

# The contagion of social defeat stress: Insights from rodent studies

Luca Carnevali<sup>a</sup>, Nicola Montano<sup>b,c</sup>, Eleonora Tobaldini<sup>b,c</sup>, Julian F Thayer<sup>d</sup>, Andrea Sgoifo<sup>a</sup>

<sup>a</sup> Stress Physiology Lab, Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Parma, Italy

<sup>b</sup> Department of Internal Medicine, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy

<sup>c</sup> Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy

<sup>d</sup> Department of Psychological Science, The University of California, Irvine, Irvine, CA, USA.

**Corresponding author:** Luca Carnevali, Stress Physiology Lab, Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Parco Area delle Scienze 11/A, 43124, Parma, Italy. Email address: [luca.carnevali@unipr.it](mailto:luca.carnevali@unipr.it)

## **Abstract**

Stressful experiences can be transmitted among individuals through social interactions. Like humans, rodents are social creatures whose behavior and physiology can be influenced by the emotional state of fellow rodents. This paper will review rodent studies which have explored two conditions of potential social stress contagion using the social defeat paradigm. In the vicarious social defeat model, mice and rats that witness a conspecific being socially defeated exhibit physiological stress responses and develop a host of depressive- and anxiety-like behavioral deficits. Likewise, social interaction with a stressed partner in the aftermath of social defeat stress results in physiological stress responses and social avoidance behavior. After summarizing the existing literature on this newly emerging area of social defeat stress contagion in rodents, we will discuss the potential utility of these rodent models for investigating the neurobiological processes and sensory channels of information that allow for the spread of psychophysiological effects of stress across individuals.

## 1. Introduction

Emotional contagion, a term coined by psychology professor Elaine Hatfield (Hatfield et al., 1993), has been construed as a simple or automatic process in which one simply “catches” aspects of another person’s emotional state, producing similar affective and physiological responses that result directly from the observation (Hatfield et al., 1993; Hoffman, 2000). Findings of brain regions with mirror properties that are active when individuals perform an action as well as when they observe others perform the same or similar actions have fueled speculations about neural mechanisms underlying the social sharing of emotions (Ferrari and Rizzolatti, 2014; Iacoboni et al., 1999). Specifically, within the social domain, mirroring would occur when the same neurons are activated by emotions experienced directly and by observing/interacting with others who are experiencing emotions (Carr et al., 2003; Rizzolatti et al., 2001; Wicker et al., 2001). Emotional contagion, also known as the “resonance” of emotions among individuals, may form the basis - together with more complex processes - for a full capacity for empathy (Preston and de Waal, 2002). Such capacity has been long considered uniquely human. However, studies in nonhuman primates (e.g., Palagi et al., 2014), pigs (e.g., Reimert et al., 2013), dogs (e.g., Huber et al., 2017) and rodents (e.g., Atsak et al., 2011) have shown that emotional contagion exists across species, does not require advanced cognitive capabilities, and is crucial to successfully navigate the social environment (Decety and Lamm, 2009; Panksepp and Panksepp, 2013). Recent years have witnessed growing interest in the study of “empathic stress” or “stress contagion” or “stress resonance”, as it has been variably called in human studies (Engert et al., 2019; White and Buchanan, 2016). Indeed, stress often occurs in social settings and can be transmitted among individuals as a consequence of social interactions in dyads and groups. Such “contagious stress” may induce emotional and physiological responses also in those who are not directly exposed to the stressor and may ultimately represent an additional pathway to the deleterious mental and physical consequences associated with stress exposure, beyond the daily stressors experienced firsthand. Therefore, in this paper, the term “contagious

28 stress” or “stress contagion” refers to the presence of behavioral (e.g., anxiety-like  
29 symptoms) and/or physiological (e.g., hypothalamic-pituitary-adrenal (HPA) axis activation)  
30 sequelae of stress exposure also in those individuals who are not directly exposed to the  
31 stressor. Specifically, we focus on two conditions of potential contagion that are both based  
32 on experiences of traumatic and stressful events but are conceptually distinct and empirically  
33 separable. One condition is the vicarious experience of traumatic life events. For example,  
34 several lines of evidence demonstrate that post-traumatic stress disorders (PTSD) can be  
35 triggered not only in people who directly experience traumatic events, but also in those who  
36 witness them (Blanchard et al., 2004; Perlman et al., 2011; van Wingen et al., 2011).  
37 Moreover, recent human studies have demonstrated similar physiological stress responses  
38 between an observer and a target undergoing a stressful challenge (e.g., Engert et al., 2014;  
39 Dimitroff et al., 2017). Another condition that can occur as part of the broader process of  
40 stress contagion is the response of an individual to the aftermath of stress of a social  
41 partner, a phenomenon often referred to as “stress crossover” (Wethington, 2000). For  
42 example, in a human study mothers were exposed to a social stressor in a separate room  
43 from their babies. Upon their reunion with their stressed mothers, babies showed increased  
44 heart rate and social avoidance compared to babies in a control condition (Waters et al.,  
45 2014), suggesting that mothers’ stressful experiences were contagious to their infants in the  
46 aftermath of actual exposure. Moreover, studies have shown that stress-related depression  
47 in family or friends may increase the likelihood that a person will exhibit depressive  
48 behaviors later in life (Bastiampillai et al., 2013; Joiner, 1994). Like humans, rodents are  
49 highly social animals whose behaviors and physiology can be influenced by the emotional  
50 state of fellow rodents. Such responses are thought to be adaptive for group survival; the  
51 observation of one individual under stress may indicate a threat, so other rodents may  
52 benefit from noticing and responding appropriately (Meyza et al., 2017; Meyza and Knapska,  
53 2018; Panksepp and Lahvis, 2011). However, prolonged or repeated emotional and  
54 physiological attunement to a stressed social partner may become maladaptive. The  
55 purpose of this paper is to review rodent studies which have explored the consequences of

56 vicarious social stress and social stress crossover using the social defeat paradigm, one of  
57 the most robust model of PTSD, depression, and other stress-related illnesses (Carnevali et  
58 al., 2017b; Hollis and Kabbaj, 2014; Padurariu et al., 2017; Schoner et al., 2017; Sgoifo et  
59 al., 2014). Importantly, we do not aim at providing a comprehensive theoretical framework to  
60 understand the existence of simple forms of empathic behaviors in rodents, which has  
61 already been elegantly done by others (Meyza et al., 2017; Panksepp and Lahvis, 2011).  
62 Instead, by describing the behavioral and physiological consequences of vicarious social  
63 defeat stress and social defeat stress crossover in mice and rats, we aim at highlighting the  
64 potential utility of these rodent models for investigating the neurobiological processes and  
65 sensory channels of information that allow for the contagion of social defeat stress across  
66 individuals.

67

## 68 **2. Traditional rodent models of emotional contagion**

69 Before addressing this newly emerging area of social defeat stress contagion in rodent  
70 research, it is worth recalling that most studies aimed at rodent empathic-like behaviors have  
71 traditionally focused on negative emotional states such as pain or fear (for a thorough review  
72 of these studies the reader is referred to Meyza et al., 2017). Briefly, the ability of rodents to  
73 sense what their fellow rodents are experiencing has been studied using experimental  
74 paradigms such as (i) exposure to a conspecific in pain, (ii) vicarious fear (i.e., witnessing a  
75 partner subjected to fear conditioning), (iii) fear learning by proxy (i.e., interacting with a  
76 conspecific that was previously conditioned during a fear memory retrieval), and (iv) socially  
77 transferred fear (i.e., interacting with a recently conditioned partner in a familiar  
78 environment). With the use of these models, it has been shown that rodents can experience  
79 contagion of pain and fear both during direct observation of an adverse event (i.e., injection  
80 of acetic acid or mild footshocks) and during social interaction with a previously exposed  
81 partner in the safe environment of the home cage. Notably, the magnitude of these  
82 behavioral responses was modulated by familiarity in models of pain contagion and, to a

83 lesser extent, in models of fear contagion (Gonzalez-Liencre et al., 2014; Langford et al.,  
84 2006). These studies convincingly demonstrated that rodents can acquire a state of distress  
85 vicariously through social observation of others suffering from adverse events. However,  
86 depression- or anxiety-like behaviors, which are common occurrences of witnessing  
87 traumatic and stressful life events, were not evaluated. Moreover, these studies have  
88 implemented physical stress of footshock and pain that bears little resemblance to the nature  
89 of stress in humans, in which social stressors predominate (Bjorkqvist, 2001; Rohde, 2001).  
90 More recently, more refined mouse and rat models of stress contagion that are based on the  
91 social defeat paradigm, an ethologically relevant model of social stress, have started to  
92 investigate the consequences of two conceptually distinct and empirically separable  
93 conditions of potential social subordination stress contagion, namely vicarious social defeat  
94 stress and social defeat stress crossover, on behavioral, physiological, and neurobiological  
95 readouts that are relevant in the context of human psychopathology.

96

### 97 **3. Vicarious social defeat**

98 Social defeat (also referred to as the resident-intruder test (Miczek, 1979)) is a relatively  
99 severe stressor in mice and rats (and also other animals) based on social hierarchy and  
100 dominance. Although there are a number of small variations of the social defeat model (for  
101 an overview of different protocols see Hollis and Kabbaj, 2014), the basic principle remains  
102 the same: a male animal is introduced into the home cage of an older and aggressive male  
103 (i.e., resident), who will then threaten and physically assault the intruder until there are clear  
104 signs of submission (i.e., social defeat). Upon social defeat, intruders are usually removed  
105 from direct physical contact with the resident by a wire partition or cage for the remainder of  
106 the test, allowing for psychogenic exposure to aggressive threats without physical harm. This  
107 model has been extensively applied to investigate the behavioral, physiological, and  
108 neurobiological consequences of single or repeated episodes of social defeat that are  
109 relevant in the context of human PTSD, depression, anxiety, and other stress-related

110 illnesses (Carnevali et al., 2017b; Hollis and Kabbaj, 2014; Padurariu et al., 2017; Schoner  
111 et al., 2017; Sgoifo et al., 2014). Notably, because socially defeated animals are exposed to  
112 both physical and emotional stress, more recent studies have added a witness component to  
113 this model in an attempt to tease apart the various aspects of social defeat stress. The result  
114 is a novel “social defeat witness model” or “vicarious social defeat stress paradigm” or  
115 “trauma witness model”, as it has been variably called (Patki et al., 2014; Sial et al., 2016;  
116 Warren et al., 2013), in which a mouse or rat is forced to witness a male conspecific  
117 undergoing social defeat from behind a wire partition or cage within the resident home cage.  
118 We will now summarize the results of studies in mice and rats that demonstrate the viability  
119 of adding a witness component to the social defeat model for delineating the consequences  
120 of vicarious social defeat stress (Table 1).

121

### 122 *3.1. Studies in mice*

123 In the very first study which addressed this topic, adult male mice witnessed the defeat of a  
124 conspecific by a CD-1 aggressor mouse for 10 consecutive days (Warren et al., 2013).  
125 Twenty-four hours after the last defeat, witness mice showed behavioral signs of social  
126 avoidance when confronted with a novel CD-1 mouse compared to the control condition.  
127 Remarkably, reduced interaction with a social target was even more evident one month after  
128 cessation of vicarious social stress exposure and similar to that exhibited by intruder mice.  
129 This behavioral change is particularly relevant because avoidance of trauma-related cues is  
130 a hallmark of PTSD and subsets of depression (Foa et al., 2006; Nemeroff et al., 2006) and  
131 strongly suggests that witnessing social defeat can vicariously provoke a lasting sensitivity to  
132 trauma-related stimuli. Of note, the expression of social avoidance behavior after witnessing  
133 social defeat was prevented by chronic fluoxetine treatment. Importantly, the authors of this  
134 study demonstrated that sensory exposure to an aggressive resident in the absence of  
135 social defeat had no effect on social interaction. Other consequences associated with the  
136 vicarious experience of social defeat in this study included (i) deficits in body weight gain, (ii)  
137 passive coping in the forced swim test, decreased time spent in the open arms of the

138 elevated plus maze, and increased plasma corticosterone levels both 24 hours and 1 month  
139 after the last defeat, and (iii) depressive-like anhedonia (i.e., reduced preference for the  
140 consumption of a sucrose solution) only one month after the last defeat (Table 1). These  
141 abnormalities nearly matched those of intruder mice, suggesting that witnessing social  
142 defeat is a potent stressor in mice with long-lasting consequences at the behavioral,  
143 physiological, and neuroendocrine level. Moreover, witnesses and intruders showed  
144 considerable overlap in gene expression dysregulation in the ventral tegmental area (Warren  
145 et al., 2013) and nucleus accumbens (Warren et al., 2014). These brain areas form part of a  
146 highly complex circuitry that plays an important role in discerning and reacting to rewarding  
147 and aversive stimuli in the environment, as well as influencing future responses based on  
148 past experience (Russo and Nestler, 2013). Importantly, alterations in this circuitry have been  
149 associated with mood disorders (Russo and Nestler, 2013). Interestingly, while the  
150 emergence of aberrant behavioral reactivity to social stimuli has been described both in adult  
151 and adolescent male witness mice (Li et al., 2018; Warren et al., 2014), neurobiological  
152 changes in the nucleus accumbens seemed to depend on the developmental stage of the  
153 witness mice (Warren et al., 2014). The emergence of contextual social avoidance behavior  
154 was also reported in adult female mice that vicariously experienced the defeat of a male  
155 counterpart (Iniguez et al., 2018). This behavioral abnormality was corrected by acute  
156 treatment with ketamine or chlordiazepoxide, pharmacological agents used to treat mood-  
157 related disorders in the clinical population (Frussa-Filho et al., 1999; Parise et al., 2013).  
158 Alongside social functioning deficits, female witness mice showed depressive-like  
159 anhedonia, passive coping in the tail suspension test, a strong trend for anxiety-like behavior  
160 on the elevated plus maze test, increased plasma corticosterone levels, and lower body  
161 weight gain (Table 1), thus extending to the female sex previously obtained results in male  
162 mice (Warren et al., 2013). The expression of aberrant behavior was recently described also  
163 in pregnant mice witnessing the defeat of their mates (Miao et al., 2018), including  
164 depressive-like behavior during the late period of gestation and anxiety-like behaviors after  
165 lactation (Table 1). These behaviors were associated with decreased brain derived



166 neurotrophic factor (BDNF) expression in the hippocampus and medial prefrontal cortex, and  
167 increased BDNF expression in the amygdala of pregnant witness mice. Taken together, the  
168 results of these studies strongly suggest that the stress of witnessing social defeat induces  
169 PTSD-like symptomatology and other depressive and anxiety-like phenotypes in mice and  
170 support the utility of the vicarious social defeat model in mice for further investigating the  
171 underlying neurobiological mechanisms in both sexes and different age groups.

172

### 173 *3.2. Studies in rats*

174 The emergence of depressive- and anxiety-like behavioral symptoms following the vicarious  
175 experience of social defeat of a cage-mate was demonstrated also in a study conducted in  
176 adult male rats (Patki et al., 2014). These behavioral abnormalities were accompanied by  
177 increased plasma corticosterone levels, deficits in body weight, and impaired long-term, but  
178 not short-term, memory function (Table 1), and resembled those of intruder rats. Notably, a  
179 subsequent study from the same group showed that anxiety-like behaviors and cognitive  
180 deficits in witness rats persisted for up to 6 weeks after the last defeat episode but seemed  
181 to be reversible beyond this time period (i.e., after 8 weeks) (Patki et al., 2015). On the  
182 contrary, the presence of a depression-like behavioral phenotype was still evident 8 weeks  
183 after the last defeat. The authors of this study argued that the different time course of  
184 normalization of behavioral and cognitive responses in witness rats may be due to the fact  
185 that depression affects more complex circuits and mechanisms as compared to anxiety and  
186 memory function, and hence could take more time to normalize (Patki et al., 2015). A more  
187 recent study investigated the cardiovascular consequences of vicarious social defeat in male  
188 rats (Finnell et al., 2017). Remarkably, witnesses exhibited increases in mean arterial  
189 pressure and heart rate that were nearly identical to those of intruders, both during acute  
190 and repeated social stress exposure. This finding is quite surprising given that witness rats  
191 were merely observing the defeat bout of a same-sex conspecific without actually being  
192 engaged in any physical effort. Moreover, re-exposure to the stress environment 6 days after  
193 the last defeat in the absence of the resident produced robust tachycardic and pressor

194 responses in witness rats that were comparable to those of intruders, which is another  
195 important indication that witnessing social defeat can vicariously provoke a lasting sensitivity  
196 to trauma-related stimuli, a hallmark of PTSD. Other consequences associated with the  
197 vicarious experience of social defeat in this study included a reduction in sucrose solution  
198 consumption preference, increases in resting systolic blood pressure, and signs of HPA axis  
199 hyperactivity (i.e., elevated plasma corticosterone levels and increased adrenal weight)  
200 (Table 1). These findings prompted the same research group to study the effects of vicarious  
201 social defeat stress in female rats (Finnell et al., 2018). Similar to the male-based results of  
202 their previous investigation, female witnesses showed robust tachycardic and pressor  
203 responses to the social defeat of a male intruder (Table 1). These responses did not  
204 habituate over time. Importantly, vicarious stress-induced tachycardia was associated with a  
205 higher, although modest, incidence of ventricular arrhythmias compared with the control  
206 condition. Moreover, daily exposure to vicarious social defeat provoked an increase in  
207 resting systolic blood pressure and heart rate and reductions in heart rate variability (Table  
208 1). From a behavioral point of view, female witness rats showed anxiety-like burying during  
209 social defeat episodes, depressive-like anhedonia, and passive coping during the forced  
210 swim test after 5 days of vicarious social defeat stress (Table 1). Notably, cardiovascular and  
211 behavioral alterations were not evident in ovariectomized female rats exposed to the same  
212 procedure of vicarious social defeat. Moreover, upon re-exposure to the stress environment  
213 in the absence of the resident, intact, but not ovariectomized, female witness rats exhibited  
214 increases in peripheral cytokine concentrations and corticotropin-releasing factor and  
215 interleukin-1 $\beta$  levels in the central amygdala. According to the authors of this study, these  
216 results provide preliminary insights into a putative neuronal mechanism by which ovarian  
217 hormones sensitize behavioral and cardiovascular responses to witness stress, as both  
218 inflammation and corticotropin-releasing factor are known to activate several brain regions,  
219 including the central amygdala (Nadjar et al., 2005; Reul et al., 1998). Taken together, the  
220 results of these studies further support the utility of the vicarious social defeat model in rats  
221 for elucidating the neurobiological processes that mediate, potentially in a sex-dependent

222 manner, the negative behavioral and cardiovascular consequences associated with vicarious  
223 social stress exposure. An important factor to consider in future studies on sex differences in  
224 the vicarious social defeat model is that the behavior of resident animals (for example, the  
225 intensity of the attacks) could also be different depending on whether the resident is  
226 observed by a male or a female observer. This, in turn, could affect male and female  
227 observers in a sex-specific manner.

228

### 229 *3.3. Sensory channels of vicarious social defeat stress perception*

230 As mentioned above, in the social defeat witness model a rodent is forced to witness a  
231 conspecific undergoing social defeat from behind a wire partition or cage within the resident  
232 home cage. Therefore, the term “witness” in this model generally refers to all sensory stimuli  
233 associated with the vicarious experience of social defeat and not visual stimuli alone. An  
234 obvious question would then be to determine the specific sensory channel(s) through which  
235 vicarious social stress can be perceived. In their original study, Warren and colleagues  
236 (Warren et al., 2013) used opaque non-perforated dividers to confine separate groups of  
237 witness male mice within the resident cage during social defeat. They found that this  
238 manipulation completely prevented the acquisition of social avoidance behavior in witness  
239 mice. Similar results were obtained in female witness mice (Iniguez et al., 2018), suggesting  
240 that visual cues play a central role in the perception of vicarious social stress. However,  
241 although visual stimuli were completely blocked in these studies by the use of opaque  
242 dividers without holes, the transmission of auditory and chemosensory stimuli might have  
243 been blunted as well. To further examine the contribution of olfactory and auditory stress vs  
244 visual reinforcement, Patki and colleagues (Patki et al., 2015) exposed male rats only to  
245 odor and urine of the aggressive rat or to ultrasound vocalizations emitted by a cage-mate  
246 undergoing social defeat (witness rats were kept outside the resident’s cage with visual  
247 stimuli blocked by opaque black paper). They demonstrated that smelling the odor and urine  
248 of the aggressive rat without social defeat (olfactory stress) or only hearing the social defeat  
249 (auditory stress) had no effect on depressive- and anxiety-like behaviors or memory function.

250 These findings indicate the importance of visually witnessing the traumatic effects of social  
251 defeat for the development of behavioral and cognitive alterations in rats.

252

#### 253 *3.4. The role of social support in buffering the effects of vicarious social defeat*

254 A related matter to the adverse effects of vicarious social stress exposure on subsequent  
255 social interaction is the fact that social interaction can in turn play a role in buffering or  
256 moderating the effects of that stressor. In rodents, most studies of social buffering have  
257 focused on the presence or absence of a conspecific such as the cage-mate after a stressor  
258 (DeVries et al., 2003; Kikusui et al., 2006). Specifically, it has been shown that the effects of  
259 social defeat on a variety of behavioral, physiological, and neurobiological outcomes were  
260 substantially reduced in animals that were group-housed after being directly exposed to the  
261 defeat episode (e.g., Lehmann and Herkenham, 2011; McQuaid et al., 2013; Nakayasu and  
262 Ishii, 2008; Ruis et al., 2001). Can social buffering also protect against the negative  
263 consequences of witnessing social defeat? In the study by Patki and colleagues (Patki et al.,  
264 2014), a group of witness and intruder rats was paired housed after each defeat episode.  
265 The authors reported that the witness rat was aloof and restless upon initial reunion with the  
266 socially defeat partner, but then tried to huddle with its mate and spent time licking and  
267 surrounding it for the next hour (Patki et al., 2014). They concluded that these qualitative  
268 assessments are representative of comforting and supporting behavior. Interestingly, they  
269 documented that depressive- and anxiety-like behaviors were significantly lower in both  
270 social defeat experiencing and witnessing rats in the pair-housing condition as compared to  
271 when rats were isolated in a single cage after firsthand or vicarious social defeat. These  
272 findings were only partially replicated in a subsequent study in adolescent mice (Li et al.,  
273 2018), in which social support following social defeat exerted beneficial effects on social  
274 behavior only in witness mice but not in mice that had directly experienced the defeat as  
275 compared to the single housing condition. In rodents, many different variables are thought to  
276 affect the efficacy of social buffering, including the familiarity of the conspecific, the relative  
277 hierarchy, sex of the individual and partner, sensory modalities of exposure to that individual,

278 timing of the availability of social support, presence or absence during stress exposure, and  
279 whether the cage-mate was also stressed (Beery and Kaufer, 2015). These last two aspects  
280 are obviously particularly important in the context of vicarious social stress, and future  
281 studies exploring these variables in all combinations will likely reveal how social support can  
282 buffer against the negative consequences of social defeat stress both in social stress  
283 experiencing and witnessing individuals.

284

#### 285 **4. Social defeat stress crossover**

286 In the vicarious social defeat model, witness rodents are exposed to a partner that is in  
287 immediate danger of being physically assaulted by the resident. Therefore, this model  
288 seems particularly suitable for addressing specific experimental questions related to the  
289 vicarious experience of traumatic life events. However, another condition that falls under the  
290 umbrella term of stress contagion is the response of an individual to the aftermath of stress  
291 of a social partner. To address this issue, the social defeat stress crossover model implies  
292 that the partner rat or mouse is still stressed due to recent social defeat but the danger is  
293 remote. For example, in a recent study by our group (Carnevali et al., 2017a), a male  
294 'demonstrator' rat was paired up with a same-sex 'observer' rat for several days to achieve  
295 familiarity before the beginning of the social defeat stress procedure. The demonstrator rat  
296 was then removed from the cage and underwent social defeat stress in another, soundproof  
297 room. Upon the return of the demonstrator rats to the original cage, the cage-mate observers  
298 showed a stress response characterized by a transient increase in heart rate and a reduction  
299 in heart rate variability compared to the control condition. Remarkably, this response  
300 occurred despite the fact that the observer rats had not seen or heard the social defeat  
301 experience of the demonstrator rats. Moreover, we ruled out the potential for olfactory  
302 signals from the aggressive rat to influence response of observers by showing that exposure  
303 to the bedding from the cage of the aggressive rat did not elicit cardiovascular responses in  
304 the observers in the absence of the demonstrator. Most importantly, following repeated

305 exposure to socially defeated demonstrators, observer rats showed clear behavioral signs of  
306 social avoidance when tested in a new social context that nearly matched those of their  
307 respective stressed demonstrators. Moreover, observer rats showed elevated plasma  
308 corticosterone levels compared to the control condition. This work is novel in showing that  
309 social subordination stress occurring out of sight and immediate hearing and smell range  
310 can be contagious between rats. Clearly, the social transmission of stress between social  
311 partners could exploit different sensory channels. We hypothesized that observer rats may  
312 have acquired the stress state of their social partners also through observation of distinctive  
313 patterns of overt behavior (e.g., freezing) expressed by demonstrator rats upon their return  
314 to the home cage following social defeat. However, future work should address which  
315 specific olfactory, visual, and/or auditory signals from the demonstrator rats induced the  
316 observer rats to respond to the aftermath of stress of their cage-mates in the safe  
317 environment of the home cage. A number of other questions arise when the results of this  
318 study are critically evaluated. What are the neurobiological mechanisms underlying  
319 emotional-state matching between observer and demonstrator rats? Do the degree of  
320 relatedness, sex and/or age of the observer and partner play a role in these contagious  
321 stress responses? Would the observer rats have shown similar behavioral and physiological  
322 responses if the demonstrator rats had been exposed to a different (nonsocial) stressor?  
323 Nevertheless, this study provides preliminary clues about how the stress of those around us  
324 may affect our behavior and physiology and prompts a systematic investigation of these  
325 research questions.

326

## 327 **5. Conclusion**

328 Many studies in humans and nonhuman primates have suggested that stressful experiences  
329 may be transmitted among individuals through social interactions within a shared social  
330 setting (de Waal and Preston, 2017; Engert et al., 2019; White and Buchanan, 2016). Such  
331 contagious stress transcends subjective feeling states to affect the individual's behavior and

332 even physiology beyond the daily stressors experienced firsthand (de Waal and Preston,  
333 2017; Engert et al., 2019; White and Buchanan, 2016). The study of stress contagion in  
334 rodent research is very much in its early days. However, the findings reviewed here  
335 demonstrate that the behavior and physiology of mice and rats can be influenced by the  
336 stress state of their conspecifics in two distinct conditions of social defeat stress contagion.  
337 In the vicarious social defeat model, witness mice and rats exhibit physiological stress  
338 responses and develop a host of behavioral deficits that include contextual social avoidance  
339 and other depressive- and anxiety-like phenotypes. Likewise, social interaction with a  
340 recently socially defeated partner in the safe environment of the home cage (social defeat  
341 stress crossover model) results in increased heart rate and corticosterone as well as  
342 increased social avoidance behavior in rats. Importantly, the behavioral and physiological  
343 consequences of vicarious social defeat stress seem relatively stable across mouse and rat  
344 strains and both sexes, whereas a systematic investigation of strain- and sex-specific  
345 responses to the social defeat crossover model is currently lacking. Thus, these rodent  
346 models seem to be well-suited for a more in-depth evaluation of the sensory channels of  
347 information that allow the contagion of behavioral and physiological effects of social defeat  
348 stress among individuals. One of the main questions to be addressed by future studies is  
349 whether the contagion is specific to the social aspect of the stressor or is just a consequence  
350 of general stress produced by social defeat. Furthermore, while some of the brain areas  
351 affected by vicarious social defeat stress exposure and the underlying neural mechanisms  
352 have been unveiled by these rodent studies, much remains to be known. The neural basis of  
353 stress (and other forms of emotional) contagion revolves around the idea of shared neural  
354 networks or neural resonance between individuals. Specifically, one of the most intriguing  
355 and intensely debated hypotheses proposed so far is that mirror neurons play an important  
356 role in the neural resonance of emotional states (Ferrari and Rizzolatti, 2014; Hickok, 2009).  
357 The availability of new techniques of imaging and manipulation of neuronal circuits with  
358 single-cell resolution in rodents encourages the use of these models of social defeat stress  
359 contagion for investigating the brain structures and neurochemistry involved in the social

360 sharing of stressful experiences and also for testing the hypothesis about the role of  
361 mirroring mechanisms. Given the frequent social situations where stress is likely to occur in  
362 our daily life, beyond the daily stressors experienced firsthand, and the deleterious mental  
363 and physical consequences associated with stress exposure, a more detailed understanding  
364 of the neurobiological processes underlying the contagion of psychophysiological effects of  
365 stress across individuals is likely to have important implications for health.

366



**Table 1.** Rodent models of social defeat stress contagion

Strain/species	Procedure	Observer response	References
Adult male c57BL/6J mice	One 10-min episode of vicarious social defeat daily for 10 consecutive days	Contextual social avoidance (SIT) Depressive- (FST and SPT) and anxiety- (EPM test) like behaviors Increased plasma corticosterone levels Deficits in body weight gain Dysregulated gene expression in the VTA and NAc	(Warren et al., 2013; Warren et al., 2014)
Adolescent male c57BL/6J mice	One 10-min episode of vicarious social defeat daily for 10 consecutive days	Contextual social avoidance (SIT) Dysregulated gene expression and altered spine density in the NAc	(Warren et al., 2014)
Adolescent male c57BL/6J mice	Ten 15-min episodes of vicarious social defeat over a 7-day period	Contextual social avoidance (SIT) Deficits in body weight gain	(Li et al., 2018)
Adult female c57BL/6J mice	One 10-min episode of vicarious social defeat daily for 10 consecutive days	Contextual social avoidance (SIT) Depressive-like behaviors (TST and SPT) and a strong trend for anxiety-like behavior (EPM test) Increased plasma corticosterone levels Deficits in body weight gain	(Iniguez et al., 2018)
Pregnant female c57BL/6J mice	One 5-min episode of vicarious social defeat daily for 17 consecutive days	Depressive-like behavior (SPT) during the late period of gestation Anxiety-like behaviors (EPM and LD tests) after lactation Deficits in body weight gain Changes in BDNF expression in the hippocampus, amygdala and medial prefrontal cortex	(Miao et al., 2018)
Adult male Sprague- Dawley rats	One episode of vicarious social defeat daily for 7 consecutive days. Each defeat episode lasted 30 min, including phases of sensory, but not physical, contact between resident and intruder rats	Depressive- (FST and SPT) and anxiety- (EPM, LD, and OPF tests) like behaviors Increased plasma corticosterone levels Impaired long-term memory function (RAVW test) Deficits in body weight gain	(Patki et al., 2014; Patki et al., 2015)
Adult male Sprague-	One 15-min episode of vicarious social	Robust pressor and tachycardic responses during acute and	(Finnell et al., 2017)

Dawley rats	defeat daily for 5 consecutive days	repeated vicarious stress exposure, and during context re-exposure Increases in resting systolic blood pressure Depressive-like anhedonia (SPT) Elevated plasma corticosterone levels Increased adrenal weight	
Adult female Sprague-Dawley rats	One 15-min episode of vicarious social defeat daily for 5 consecutive days	Robust pressor and tachycardic responses during acute and repeated vicarious stress exposure Larger vulnerability to arrhythmias during acute vicarious stress exposure Increases in resting systolic blood pressure and heart rate and reductions in heart rate variability Depressive- (FST and SPT) and anxiety (burying)-like behaviors Elevated peripheral cytokine levels and increased corticotropin-releasing factor and interleukin-1 $\beta$ levels in the central amygdala after context re-exposure	(Finnell et al., 2018)
Adult male Wistar rats	Cohabitation with a socially defeated male partner without witnessing the social defeat experience of the partner. Each defeat episode lasted 15 min and was repeated for 4 consecutive days	Increases in heart rate and decreases in heart rate variability upon return of the socially defeated partner in the home cage Social avoidance behavior in a new social context (SAAP test) Elevated plasma corticosterone levels	(Carnevali et al., 2017a)

369

370 Abbreviations: BDNF: brain derived neurotrophic factor; LD: light-dark; EPM: elevated plus  
371 maze; FST: forced swim test; NAc: nucleus accumbens; OPF: open field; RAVW: radial arm  
372 water maze; SAAP: social approach/avoidance test; SIT: social interaction test; SPT:  
373 sucrose preference test; TST: tail suspension test; VTA: ventral tegmental area. Detailed  
374 experimental procedures are described in the original papers.

375 **References**

- 376 Atsak, P., Orre, M., Bakker, P., Cerliani, L., Roozendaal, B., Gazzola, V, Moita M., Christian  
377 Keysers, C., 2011. Experience modulates vicarious freezing in rats: a model for empathy.  
378 PLoS One 6, e21855. <https://doi.org/10.1371/journal.pone.0021855>.
- 379 Bastiampillai, T., Allison, S., Chan, S., 2013. Is depression contagious? The importance of  
380 social networks and the implications of contagion theory. *Aust. N. Z. J. Psychiatry* 47, 299-  
381 303. <https://doi.org/10.1177/0004867412471437>.
- 382 Beery, A.K., Kaufer, D., 2015. Stress, social behavior, and resilience: insights from rodents.  
383 *Neurobiol. Stress* 1, 116-127. <https://doi.org/10.1016/j.ynstr.2014.10.004>.
- 384 Bjorkqvist, K., 2001. Social defeat as a stressor in humans. *Physiol. Behav.* 73, 435-442.  
385 [https://doi.org/10.1016/s0031-9384\(01\)00490-5](https://doi.org/10.1016/s0031-9384(01)00490-5).
- 386 Blanchard, E.B., Kuhn, E., Rowell, D.L., Hickling, E.J., Wittrock, D., Rogers, R.L., Johnson,  
387 M.R., Steckler, D.C., 2004. Studies of the vicarious traumatization of college students by the  
388 September 11th attacks: effects of proximity, exposure and connectedness. *Behav. Res.*  
389 *Ther.* 42, 191-205. [https://doi.org/10.1016/S0005-7967\(03\)00118-9](https://doi.org/10.1016/S0005-7967(03)00118-9).
- 390 Carnevali, L., Montano, N., Statello, R., Coude, G., Vacondio, F., Rivara, S., Ferrari, P.F.,  
391 Sgoifo, A., 2017a. Social stress contagion in rats: Behavioural, autonomic and  
392 neuroendocrine correlates. *Psychoneuroendocrinology* 82, 155-163.  
393 <https://doi.org/10.1016/j.psyneuen.2017.05.017>.
- 394 Carnevali, L., Montano, N., Statello, R., Sgoifo, A., 2017b. Rodent models of depression-  
395 cardiovascular comorbidity: Bridging the known to the new. *Neurosci. Biobehav. Rev.* 76,  
396 144-153. <https://doi.org/10.1016/j.neubiorev.2016.11.006>.
- 397 Carr, L., Iacoboni, M., Dubeau, M.C., Mazziotta, J.C., Lenzi, G.L, 2003. Neural mechanisms  
398 of empathy in humans: a relay from neural systems for imitation to limbic areas. *Proc. Natl*  
399 *Acad. Sci. USA* 100, 5497–5502. <https://doi.org/10.1073/pnas.0935845100>
- 400 de Waal, F.B.M., Preston, S.D., 2017. Mammalian empathy: behavioural manifestations and  
401 neural basis. *Nat. Rev. Neurosci.* 18, 498-509. <https://doi.org/10.1038/nrn.2017.72>.

402 Decety, J., Lamm, C., 2009. The biological bases of empathy. John Wiley and Sons.

403 DeVries, A.C., Glasper, E.R., Detillion, C.E., 2003. Social modulation of stress responses.

404 *Physiol. Behav.* 79, 399-407. [https://doi.org/10.1016/s0031-9384\(03\)00152-5](https://doi.org/10.1016/s0031-9384(03)00152-5).

405 Dimitroff, S.J., Kardan, O., Necka, E.A., Decety, J., Berman, M.G., Norman, G.J., 2017.

406 Physiological dynamics of stress contagion. *Sci. Rep.* 7, 6168.

407 <https://doi.org/10.1038/s41598-017-05811-1>.

408 Engert, V., Linz, R., Grant, J.A., 2019. Embodied stress: The physiological resonance of

409 psychosocial stress. *Psychoneuroendocrinology* 105, 138-146.

410 <https://doi.org/10.1016/j.psyneuen.2018.12.221>.

411 Engert, V., Plessow, F., Miller, R., Kirschbaum, C., Singer, T., 2014. Cortisol increase in

412 empathic stress is modulated by emotional closeness and observation modality.

413 *Psychoneuroendocrinology* 45, 192–201. <https://doi.org/10.1016/j.psyneuen.2014.04.005>.

414 Ferrari, P.F., Rizzolatti, G., 2014. Mirror neuron research: the past and the future. *Philos*

415 *Trans. R. Soc. Lond. B. Biol. Sci.* 369, 20130169. <https://doi.org/10.1098/rstb.2013.0169>.

416 Finnell, J.E., Lombard, C.M., Padi, A.R., Moffitt, C.M., Wilson, L.B., Wood, C.S., Wood, S.K.,

417 2017. Physical versus psychological social stress in male rats reveals distinct

418 cardiovascular, inflammatory and behavioral consequences. *PLoS One* 12, e0172868.

419 <https://doi.org/10.1371/journal.pone.0172868>.

420 Finnell, J.E., Muniz, B.L., Padi, A.R., Lombard, C.M., Moffitt, C.M., Wood, C.S., Wilson, L.B.,

421 Reagan, L.P., Wilson, M.A., Wood, S.K., 2018. Essential Role of Ovarian Hormones in

422 Susceptibility to the Consequences of Witnessing Social Defeat in Female Rats. *Biol.*

423 *Psychiatry* 84, 372-382. <https://doi.org/10.1016/j.biopsych.2018.01.013>.

424 Foa, E.B., Stein, D.J., McFarlane, A.C., 2006. Symptomatology and psychopathology of

425 mental health problems after disaster. *J. Clin. Psychiatry* 67 Suppl 2, 15-25.

426 Frussa-Filho, R., Barbosa-Junior, H., Silva, R.H., Da Cunha, C., Mello, C.F., 1999.

427 Naltrexone potentiates the anxiolytic effects of chlordiazepoxide in rats exposed to novel

428 environments. *Psychopharmacology (Berl)* 147, 168-173.

429 <https://doi.org/10.1007/s002130051157>.

430 Gonzalez-Liencre, C., Juckel, G., Tas, C., Friebe, A., Brune, M., 2014. Emotional contagion  
431 in mice: the role of familiarity. *Behav. Brain. Res.* 263, 16-21.  
432 <https://doi.org/10.1016/j.bbr.2014.01.020>.

433 Hatfield, E., Cacioppo, J., Rapson, R., 1993. *Emotional Contagion*. Cambridge University  
434 Press.

435 Hickok, G., 2009. Eight problems for the mirror neuron theory of action understanding in  
436 monkeys and humans. *J. Cogn. Neurosci.* 21, 1229-1243.  
437 <https://doi.org/10.1162/jocn.2009.21189>.

438 Hoffman, M.L., 2000. *Empathy and moral development: Implications for caring and justice*.  
439 Cambridge University Press, New York.

440 Hollis, F., Kabbaj, M., 2014. Social defeat as an animal model for depression. *ILAR J.* 55,  
441 221-232. <https://doi.org/10.1093/ilar/ilu002>.

442 Huber, A., Barber, A.L.A., Farago, T., Muller, C.A., Huber, L., 2017. Investigating emotional  
443 contagion in dogs (*Canis familiaris*) to emotional sounds of humans and conspecifics. *Anim.*  
444 *Cogn.* 20, 703-715. <https://doi.org/10.1007/s10071-017-1092-8>.

445 Iacoboni, M., Woods, R.P., Brass, M., Bekkering, H., Mazziotta, J.C., Rizzolatti, G., 1999.  
446 Cortical mechanisms of human imitation. *Science* 286, 2526-2528.  
447 <https://doi.org/10.1126/science.286.5449.2526>.

448 Iniguez, S.D., Flores-Ramirez, F.J., Riggs, L.M., Alipio, J.B., Garcia-Carachure, I.,  
449 Hernandez, M.A., Sanchez, D.O., Lobo, M.K., Serrano, P.A., Braren, S.H., Castillo, S.A.,  
450 2018. Vicarious Social Defeat Stress Induces Depression-Related Outcomes in Female  
451 Mice. *Biol. Psychiatry* 83, 9-17. <https://doi.org/10.1016/j.biopsych.2017.07.014>.

452 Joiner, T.E., Jr., 1994. Contagious depression: existence, specificity to depressed  
453 symptoms, and the role of reassurance seeking. *J. Pers. Soc. Psychol.* 67, 287-296.  
454 <https://doi.org/10.1037//0022-3514.67.2.287>.

455 Kikusui, T., Winslow, J.T., Mori, Y., 2006. Social buffering: relief from stress and anxiety.  
456 *Philos. Trans. R. Soc. Lond. B. Biol. Sci.* 361, 2215-2228.  
457 <https://doi.org/10.1098/rstb.2006.1941>.

458 Langford, D.J., Crager, S.E., Shehzad, Z., Smith, S.B., Sotocinal, S.G., Levenstadt, J.S.,  
459 Chanda, M.L., Levitin, D.J., Mogil, J.S., 2006. Social modulation of pain as evidence for  
460 empathy in mice. *Science* 312, 1967-1970. <https://doi.org/10.1126/science.1128322>.

461 Lehmann, M.L., Herkenham, M., 2011. Environmental enrichment confers stress resiliency  
462 to social defeat through an infralimbic cortex-dependent neuroanatomical pathway. *J.*  
463 *Neurosci.* 31, 6159-6173. <https://doi.org/10.1523/JNEUROSCI.0577-11.2011>.

464 Li, M., Xu, H., Wang, W., 2018. An Improved Model of Physical and Emotional Social Defeat:  
465 Different Effects on Social Behavior and Body Weight of Adolescent Mice by Interaction With  
466 Social Support. *Front. Psychiatry* 9, 688. <https://doi.org/10.3389/fpsy.2018.00688>.

467 McQuaid, R.J., Audet, M.C., Jacobson-Pick, S., Anisman, H., 2013. The differential impact of  
468 social defeat on mice living in isolation or groups in an enriched environment: plasma  
469 corticosterone and monoamine variations. *Int. J. Neuropsychopharmacol.* 16, 351-363.  
470 <https://doi.org/10.1017/S1461145712000120>.

471 Meyza, K., Knapska, E., 2018. What can rodents teach us about empathy? *Curr. Opin.*  
472 *Psychol.* 24, 15-20. <https://doi.org/10.1016/j.copsyc.2018.03.002>

473 Meyza, K.Z., Bartal, I.B., Monfils, M.H., Panksepp, J.B., Knapska, E., 2017. The roots of  
474 empathy: Through the lens of rodent models. *Neurosci. Biobehav. Rev.* 76, 216-234.  
475 <https://doi.org/10.1016/j.neubiorev.2016.10.028>.

476 Miao, Z., Mao, F., Liang, J., Szyf, M., Wang, Y., Sun, Z.S., 2018. Anxiety-Related  
477 Behaviours Associated with microRNA-206-3p and BDNF Expression in Pregnant Female  
478 Mice Following Psychological Social Stress. *Mol. Neurobiol.* 55, 1097-1111.  
479 <https://doi.org/10.1007/s12035-016-0378-1>.

480 Miczek, K.A., 1979. A new test for aggression in rats without aversive stimulation: differential  
481 effects of d-amphetamine and cocaine. *Psychopharmacology (Berl)* 60, 253-259.  
482 <https://doi.org/10.1007/bf00426664>.

483 Nadjar, A., Bluthé, R.M., May, M.J., Dantzer, R., Parnet, P., 2005. Inactivation of the  
484 cerebral NFkappaB pathway inhibits interleukin-1beta-induced sickness behavior and c-Fos

485 expression in various brain nuclei. *Neuropsychopharmacology* 30, 1492-1499.  
486 <https://doi.org/10.1038/sj.npp.1300755>.

487 Nakayasu, T., Ishii, K., 2008. Effects of pair-housing after social defeat experience on  
488 elevated plus-maze behavior in rats. *Behav. Processes* 78, 477-480. <https://doi.org/>  
489 Nemeroff, C.B., Bremner, J.D., Foa, E.B., Mayberg, H.S., North, C.S., Stein, M.B., 2006.  
490 Posttraumatic stress disorder: a state-of-the-science review. *J. Psychiatr. Res.* 40, 1-21.  
491 <https://doi.org/10.1016/j.beproc.2008.02.007>.

492 Padurariu, M., Antioch, I., Balmus, I., Ciobica, A., El-Lethey, H.S., Kamel, M.M., 2017.  
493 Describing some behavioural animal models of anxiety and their mechanistics with special  
494 reference to oxidative stress and oxytocin relevance. *Int. J. Vet. Sci. Med.* 5, 98-104.  
495 <https://doi.org/10.1016/j.ijvsm.2017.08.003>.

496 Palagi, E., Norscia, I., Demuru, E., 2014. Yawn contagion in humans and bonobos:  
497 emotional affinity matters more than species. *PeerJ* 2, e519.  
498 <https://doi.org/10.7717/peerj.519>.

499 Panksepp, J., Panksepp, J.B., 2013. Toward a cross-species understanding of empathy.  
500 *Trends Neurosci.* 36, 489-496. <https://doi.org/10.1016/j.tins.2013.04.009>.

501 Panksepp, J.B., Lahvis, G.P., 2011. Rodent empathy and affective neuroscience. *Neurosci.*  
502 *Biobehav. Rev.* 35, 1864-1875. <https://doi.org/10.1016/j.neubiorev.2011.05.013>.

503 Parise, E.M., Alcantara, L.F., Warren, B.L., Wright, K.N., Hadad, R., Sial, O.K., Kroeck, K.G.,  
504 Iniguez, S.D., Bolanos-Guzman, C.A., 2013. Repeated ketamine exposure induces an  
505 enduring resilient phenotype in adolescent and adult rats. *Biol. Psychiatry* 74, 750-759.  
506 <https://doi.org/10.1016/j.biopsych.2013.04.027>.

507 Patki, G., Salvi, A., Liu, H., Salim, S., 2015. Witnessing traumatic events and post-traumatic  
508 stress disorder: Insights from an animal model. *Neurosci. Lett.* 600, 28-32.  
509 <https://doi.org/10.1016/j.neulet.2015.05.060>.

510 Patki, G., Solanki, N., Salim, S., 2014. Witnessing traumatic events causes severe  
511 behavioral impairments in rats. *Int. J. Neuropsychopharmacol.* 17, 2017-2029.  
512 <https://doi.org/10.1017/S1461145714000923>.

513 Perlman, S.E., Friedman, S., Galea, S., Nair, H.P., Eros-Sarnyai, M., Stellman, S.D., Hon, J.,  
514 Greene, C.M., 2011. Short-term and medium-term health effects of 9/11. *Lancet* 378, 925-  
515 934. [https://doi.org/10.1016/S0140-6736\(11\)60967-7](https://doi.org/10.1016/S0140-6736(11)60967-7)

516 Preston, S.D., de Waal, F.B., 2002. Empathy: Its ultimate and proximate bases. *Behav.*  
517 *Brain. Sci.* 25, 1-20; discussion 20-71.

518 Reimert, I., Bolhuis, J.E., Kemp, B., Rodenburg, T.B., 2013. Indicators of positive and  
519 negative emotions and emotional contagion in pigs. *Physiol. Behav.* 109, 42-50.  
520 <https://doi.org/10.1016/j.physbeh.2012.11.002>.

521 Reul, J.M., Labeur, M.S., Wieggers, G.J., Linthorst, A.C., 1998. Altered  
522 neuroimmunoendocrine communication during a condition of chronically increased brain  
523 corticotropin-releasing hormone drive. *Ann. N. Y. Acad. Sci.* 840, 444-455.  
524 <https://doi.org/10.1111/j.1749-6632.1998.tb09583.x>.

525 Rizzolatti, G., Fogassi, L., Gallese, V., 2001. Neurophysiological mechanisms underlying the  
526 understanding and imitation of action. *Nat. Rev. Neurosci.* 2, 661-670.  
527 <https://doi.org/10.1038/35090060>.

528 Rohde, P., 2001. The relevance of hierarchies, territories, defeat for depression in humans:  
529 hypotheses and clinical predictions. *J. Affect. Disord.* 65, 221-230.  
530 [https://doi.org/10.1016/s0165-0327\(00\)00219-6](https://doi.org/10.1016/s0165-0327(00)00219-6).

531 Ruis, M.A., de Groot, J., te Brake, J.H., Dinand Ekkel, E., van de Burgwal, J.A., Erkens, J.H.,  
532 Engel, B., Buist, W.G., Blokhuis, H.J., Koolhaas, J.M., 2001. Behavioural and physiological  
533 consequences of acute social defeat in growing gilts: effects of the social environment. *Appl.*  
534 *Anim. Behav. Sci.* 70, 201-225.

535 Russo, S.J., Nestler, E.J., 2013. The brain reward circuitry in mood disorders. *Nat. Rev.*  
536 *Neurosci.* 14, 609-625. <https://doi.org/10.1038/nrn3381>.

537 Schoner, J., Heinz, A., Endres, M., Gertz, K., Kronenberg, G., 2017. Post-traumatic stress  
538 disorder and beyond: an overview of rodent stress models. *J. Cell. Mol. Med.* 21, 2248-2256.  
539 <https://doi.org/10.1111/jcmm.13161>



540 Sgoifo, A., Carnevali, L., Grippo, A.J., 2014. The socially stressed heart. Insights from  
541 studies in rodents. *Neurosci. Biobehav. Rev.* 39, 51-60.  
542 <https://doi.org/10.1016/j.neubiorev.2013.12.005>

543 Sial, O.K., Warren, B.L., Alcantara, L.F., Parise, E.M., Bolanos-Guzman, C.A., 2016.  
544 Vicarious social defeat stress: Bridging the gap between physical and emotional stress. *J.*  
545 *Neurosci. Methods* 258, 94-103. <https://doi.org/10.1016/j.jneumeth.2015.10.012>.

546 van Wingen, G.A., Geuze, E., Vermetten, E., Fernandez, G., 2011. Perceived threat predicts  
547 the neural sequelae of combat stress. *Mol. Psychiatry* 16, 664-671.  
548 <https://doi.org/10.1038/mp.2010.132>.

549 Warren, B.L., Sial, O.K., Alcantara, L.F., Greenwood, M.A., Brewer, J.S., Rozofsky, J.P.,  
550 Parise, E.M., Bolanos-Guzman, C.A., 2014. Altered gene expression and spine density in  
551 nucleus accumbens of adolescent and adult male mice exposed to emotional and physical  
552 stress. *Dev. Neurosci.* 36, 250-260. <https://doi.org/10.1159/000362875>.

553 Wicker, B., Keysers, C., Plailly, J., Royet, J.P., Gallese, V., Rizzolatti, G.. 2003. Both of us  
554 disgusted in my insula: the common neural basis of seeing and feeling disgust. *Neuron* 40,  
555 655–664. [https://doi.org/10.1016/S0896-6273\(03\)00679-2](https://doi.org/10.1016/S0896-6273(03)00679-2).

556 Warren, B.L., Vialou, V.F., Iniguez, S.D., Alcantara, L.F., Wright, K.N., Feng, J., Kennedy,  
557 P.J., Laplant, Q., Shen, L., Nestler, E.J., Bolanos-Guzman, C.A., 2013. Neurobiological  
558 sequelae of witnessing stressful events in adult mice. *Biol. Psychiatry* 73, 7-14.  
559 <https://doi.org/10.1016/j.biopsych.2012.06.006>.

560 Waters, S.F., West, T.V., Mendes, W.B., 2014. Stress contagion: physiological covariation  
561 between mothers and infants. *Psychol. Sci.* 25, 934-942.  
562 <https://doi.org/10.1177/0956797613518352>.

563 Wethington, E., 2000. Contagion of Stress. *Advances in Group Processes* 17, 229-253.

564 White, C.N., Buchanan, T.W., 2016. Empathy for the Stressed. *Adapt. Hum. Behav. Physiol.*,  
565 311-324.