear occurred in this condition. As with *Studies 1 & 2*, this pattern of results indicates that high lonely individuals had poorer extinction of fear (see Fig. 3).

As with investigations of the social support paired conditions in *Studies 1 & 2*, here we investigated the effects of the warmth paired condition to evaluate whether physical warmth, which shares overlap with experiences of social connection (Inagaki & Eisenberger, 2013) and has also been shown to improve fear extinction in those who are not specifically lonely (Hornstein et al., 2021), influences fear extinction in those who are lonely. These investigations showed that there was no significant or marginal conditional fear responding in either group in the warmth paired condition (high lonely $t(12) = 0.472$, $p = .645$, Cohen's $d = 0.13$; low lonely $t(16) = 0.673$, $p = .511$, Cohen's $d = 0.16$), suggesting that return of fear did not occur for either group. This pattern of findings was similar to what was observed in *Studies 1 & 2* in the presence of the social support figures, suggesting that physical warmth may also mitigate the effects of loneliness on fear learning. This is notable, for while many individuals who are lonely are still able to identify at least one close, supportive other, some may have difficulty doing so—rendering warmth a useful alternative to enhance extinction processes.

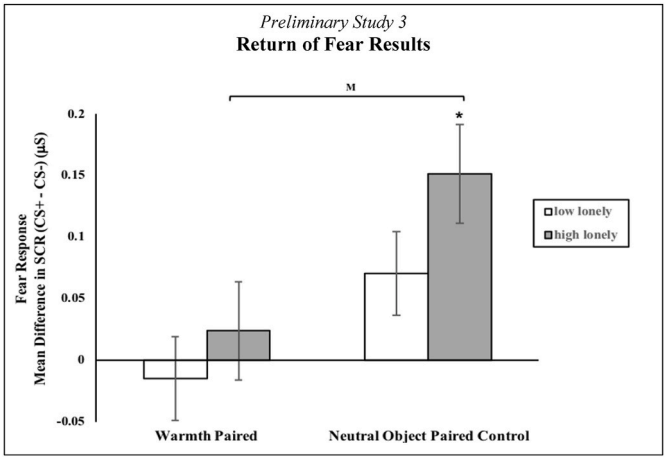

Fig. 3. Results from the test stage of *Study 3*. All error bars indicate standard error. All SCR measurements are presented post-square-root-transformation and are reported in micro-siemens (μS). Asterisk indicates a significant difference score ($p < .05$). Results show that for high lonely individuals, return of fear occurred in the neutral object paired control condition, but not in physical warmth paired condition. No return of fear occurred for low lonely individuals in either condition. Additionally, in high lonely individuals there was marginally less conditional fear responding in the warmth paired condition compared to the neutral object paired condition.

Finally, we investigated whether there was an interaction of pairing condition and loneliness group on fear learning. Results showed an almost significant effect of pairing condition, ($F(1,30) = 4.158$, $p = .051$, $\eta_p^2 = 0.129$, Cohen's $f = 0.38$), such that there was higher conditional fear responding in the neutral object condition, but no interaction ($F(1,28) = 0.142$, $p = .709$ $\eta_p^2 = 0.005$, Cohen's $f = 0.07$), suggesting that physical warmth benefitted both the high low lonely groups similarly.

2.6. Meta-analytic integration

Because these preliminary investigations included smaller sample sizes, we used *Meta-Essentials version 1.5* (Suurmond, van Rhee, & Hak, 2017; Van Rhee, Suurmond, & Hak, 2015) to conduct several random-effects meta-analyses to examine the overall effects of loneliness on fear extinction in high and low lonely participants, as well as across groups. Specifically, we examined the strength of fear extinction, assessed via levels of fear reinstatement (*Studies 1 & 2*) or return of fear (*Study 3*) in high and low lonely groups in both the control (*Study 1*: stranger image; *Study 2*: safety signal, *Study 3*: neutral object) or intervention (*Studies 1 & 2*: social support figure image; *Study 3*: warm object) conditions. Additionally, we assessed differences in strength of fear extinction across the control and intervention conditions for both high and low lonely groups.

In line with the separate preliminary investigations, in the control conditions, conditional fear responding occurred to a larger degree in high lonely individuals, Hedge's $g = 0.72$, $z = 8.11$, $p < .001$, 95% CI [0.34,1.10], suggesting fear reinstatement or return of fear occurred in this group, and to a smaller degree in low lonely individuals, Hedge's $g = .26$, $z = 4.87$, $p < .001$, 95% CI [0.03, 0.50] (while none occurred in either group in the intervention condition: Hedge's gs < 0.26, all 95% CIs included 0),. Additionally, poorer fear extinction occurred in high lonely compared to low lonely individuals in the control condition, indicated by conditional fear responding, Hedge's $g = 0.53$, $z = 8.10$, $p < .001$, 95% CI [0.25, 0.81], suggesting that greater fear reinstatement or return of fear occurred and that fear extinction is impaired by loneliness. Importantly, in high lonely individuals, fear extinction was marginally improved (less fear reinstatement or return of fear) in the intervention conditions in which conditional fear responding was lower compared to the control conditions, Hedge's $g = 0.49$, $z = 4.08$, $p < .001$, 95% CI [-0.03, 1.02], suggesting that interventions designed to increase feelings of social connectedness may reduce or offset these extinction-impairing effects of being lonely.

3. Summary

Although preliminary, these investigations indicate that lonely individuals exhibit poorer extinction of fear, mirroring findings from the animal literature (Lukkes et al., 2009; Naert et al., 2011; Zelikowsky et al., 2018). Notably, these investigations also indicate that images of social support figures or physically warm objects mitigate these effects. It is possible that the presence of these cues during fear extinction reduces participants' acute experiences of loneliness, reminding them of social bonds they do have. Indeed, although loneliness is defined as the perception of social isolation (Weiss, 1973), lonely individuals are not necessarily socially isolated—just perceive themselves to be. Thus, reminders of social support figures (via images) or the experience of physical warmth (which has been shown to be a critical component in feelings of social connectedness: Williams & Bargh, 2008; Bargh & Shalev, 2012; Inagaki & Eisenberger, 2013), may reduce these perceptions of being socially disconnected in the moment. However, given that viewing images of or thinking about social support figures (Hornstein

et al., 2016; Hornstein et al., 2018; Hornstein et al., in prep; Toumbelekis et al., 2021) and holding physically warm objects (Hornstein et al., 2021) have been shown to bring about enhanced extinction in populations that were not specifically lonely, it is also possible that these cues may counteract the effects of loneliness simply by enhancing extinction processes and not by reducing loneliness itself.

Additional work is required not only to test these effects in a well-powered sample, but also to investigate whether the impaired extinction in high lonely individuals demonstrated here is a result of more robust fear acquisition or weaker fear extinction, although the ability of images of social support figures (*Studies 1 & 2*) or physical warm stimuli (*Study 3*) to mitigate these effects when present during extinction procedures suggests that it is during this stage of the learning processes that loneliness may be impacting fear learning outcomes.

4. Discussion

One unfortunate consequence of the necessary measures taken to combat the COVID-19 pandemic has been the creation of circumstances that foster feelings of social disconnection. Whether under strict stay-at-home orders, practicing social distancing, or simply having diminished contact with others due to remote work, reduced travel, or local closures, individuals have been living in conditions that foster feelings of loneliness and social isolation for almost the past two years. In combination with the very real threats to health and well-being brought about by this pandemic, these increased levels of social disconnectedness may be especially harmful, leading to maladaptive and dysfunction fears.

Although animal research sheds light on the impact of social isolation on fear learning, and human research provides evidence of the impact of loneliness and poor quality social bonds on fear-disorder symptomology, no work has directly examined whether the relationship between social disconnection and fear disorders might be driven by changes in fear learning itself. In light of current events, insight into this question is crucial in order to better understand how and when it might be possible to mitigate the effects of COVID-19-induced social disconnection on the development of trauma or lasting dysfunctional fears.

Thus, here we present Results from three preliminary investigations which demonstrate that loneliness leads to poorer extinction of conditional fears. While these results must be interpreted with caution, as these investigations are preliminary and thus underpowered, they are consistent across all three studies and are in-line with the animal literature, which shows that animals in social isolation exhibit increased anxious behavior, poorer fear extinction, and persistent fear responding (Lukkes et al., 2009; Naert et al., 2011; Zelikowsky et al., 2018). Furthermore, they complement the human literature, which shows social disconnection to be related to occurrence and persistence of disordered-fear symptoms in individuals with anxiety and PTSD (Hawkley & Cacioppo, 2010; Chou et al., 2011; Cacioppo, Cacioppo, Cole, Capitanio, & Goossens, 2015; Cacioppo, Grippo, et al., 2015; Cacioppo, Hughes, et al., 2006; Solomon, Waysmun, & Mikulincer, 1990; Charuvastra & Cloitre, 2008; Kaniasty & Norris, 2008; Solomon et al., 2008; Freedman et al., 2015), suggesting that social disconnectedness may contribute to symptomology via learning processes. Importantly, in addition to shedding light on a potential link between social disconnection and fear-disorder outcomes, these preliminary investigations also reveal potential methods to mitigate these effects. The presence of stimuli that directly remind individuals of close social bonds (e.g., images of social support figures) or that play a role in social connection processes (e.g., physically warm objects) were shown to enhance fear extinction in high lonely individuals, returning levels of fear extinction to those exhibited by low lonely individuals.

Although they are preliminary in nature and future investigation is needed, the findings discussed in this manuscript are notable, not only for the window they provide into the relationship between social disconnection and fear, but also because of their implications for treatment. Indeed, as mentioned above, individuals with anxiety or PTSD who are also high in loneliness or who report poor quality social bonds have poorer treatment outcomes (Price et al., 2013; Price et al., 2018; Thrasher, Power, Morant, Marks, & Dalgeish, 2010; Dour et al., 2014; Lindfors et al., 2014). To date, the most effective treatment for these fear disorders are exposure therapies, during which individuals are repeatedly presented with cues or situations that trigger their dysfunctional fears (Craske, Hermans, & Vervliet, 2018). These therapeutic procedures are based on fear extinction processes, during which the repeated presentation of a fearful cue or context in the absence of an aversive outcome leads to new learning that these cues or contexts do not always predict threat (Bouton, 2004). Therefore, by impacting fear extinction processes, feelings of social disconnection may be undermining these treatment procedures and the application of social support reminders may be mitigating these effects.

While there is mixed evidence for whether occurrence of loneliness changed during the COVID-19 pandemic, with some literature demonstrating an increase (Ausín et al., 2021; Holaday et al., 2022; Elran-Barak & Mozeikov, 2020) and some demonstrating no change (Luchetti et al., 2020; McGinty, Presskreischer, Han, & Barry, 2020; Latikka, Koivula, Oksa, Savela, & Oksanen, 2022), examinations have shown that certain groups, including women, those living alone, and those who are younger, were all at higher risk of increased loneliness during COVID-19 (Bu, Steptoe, & Fancourt, 2020; Li & Wang, 2020) as well as increased risk of psychiatric disorder (Li & Wang, 2020). Importantly, work has also revealed that loneliness was linked to greater increases in psychological distress and anxiety during the pandemic, especially in these groups (Latikka et al., 2022; McDonald et al., 2022). Thus, members of these groups, as well as individuals who were already lonely, may have been at higher risk for developing disordered-fear or trauma during COVID-19 and may also especially benefit from the addition of social support reminders to procedures designed to reduce fear symptoms. As we develop systems to address future surges of COVID-19 or other pandemics that may occur, understanding of these issues will provide insight into targeted methods to reduce fear symptoms and for whom they will be most beneficial.

There are several limitations of the current work, the most important of which are the low sample sizes used in each of these three studies and the fact that they were not designed to specifically look at the effects of loneliness on fear acquisition or extinction. Because of this, none of the studies included an alone (in the absence of any added stimuli) extinction condition and, in all studies, participants were required to acquire fear in order to be included in data analysis, and thus it was also not possible to assess the effects of loneliness on fear acquisition. Additionally, this work was focused entirely on the effects of loneliness—not objective social isolation or poor quality social networks and bonds—leaving questions as to whether these other types of social disconnection experiences would bring about similar effects. These limitations must be addressed in future work.

Due to the emerging nature of this area of inquiry, there are many next steps that are required, but here we outline three that we believe are the most pressing. The most important next step is to examine the effect of loneliness on fear extinction outcomes using a larger sample size, to determine if the effects demonstrated here also occur in a well-powered investigation. In addition to this, future studies should augment fear acquisition by increasing the number of trials used during fear acquisition procedures. This will not only reduce the number of participants excluded due to not acquiring fear associations for both CS + s, but will also provide conditions under which it possible to assess whether loneliness influences fear acquisition outcomes as well as fear extinction outcomes. Finally, future examinations should not only augment acquisition procedures, as described above, but also conduct fear extinction procedures in the absence of other stimuli. Additionally, the inclusion of measures to reduce acute loneliness during acquisition instead of during extinction, may help to provide clearer data from which to parse apart whether the effects of loneliness demonstrated in this preliminary work are a result of acquired fears that are more

persistent (i.e., less able to be extinguished) or weaker fear extinction learning. Specifically, by comparing extinction outcomes in lonely individuals who previously acquired fears when in an acute state of high or low loneliness (i.e., in the presence of a social support reminder vs alone), it will be possible to assess the effects of loneliness on persistence of acquired fears**.** However, despite these needed steps, the consistency of the Results across these three preliminary investigations suggests that the demonstrated effects of loneliness on fear extinction are reliable.

Although only one amongst many extreme impacts of the COVID-19 pandemic, the abrupt shift into a state of social disconnection experienced by many individuals as they took measures to prevent the spread of the virus nevertheless requires consideration. Indeed, in the case of COVID-19-induced social disconnection, the combination of increased environmental threats and increased feelings of loneliness may have created potent conditions under which dysfunctional fear or trauma is likely to occur. Although the outcomes of this combination of events can only be begun to be examined, the initiation of a discussion regarding what we know from previous literature and implications from preliminary findings is crucial as we move forward. This dialogue has the potential to guide understanding of how to approach understanding of disordered fear and trauma resulting from during the pandemic as well as potential methods to boost current treatments that might be especially effective for those experiencing COVID-19-induced social disconnection.

CRediT authorship contribution statement

Erica A. Hornstein: Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review & editing, Supervision, Project administration. **Naomi I. Eisenberger:** Conceptualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

Drs. Hornstein & Eisenberger have no financial disclosures or conflicts of interest to declare.

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