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Feature Review

Emotional contagion and prosocial behavior in rodents

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Empathy is critical to adjusting our behavior to the state of others. The past decade dramatically deepened our understanding of the biological origin of this capacity. We now understand that rodents robustly show emotional contagion for the distress of others via neural structures homologous to those involved in human empathy. Their propensity to approach others in distress strengthens this effect. Although rodents can also learn to favor behaviors that benefit others via structures overlapping with those of emotional contagion, they do so less reliably and more selectively. Together, this suggests evolution selected mechanisms for emotional contagion to prepare animals for dangers by using others as sentinels. Such shared emotions additionally can, under certain circumstances, promote prosocial behavior.

Highlights

Rats and mice show robust emotional contagion by aligning their fear and pain to that of others.

Brain regions necessary for emotional contagion in rodents closely resemble those associated with human empathy; understanding the biology of emotional contagion in rodents can thus shed light on the evolutionary origin and mechanisms of human empathy.

Cingulate area 24 in rats and mice contains emotional mirror neurons that map the emotions of others onto the witnesses' own emotions.

Emotional contagion prepares animals to deal with threats by using others as sentinels; the fact that rodents approach individuals in distress facilitates such contagion.

In some conditions, rats and mice learn to prefer actions that benefit others, with notable individual differences. This effect depends on structures that overlap with those of emotional contagion.

Rodents share and respond to emotions of others

Our ability to place ourselves in the shoes of others, share their **emotions** (see Glossary), and feel their **feelings** is thought to provide important information and motivation to adjust our behavior to the state of others and our environment (Box 1). These abilities have long been considered a top candidate for what makes us prosocial [1,2] and their deficits are some of the most debilitating and hard to treat symptoms of several psychiatric and neurological disorders [3]. The past decade has seen a dramatic deepening of our understanding of the biology of how rodents share and respond to the emotions of others. As we will discuss in the first part of our review, leveraging a combination of robust behavioral paradigms and the powerful neuroscience tools available in mice and rats, we now understand that rodents robustly show **emotional contagion** of **distress**, showing signs of **fear** and altered **pain** sensitivity when they witness other rodents in fear or pain, and that this relies on neural structures homologous to those activated while humans witness the pain of others. Although emotional contagion is only part of the fully-fledged **affective empathy** humans experience (Box 2), rodent work sheds light on the neural mechanisms and evolutionary origin of this emotional link across individuals [4,5]. Conceptually, while empathy for pain in humans is often seen romantically as an other-regarding emotion in which we feel distressed for the victim, the rodent literature affords the distance to consider a more selfish explanation: sharing the distress of others is a powerful way to save one's own skin. In the second part of our review, we will discuss the related literature showing that rodents actively approach individuals in distress, thereby increasing emotional contagion. Instrumental learning tasks also provide evidence that rodents can find benefits for others reinforcing, thereby learning to favor **prosocial behaviors** (i.e., behaviors that benefit others), but do so less reliably and more selectively than catching emotions. That prosocial behavior depends on neural structures overlapping with those of emotional contagion could indicate that mechanisms that prepare individuals for threats contribute to prosociality, but through filters that restrict prosociality to a subset of the situations that trigger contagion.

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Box 1. The contentious concept of emotion

To discuss emotional contagion we must address the debate revolving around 'what is an emotion' and 'how can we study it' [90]. Scientists have used the word emotion in one of two ways [90,149].

(i) Emotions are internal states, consisting of a combination of neural, physiological, and behavioral states that can be categorized according to their function. They are triggered by relevant external stimuli and serve to flexibly organize behavior and promote fitness. They can be observed across a wide range of animals (evidence for their adaptive value). These intervening variables may cause, but do not require, the conscious experiences we call feelings. In fear, the stimulus is a threat; the emotion, an activity pattern across various brain regions (e.g., amygdala, hypothalamus) and physiological changes (accelerated heart rate, hormonal releases); the function, to prioritize behaviors that avoid or mitigate the threat such as hiding, freezing, or fighting.

(ii) Emotions are conscious experiences, conceptual constructs built upon the perception of external and internal stimuli and their integration with past, similar experiences and/or schemas. Here, fear emerges from the perception of danger and the interoception of the altered bodily state and is consciously construed as fear based on prior experiences of threat.

While the former emphasizes the functional aspect of emotions as intervening variables between stimuli and adaptive responses and can be studied in all animals (regardless of conscious experiences, only accessible in humans), the latter establishes the conscious experience as the emotion itself. As emphasized by LeDoux [150], we must specify how we use emotion here, because a biological understanding of emotion and its contagion in the first meaning is not an understanding of the biology of the conscious experience. Rather than abandoning the attribution of emotions to animals, here we disambiguate these meanings by reserving the words emotion**,** fear**,** and pain to refer to intervening variables while remaining agnostic about their conscious experience in rodents. We will instead use the word feeling to refer to the conscious experiences of emotions [151–153].

A core challenge for the future will be to unravel how emotions can become feelings, as the biology of that process will be key to understanding our social and affective experiences and the clinical disorders thereof.

Emotional contagion

Emotional contagion of distress

Following the lead of classic studies from the past century [6,7], recent rodent paradigms investigating emotional contagion have mostly focused on negative emotional states that we jointly refer to as distress (Figure 1A–E, Key figure). These states are evoked by threat or noxious stimuli. The induced defensive and nocifensive behavioral responses are used by investigators to measure the intensity of

Box 2. Emotional contagion is not full affective empathy

The terms emotional contagion and empathy are often used almost interchangeably in the recent animal literature. However, their meanings are different in important ways. Emotional contagion stems from the German 'Stimmungsübertragung' (Stimmung = mood, übertragung = transfer) introduced by Konrad Lorentz to refer to how in non-human animals, witnessing a conspecific emotion, expressed via movements and sounds, triggers a similar emotion in the observer [154]. Empathy stems from the German 'Einfühlung' (Ein = into, fühlung = to feel), introduced by Vischer [155] and Lipps [156] as a combination of resonating with the inner states of others and projecting the resonant feelings back onto them, to explain how humans perceive the inner lives of others so immediately.

That emotional contagion stems from a tradition of animal ethology while empathy stems from philosophy encapsulates the differences between these related concepts. Ethologists have limited access to their animals' mental states, and the definition of emotional contagion, therefore, hinges on behavioral observations and avoids references to higher mental states. In contrast, human psychologists can access verbal reports and introspection and the definition of empathy therefore naturally includes an individual's ability to project or attribute the resonant state to others.

Some argue that the term empathy should be used liberally as an umbrella term for all cases of affective resonance across individuals [5], and several scientists consider the rodent paradigms of Figure 1 (in main text) models of empathy [18,28,29,31]. Doing so, however, hides what we do not know in animals: does the observer know that the fear or pain is the demonstrator's? So far, there is little evidence that freezing or hyperalgesia reflects an attribution to the demonstrator.

Speaking of emotional contagion thus more honestly highlights what we do and what we do not know and keeps us aware that the field must find ways to test the degree of attribution to claim a true model of empathy. Testing the presence of such attribution might eventually reveal the evolution and neurobiology of the mechanisms elevating emotional contagion to empathy and afford a biological distinction between psychiatric disorders of emotional contagion and social attribution [157].

Glossary

Affective empathy: feeling what another person is feeling while at the same time being aware that the shared emotion originates in the other.
Allogrooming: the grooming of one animal towards another of the same species, by licking or carefully nibbling.
Distress: the overarching category of negatively valenced emotional states encompassing fear and pain that motivate avoidance.
Emotional contagion: the process through which an individual's emotional state comes to resemble that of another individual. Unlike affective empathy, emotional contagion does not require the recipient of the emotion to be aware that the emotion originates in the other individual; nor does it require that either individual be aware of their emotional state.
Emotional mirror neurons: neurons selectively activated while an individual experiences a subset of emotions and while witnessing another appearing to experience a similar subset of emotions.
Emotions: states characterized by complex neural and physiological responses to significant actual or suspected events that act as latent variables to promote fitness by organizing priorities and motivating behavior, whether these states are consciously perceived (i.e., feelings) or not.
Fear: the category of emotional states triggered by external threats and whose function is the protection of the organism against the threat. Fear states can be diverse, depending on the nature of the threat and the context, external and internal, in which it occurs. For example, if the threat, such as a predator, is distant or inescapable an animal might freeze and its heart slow down, whereas if there is a shelter the animal might escape to it, while the heart speeds up. Both fear states contribute to the animal's survival, in the first case it might avoid detection by the predator and in the second case it decreases the chances of being caught by the predator.
Feelings: conscious experiences of emotions. Feelings arise from the integration of external and internal/bodily cues, the context in which they occur, and our schemas of the world (structured semantic representations of past experiences). This process allows the categorization of the conscious

Key figure

Paradigms revealing emotional contagion

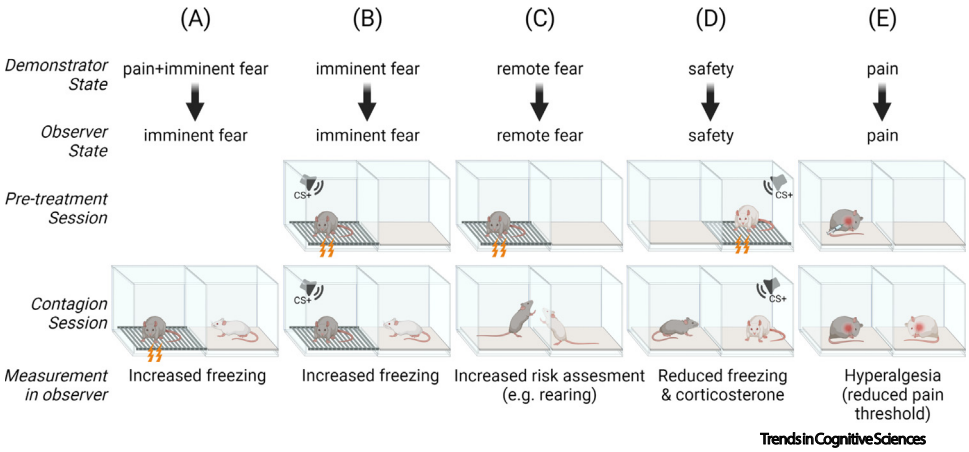

Figure 1. (A) Observers (white) witnessing a demonstrator (gray) receive shocks show increased freezing. (B) Observers witnessing a demonstrator displaying defensive behaviors triggered by a CS+ playback show increased freezing. (C) Observers interacting with a demonstrator that was recently shocked show increased risk assessment. (D) Animals experiencing fear show reduced freezing when exposed to a nonstressed conspecific. (E) Observers interacting with a demonstrator subjected to a noxious stimulus (injection of a painful substance) show changes in their pain threshold.

a negative state. Most paradigms experimentally alter the state of a demonstrator animal and then measure the state of an observer to infer the presence and intensity of the contagion. Note that many senses (e.g., hearing, seeing, and smelling) [8–14] may contribute to the contagion.

A very robust paradigm involves the delivery of footshocks to the demonstrator while the observer is exposed to the demonstrator's reaction through a perforated transparent divider (Figure 1A). In both mice and rats, observer **freezing** significantly increases in response to the demonstrator's reaction, in ways that correlate with how much freezing the demonstrator displays [8,10,15–18]. In this paradigm, the demonstrator undergoes pain during the shocks and fear between them. The former can be observed and transmitted through pain-squeaks, a vocalization in the audible range, and rapid nocifensive movements, including jumping; the latter through freezing and ultrasonic vocalizations around 22 kHz [19]. The observed increase in observer freezing, which is called '**vicarious freezing**', is taken as evidence that a defensive emotional state was triggered through emotional contagion. We therefore refer to this paradigm as evidence for $(\text{pain} + \text{fear})_{\text{demo}} \rightarrow \text{fear}_{\text{observer}}$ contagion, where the demonstrator state reflects what was induced by the experimenter and the observer state reflects what was measured. In some experiments, the observer is later placed again in the witnessing context without a demonstrator and increased freezing then shows that the observer learned to associate vicariously experienced distress with the context [18]. Another variant replaces the footshocks with witnessing an aggressor defeat the demonstrator. In this vicarious social defeat test, observers show increased physiological stress, reduced body weight gain, and social avoidance as if they had suffered social defeat themselves [20,21], suggesting an emotional contagion of stress.

A second paradigm involves threat conditioning of a demonstrator to a tone (CS+) prior to the main session. During the main session, the observer then witnesses the demonstrator freeze in

experience of emotional states into distinct concepts/categories, or feelings.
Freezing: a reaction to threat characterized by the cessation of movement, except for respiration.
Pain: the category of emotional states triggered by noxious stimuli, whose function is the protection of the organism from injury or damage. Just as fear, pain may include a diversity of states characterized by different combinations of physiological and behavioral responses, sharing the function of protection against noxious stimuli.
Prosocial behavior: behavior that benefits others, be it intentionally or not.
Risk assessment: vigilant approach and exploratory behavior that serves to collect information about a suspected threat in the environment, including rearing, sniffing, and exploration.
Vicarious freezing: freezing triggered by witnessing the distress of another individual.

reaction to a playback of the CS+ (Figure 1B) [9,11,13]. Increased freezing of the observer is again taken as evidence of a defensive state triggered by emotional contagion. This represents a case of $fear_{demo} \rightarrow fear_{observer}$ paradigm, as the demonstrator does not experience pain during the interaction period.

In a somewhat related paradigm (Figure 1C), the demonstrator receives electroshocks prior to the main session. In the main session, an observer then interacts with the previously shocked demonstrator in a new environment. The observer then shows increased **risk assessment** (e.g., rearing) typical for exposure to a remote threat [17,22]. Because the danger is remote for the demonstrator during the interaction, this can be considered a $remote\text{-}fear_{demo} \rightarrow remote\text{-}fear_{observer}$ paradigm, while the former two paradigms are $imminent\text{-}fear_{demo} \rightarrow imminent\text{-}fear_{observer}$ paradigms. This distinction highlights the fine-grained nature of the state that is being transmitted, including information about the imminence of the danger [17,23].

Finally, in social buffering paradigms (Figure 1D), one animal is in distress, be it because it is currently exposed to footshocks or because it is exposed to a previously conditioned CS+, yet freezing and physiological stress indicators (e.g., glucocorticoids such as corticosterone) are reduced if another, nonstressed animal is close by compared with when the stressed animal is alone [24–26].

In all of these paradigms, the state altered in the observer via emotional contagion is expressed as threat responses, even if the induction in the demonstrator involves noxious stimuli. In the first three, relatively high levels of threat responses, which indicate a highly negative emotional state in the demonstrator, spill over to the observer. In the last, the reverse is true and the low level of threat responses in the demonstrator spill over and moderate defensive states and reactions of the observer. Jointly, these processes are starting to be considered as a mutual transfer of emotional state, so that the individual risk assessment and defensive states converge across animals, combining each individual's first-hand threat evidence with that perceived through the state of others to reach a more veridical assessment of the danger or safety level in the environment [12,15,23].

In a different family of paradigms, observers are tested for signs of changes in their pain sensitivity in response to lasting nocifensive responses in the demonstrator (Figure 1E). One of the earliest tests showed that when injecting acetic acid into the peritoneal cavity of the observer, the number of writhes (an index of pain intensity) increased if the mouse or rat witnessed another familiar animal also writhing in pain [27,28]. More recent experiments showed that pain-evoking agents that cause visually identifiable nocifensive behaviors in demonstrators, like acetic acid, formalin, or bee venom, instantly increase pain sensitivity in naive observers and such hypersensitivity lasts several hours [29]. The more chronic and less visually identifiable responses caused by complete Freund's adjuvant injection or peripheral nerve injury need more time [29–31] but also increase pain sensitivity in observers. Similarly, 'bystander' mice, housed in the same room but in a different cage as mice in inflammatory pain, also exhibit hyperalgesia mediated by olfactory cues [14].

In addition to social buffering, a small number of experiments have looked at the transmission of other positive states. Witnessing a conspecific receive rewards leads to dopamine release resembling that when the observer receives a reward [32], possibly mediated by 50-kHz vocalizations [33]. Behavioral evidence that the observer experiences the sight of a conspecific receiving reward as reinforcing comes from studies showing that witnessing such rewards can unblock learning [34] and that rats prefer actions that trigger rewards to others in addition to themselves over actions only triggering reward for themselves [35–38].

Emotional contagion or mimicry?

In paradigms investigating vicarious freezing, freezing levels in the observer resemble, in intensity and duration, those of the demonstrator [15–17] and vice versa (Figure 2). Similarly, witnessing a demonstrator grasping an object primes the observer to grasp [39], and witnessing a demonstrator writhe to alleviate its own pain primes the observer to writhe [28]. The manifestation of a similar behavioral response in the observer and demonstrator may suggest the observer simply mimics the behavior of the demonstrator, rather than being contaged by its emotional state. What speaks against mimicry being the main responsible phenomenon are observations that the observer's responses are often temporarily decoupled from the demonstrator's [17,28] and may far outlast the observation of the demonstrator's behavior in the case of altered pain sensitivity [28]. Furthermore, witnessing shocks [40] or optogenetically reactivating neurons previously recruited by shock witnessing [17] flexibly triggers responses adequate to the observer's own situation rather than stereotypically copying the behavior of the demonstrator: observers of a freezing demonstrator will instead hide or escape if given a chance and only freeze if they cannot. Altogether, the data suggest that, while mimicry can play a role in the transmission of defensive behaviors across animals, emotional contagion seems to be the dominant driver, thereby adding flexibility and situation-appropriateness to the reaction of the observer.

Ultimately, understanding what observers experience in these paradigms is important. Do they 'coldly' gather information from the demonstrator's behavior to optimize their behavior without hedonic aversiveness? Do observers come to have an aversive emotional state without a conscious experience? Do they experience feelings of fear and pain in ways that resemble our fully-fledged feeling states? And how precisely does that putative emotion or feeling correspond to that of the demonstrator [41]? Distinguishing between these alternatives from observable data will require us to combine many different readouts (Box 3).

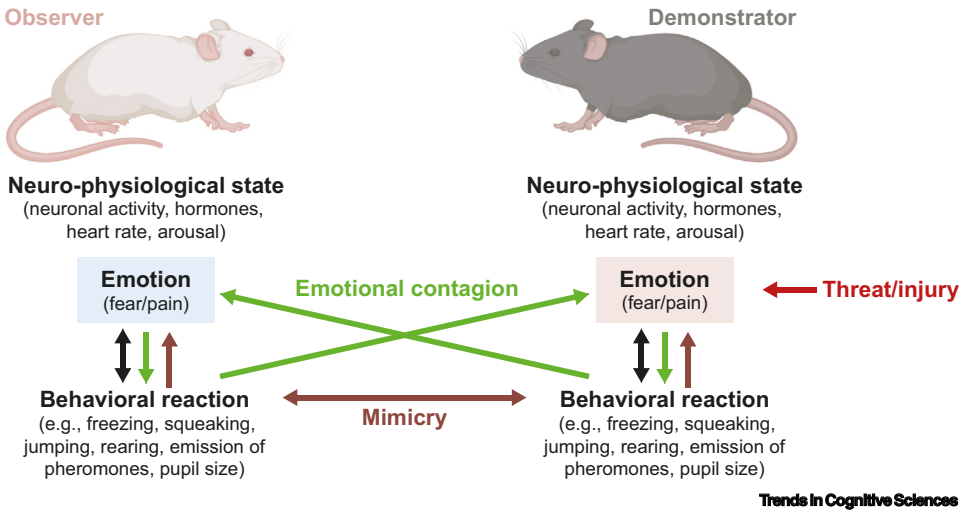

Figure 2. Emotional contagion versus mimicry. Emotional contagion occurs when an observer's brain transforms the observed behavioral reactions of a demonstrator into an emotional state that would fit these behaviors (green arrows). That is to say, if the observer freezes when it detects a threat first-hand, and witnessing a demonstrator freeze triggers an emotional state matching the one evoked by a direct exposure to threat, this would fit most definitions of emotional contagion. Thus, the matching emotional states of the observer and demonstrator results from a similar link between emotional states and behavior in self and other. Mimicry occurs when an observer's brain directly transforms a certain behavior in the demonstrator into a matching behavior in the observer (brown horizontal arrows). This can occur without any emotional state being triggered in the observer. Both of these phenomena can occur at the same time, and in human psychology, the concept of somatic feedback (vertical brown arrows) suggests that mimicking someone's emotional bodily actions will actually trigger an internal state via feedback from the body and the face in particular [173].

Box 3. The power and perils of reverse inference

Gathering observable data from the brain, body, or behavior and trying to infer back the mental state that caused them is what is called 'reverse inference'. Cognitive neuroimaging matured when it realized the perils of naive reverse inference [158]. While early neuroimagers liberally concluded that participants were experiencing fear if the amygdala was activated or in pain if the cingulate was activated, it later became apparent that taking activity in a single brain region as evidence for a particular emotion [159] is problematic because a brain region is rarely activated by only one mental state [160]. For instance, while noxious stimuli reliably activate the cingulate, activity in the cingulate is not a reliable indication of the presence of pain because the cingulate is also activated by several tasks not triggering a feeling of pain [160]. In Bayesian terms, the probability of cingulate activity given the presence of pain, p(cingulate|pain), can be high, while the probability of the presence of pain given cingulate activity, p(pain|cingulate), can be low. Confusing these two probabilities is the fallacy at the center of naive reverse inference. Instead, the combination of multiple readouts, for instance, a pattern of activity over many brain regions in several conditions, can provide more specific and valid reverse inference because the patterns are more uniquely attributed to a particular mental state [41,161].

When it comes to determining what a rodent experiences while witnessing the fear or pain of another, this neuroimaging debate teaches us to search for a pattern of readouts that is sufficiently uniquely associated with a particular emotion so that p(emotion|pattern) becomes high enough to infer the presence of that emotion. Such a pattern could include neural circuit activity spanning multiple brain regions and cell types that could be decoded using neural activity patterns measured while the observer experiences similar emotions firsthand [19,41]; psychophysiological measurements such as heart rate, respiration, pupil dilation, and endocrine responses; motivated behaviors that can reveal the valence of affective experiences such as approach/avoidance assays [162]; facial expressions that may be tightly associated with particular emotions [163]; and stereotypical defensive behaviors such as freezing. In the spirit of emotions being longer-lasting, evolved neural states that flexibly coordinate physiological and behavioral responses [90], such a multipronged approach appears best poised to infer the nature of the experience triggered by witnessing the emotional state of another.

Contagion and familiarity: an evolutionary perspective

Why do animals increase their defensive behavior and pain-sensitivity based on the threat and pain experienced by a demonstrator?

Some argue mammals experience emotional contagion because feeling distressed when their pups are distressed motivates mothers to provide the nurturing that mammalian offspring depend on [5]. Offspring-to-mother emotional contagion is then thought to generalize to other conspecifics along a gradient of kinship and familiarity. This view has been encouraged by the fact that oxytocin, associated with maternity, augments emotional contagion [40,42] and there have been observations that emotional contagion amongst mice is stronger for siblings [10,28].

The effect of familiarity is, however, less consistently observed than one would predict based on this theory. In fear contagion, vicarious freezing of rats is significant amongst familiar and unfamiliar dyads [15,43] without significant difference across familiarity, even across different strains [15]. Amongst mice, strong and frequent shocks to a demonstrator trigger vicarious freezing in familiar and unfamiliar male dyads [10,40,44]. Whether the effect is increased with familiarity remains unclear across conflicting studies [10,44]. If shocks are weaker, only familiar male observers respond with freezing [45,46]. In social buffering, a fear-conditioned rat freezes less when smelling another rat, even unfamiliar [47], although slightly more when familiar [48]. In pain contagion, hyperalgesia is significant irrespective of familiarity for observers with [49] but not without prior experience of the specific injury [27,50,51]. Both female and male mice writhe more when paired with familiar rather than unfamiliar mice in pain [28] but for male mice, which often engage in fighting (Box 4), fight/flight responses close to unfamiliar males even suppress pain behavior compared with being alone [28,52,53]. If paired with a female, a castrated male, or in the presence of barriers that prevent direct physical contact, this stress is reduced and emotional contagion across strangers is restored, confirming that reduced contagion across unfamiliar males represents an adaptation to physical fights [14,54]. Anxiolytic metyrapone injections, systemic or in the prelimbic area 32 [52,55], have the same contagion-restoring effect. Overall, despite significant effects of familiarity, be it of kinship or length of cohousing, in some conditions and more so in mice than

Box 4. A mouse is not just a small rat

Both rats and mice tend to engage in nonviolent social interactions: they crawl under or over each other, allogroom, huddle, follow, and sniff each other [164,165]. Both species recognize individual conspecifics and adapt their social behaviors to the partner's identity [166,167]. Both are social species and the many neural homologies encourage us to combine data across the two species to understand the biology of emotional contagion. However, while laboratory rats show mainly amicable social behavior and rarely fight, laboratory mice can be much more aggressive. This difference reflects the species-specific behavior in the natural environment. In the wild, rats most commonly live in mixed-sex groups of 10–15, in which they rarely fight but do attack intruders [168]. In contrast, wild male mice usually occupy a territory they share only with females and actively defend [169,170]. Species-specific characteristics also bring about differences in fear contagion between rats and mice. Footshocks to a demonstrator result in higher levels of freezing in both demonstrator and observer rats than mice [10,15,17,18,45,67] (Figure I), even though the number and intensity of shocks to the demonstrator mice (typically 20 × 2 s × 1 mA) are typically much higher than those applied to demonstrator rats (typically 5 × 1 s × 0.8 mA). Laboratory mice are also more genetically diverse than rats [171], translating to more variability in sociability and aggressiveness [165,172] that lead to considerable strain differences in fear contagion [146]. It is important to take stock of these differences in behavior and social structure when interpreting the differences and similarities in findings across studies using these species.

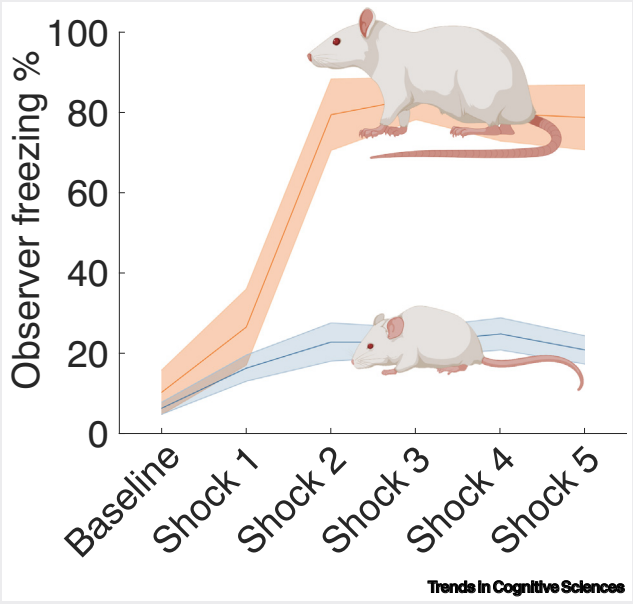

Figure I. Rats freeze more than mice. When using a similar shock paradigm, rat observers pre-exposed to shocks freeze almost four times as much as mice (data from ref. [67] for C57BL/6J mice and ref. [15] for Long-Evans rats).

rats, males than females, and in protocols using weaker stimuli, when combining over 100 studies in a quantitative meta-analysis, studies using familiar dyads did not report significantly stronger emotional contagion than studies using unfamiliar dyads, be it for rats or mice [56]. This challenges the idea that familiarity is the primary evolutionary drive for the emergence of emotional contagion.

Alternatively, using the fear or pain signals of others to trigger one's own defensive behaviors could serve to increase the preparedness of observers to deal with similar threats, before the potentially deadly encounters needed to directly sense the threat. Indeed, simulations show that emotionally coupled animals deploy defensive behavior more effectively than either member alone [15]. Further evidence comes from optogenetic experiments: reactivating central amygdala neurons that were previously activated when witnessing a demonstrator in imminent or remote fear, respectively, can later trigger defensive behaviors in the observer appropriate to imminent or remote threats even when the observer is alone [17]. This shows that the affective state evoked in the observer can serve to optimize the observer's own safety [17,23]. Through the same lens, the hyperalgesia displayed by observers of injured demonstrators can serve as a way to prepare

for similar bodily threats [14]. This preparedness perspective does not negate that demonstrator-directed behaviors can also be triggered in observers (as we discuss later in the review), but emphasizes that conceiving of emotional contagion as primarily care-promoting may be incomplete.

The primacy of a self-serving purpose is also borne out by similar phenomena in simpler animals that do not nurture their offspring: fruit flies freeze more when those around them freeze and resume activity when the others move [57]; zebrafish increase defensive responses around conspecifics expressing such responses [58,59] and reduce such responses around conspecifics that do not [60]; even trees show stress responses when other trees are attacked [61]. Emotional contagion even occurs across animals of different species, a phenomenon referred to as 'eavesdropping', where kin selection is irrelevant [62].

In contrast to the alarm calls certain animals emit to warn others [63], which have a cost for the emitter by increasing its risk of detection, most of the emotional contagion we discussed here is triggered by witnessing the demonstrator's self-defensive behavior. This increases the preparedness of the observer without a cost for the demonstrator. The economy of this transfer may explain why emotional contagion has evolved to be present in so many taxa. In addition, given the interdependence of individuals in a group, what is good for the observer is not at odds with what is good for the demonstrator.

Sex differences in emotional contagion

In humans, women appear to be slightly more empathic than men [64]. Although most rodent studies only use males, a few compared emotional contagion in males and females. That female rodents respond to threats with more escape behaviors and less freezing than males [65] complicates comparisons: if a female observer shows less freezing than a male, her emotional state might be less altered, or she might express her emotional state less, or her demonstrator may have frozen less [15]. In rats witnessing shocks (Figure 1A) both female demonstrators and female observers froze less than males. However, the relationship between their freezing, as revealed using regression or Granger causality analyses, did not differ from that across males. Familiar same-sex dyads of mice also did not reveal sex differences in emotional contagion [66,67]. Only amongst unfamiliar mice do females show more vicarious freezing and hyperalgesia than males [28,40], reflecting the higher risk of aggression between males (Box 4). Social buffering is also difficult to directly compare due to sex-specific freezing propensities, but is significant in both sexes [25]. Sex differences in emotional contagion *per se* are thus limited in rodents, but competitiveness amongst unfamiliar male mice can sometimes mask this emotional contagion. This is reminiscent of findings in humans that men and women show similar levels of elevated activity in pain-related regions for fair demonstrators receiving shocks, but only women do for unfair demonstrators [68].

Pre-exposure: enhancing but not necessary

Another question of interest is the impact of prior experience. For an observer to resonate with the state of a demonstrator, observers must associate the demonstrator's behavior with a matching inner state. Amongst the range of behaviors displayed by demonstrators, some might have innate associations with inner states (e.g., stress pheromones), while others may require these associations to be learned.

Several experiments have shown that prior experience can indeed increase emotional contagion. Although observers that have never experienced footshocks do freeze when witnessing a demonstrator receive footshocks [10,15], observers that have prior experience with footshocks show stronger responses in rats [8] and mice [67], particularly when observing fewer or weaker

shocks to the demonstrator [46]. Observers also freeze to silence caused by a demonstrator's freezing [69], but only if the observer has prior experience of receiving footshocks and freezing [9]. Similarly, hyperalgesia caused by interacting with an unfamiliar demonstrator injected with bee venom only occurs if the observer has experienced bee venom previously [49].

Hebbian learning may explain this phenomenon [70]: during the personal experience of footshocks, observers experience an aversive inner pain state while hearing themselves squeak, jump, and then freeze. These contingencies between inner states and hearing their own reactions could reinforce synaptic connections between these emotional and sensory neural engrams. When later hearing similar reactions of the demonstrator, these connections would reactivate the inner distress that would then result in increased observer freezing. Prior stressful experiences that do not trigger freezing (e.g., a cold swim challenge, or prior footshock protocols not allowing freezing) do not increase vicarious freezing [9], which shows that what is learned during pre-exposure is not simply that danger looms, but a more specific association. This specificity echoes findings in fear conditioning, where prior experience with footshocks but not forced swimming can increase later fear conditioning to footshocks [71,72].

These experiments raise multiple questions for future research: Where in the brain does prior experience generate these associations? What sensory signals (e.g., pain squeaks, ultrasonic vocalizations, pheromones) become associated with what inner state? Does the inner state triggered in the observer match the one while experiencing shocks (pain) or while expecting further shocks (fear)? Recent experiments start to answer some of these questions by showing that the effect of prior experience requires a pathway from the hippocampus to the basolateral amygdala, where it creates an engram that is reactivated during shock observation and creates a sensitivity to previously ineffective auditory cues [46].

Other signals emitted by the demonstrator may not require such prior experience, including stress pheromones or ultrasonic vocalizations, and may account for the significant emotional contagion in naive observers. That the neural pathway responsible for this naive contagion differs from that conveying the added effect of prior experience [46] illustrates the richness of emotional transfer, much as eavesdropping across species has been shown to leverage multiple mechanisms combining inborn and learned cues [62].

Neurobiology

While a decade ago many doubted whether rodents show emotional contagion through neural mechanisms relevant to human empathy, recent work has established that regions associated with empathy for pain in humans are activated by, or necessary for, emotional contagion in rodents (Figure 3) [73]. This similarity suggests that strong evolutionary forces must have stabilized the neural mechanisms responsible for these phenomena across the 70–120 million years since the last common ancestor of humans, mice, and rats [74–76].

In particular, human fMRI experiments consistently report that the anterior insula and anterior-mid cingulate cortices are activated by the pain of other individuals [77–79]. Signals in these structures increase with the intensity of the observed pain, are modulated by the level of responsibility, agency, and ingroup affiliation, and are stronger in more empathic individuals [78–83]. Additional structures such as the ventral striatum and amygdala, medio-dorsal thalamus, somatosensory, and prefrontal regions can also be recruited by the pain of others, depending on the experimental conditions used [78,79,84]. Often, regions recruited during the observation of other's pain, fall within the wider circuit activated by pain self-experience, suggesting the existence of mirror neurons for pain [85,86].

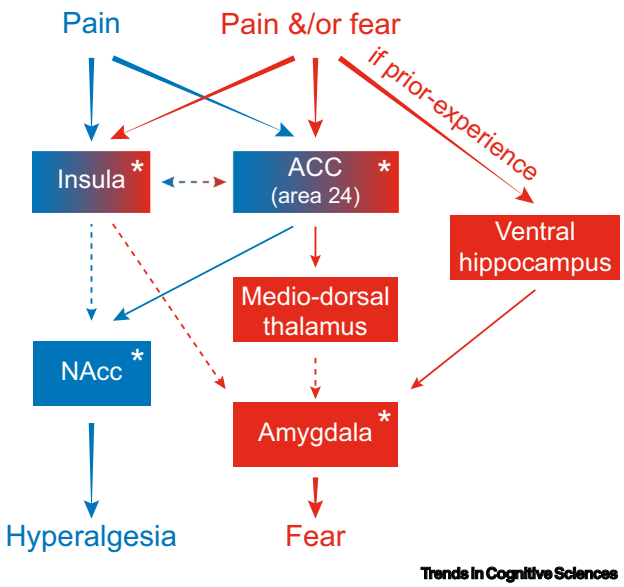

Figure 3. Circuitry of emotional contagion. Witnessing an injured demonstrator ultimately triggers hyperalgesia (blue) via a circuitry involving the insula, anterior cingulate (ACC) area 24 and the nucleus accumbens (NAcc). Witnessing a demonstrator in fear and/or acute pain ultimately triggers nocifensive reactions (red) indicative of fear via a network involving the amygdala. While witnessing footshocks, the amygdala receives input from area 24 and the medio-dorsal thalamus. While hearing the silence indicative of demonstrator freezing, the amygdala receives input from the ventral auditory cortex and the dorsomedial geniculate (not shown). When animals have prior experience of footshock, input from the ventral hippocampus plays an additional role. Familiarity can have effects on behavior through prelimbic area 32, but it is uncertain how this activity modulates the circuitry of emotional contagion. Straight arrows between brain regions are shown as unbroken lines when altering the connection has been shown to alter hyperalgesia (blue) or fear behavior (e.g., freezing, red), whilst broken lines represent likely routes without causal evidence. Tapering arrows represent stimuli or readouts. Brain regions marked with an asterisk appear to be also involved in certain prosocial behaviors. How the nature of the sensory modality (e.g., olfaction, vision, audition) and/or behavioral readout (e.g., pain threshold vs. freezing) determine the necessary and sufficient neural pathway remains incompletely understood.

Studies in humans focus on brain regions recruited while witnessing others receive acute noxious stimulation by letting observers know that others receive electroshocks or see body parts in painful situations. In contrast, the rodent work has aimed to trace two partially separate circuits: one mapping witnessed chronic pain onto altered pain thresholds and one mapping witnessed acute pain onto freezing.

Chronic pain studies (Figure 3, blue) show that early gene expression in both the anterior insula and area 24 is modulated by mice cohabiting with others in chronic pain [87,88]. Chemical deactivation of these regions reversed vicarious hyperalgesia [31,87,88]. Both regions additionally project to the nucleus accumbens (NAcc) in the ventral striatum, a structure known to be involved in reward and pain processing [89,90] and to release dopamine when witnessing others receive rewards [32], where c-Fos expression is also increased when witnessing an injured conspecific [88].

Acute pain studies in both rats and mice show that some area 24 neurons also respond to shock observation [19,30,91,92]. Importantly, in rats, 57% of the neurons that respond to shock observation showed characteristic mirror neuron activity: they also respond to self-pain [19] and encode the intensity of noxious stimuli experienced by the self and others in a similar population code [19]. Neurons in posterior area 24 show stronger responses to demonstrator shocks when the observer could also get shocks [93], as expected if they served to inform the observer about its own risk level. Neurons in this brain region can show different degrees of specificity, some responding only to noxious stimuli and others to salient stimuli more generally, whether aversive or rewarding [19,93]. Together, this mix of area 24 neurons can provide rich information about the situation an animal is in, either through first-hand experience or by witnessing the reactions of others [41]. Deactivating area 24 dramatically reduces vicarious freezing during shock witnessing [10,15,18,19,44,94]. While for vicarious hyperalgesia after witnessing chronic pain, inputs from area 24 to the accumbens are necessary, this is not the case for vicarious freezing following

shock observation [30]. Instead, the amygdalar complex is necessary for vicarious freezing [10,46]. In mice, 10% of basolateral amygdala (BLA) neurons respond to witnessing another receive shocks [91] and deactivation reduces vicarious freezing [10]. The BLA has strong interconnections with area 24. How information from area 24 reaches the BLA remains unclear, as direct projections do not appear to be necessary [30,91], while connections via the medial thalamus might be [95].

Efforts to unravel the circuitry responsible for particular social cues have refined our understanding of the circuitry. The auditory thalamus and ventral auditory cortex, projecting to the lateral amygdala, drive observer freezing to the onset of silence [13]. The basal and lateral amygdala projects to the central amygdala where these inputs are integrated with contextual information to trigger context-appropriate behavioral responses to threats, including freezing in a confined space and hiding in larger spaces [17]. Social buffering of fear is mediated by olfactory cues, sensed by the main olfactory bulb, which conveys information to the lateral and central amygdala via the olfactory peduncle [96]. The modulation of vicarious freezing by familiarity in male mice is mediated by glucocorticoids in prelimbic area 32, where microinjection of a glucocorticoid antagonist unblocks contagion in unfamiliar males and microinjection of an agonist blocks contagion in familiar animals [55]. Finally, the effect of prior shock experience appears to depend on amygdalar input from the shock-engrams in the ventral hippocampus [46].

Overall, showing that area 24, which plays a central role in human pain empathy, contains **emotional mirror neurons** in rodents, illuminates the mechanistic basis of emotional contagion: the emotions of others alter behavior not through a dedicated route, but by being mapped onto the substrates of an observer's own emotions. Rodent neuroscience reveals that human empathy shares core aspects of its hardware with rodent empathy and thus has a long evolutionary history. Interrogating single-cell activity teaches us that cingulate activity combines signals about the salience of other individuals' states that can arouse the observer and increase vigilance, with specific signals preparing the observer for specific threat situations. Relayed to the amygdala, it can trigger situation-appropriate actions. Relayed to the NAccs, it can alter pain sensitivity and, as we will see later, reinforce certain prosocial behaviors.

Beyond dyads without escape

Dyad testing in small experimental compartments has been the bread and butter of the effort to study emotional contagion: the lack of distractions, vicinity to the demonstrator, and controlled timing of the demonstrator's distress have revealed the robustness of emotional contagion. To start addressing the fact that, in real life, emotional transfer depends on social structures and decisions to approach or avoid emotional contagion [97,98], an emerging trend is to use socially and physically more complex situations, aided by systems for automated, long-term tracking of social behavior [99–106].

When humans cannot avoid a distressed individual, most participants will help the victim, some selfishly to reduce personal distress triggered by emotional contagion, some out of other-regarding concern. Providing an opportunity to escape the situation helps tease these two reactions apart: those motivated to reduce personal distress choose to escape, while those motivated by empathic concern choose to help [97]. Rodent experiments are starting to suggest that personal distress is dominant in rodents: optogenetic activation of amygdala neurons responding to witnessing footshocks leads animals to hide in a shelter if they have that option [17] and mice to eventually run away from demonstrators receiving shocks [40]. Such approaches promise to shed more light on how emotional contagion motivates helping.

Prosocial behavior: improving the state of others

What should count as prosocial behavior in rodents?

Clever behavioral paradigms have also revealed that rodents can be prosocial: they approach distressed individuals, free trapped conspecifics, avoid actions that harm, and prefer actions that reward others (Figure 4A–E). Adopting a consequentialist point of view, we consider as prosocial, any behavior that prevents damage to or improves the state of another individual, whether it does so intentionally or not, and whether it is altruistically motivated to improve the state of the other, or selfishly motivated to reduce the unpleasantness of sharing the distress of the other [107]. These paradigms have begun to reveal exciting insights into the biology of prosociality. We will start with experiments showing that observers seem to have a biological tendency to approach demonstrators in distress. This approach increases opportunities for interactions that can benefit the demonstrator. Thereafter, we will look at evidence from instrumental learning paradigms which establish that benefits for others can reinforce prosocial acts.

Close contact increases risk assessment and consolation

Humans counterintuitively choose to view stimuli of pain and suffering over positive or neutral stimuli [108]. Similarly, rats and mice are attracted to individuals in a mildly distressed state over those in a neutral state, even when the distressed animal is physically separated from the observer by a barrier [109–112] (Figure 4A). This preference is modulated by sex and age and by the demonstrator's stress level [109,110,112,113]. In related paradigms without barrier

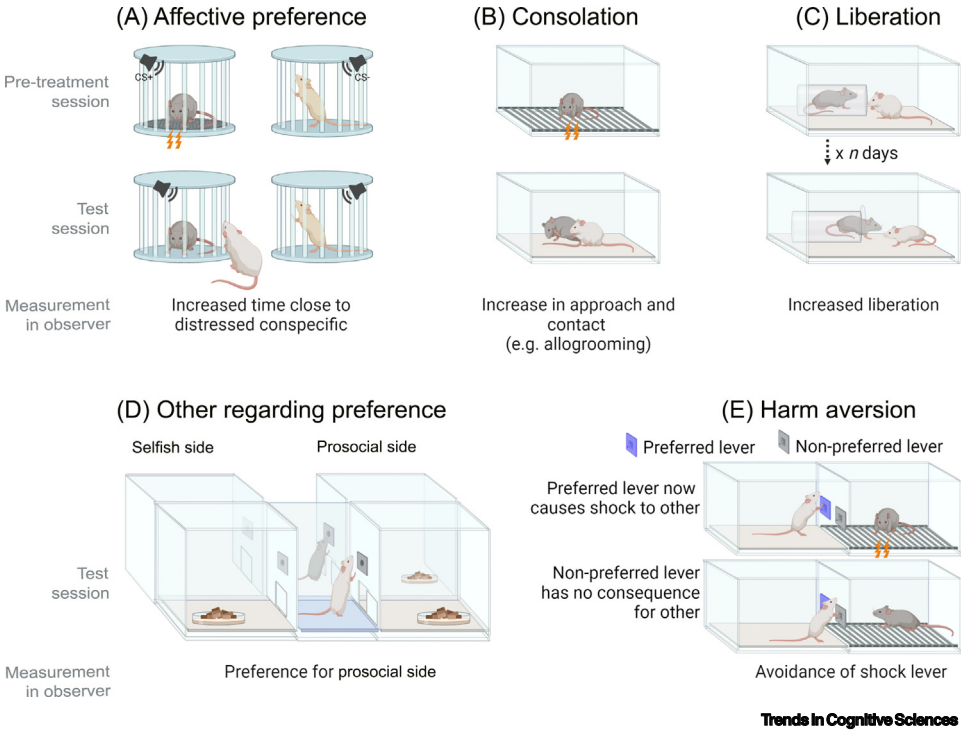

Figure 4. Paradigms revealing prosocial behavior. (A) Focal animals (white, i.e., the animal whose choices are being monitored) spend more time close to a demonstrator that is in a state of fear (gray, triggered by a CS+ playback) than one in a neutral state (beige). (B) Focal animals (white) show increased allogrooming towards a distressed animal. (C) Focal animals (white) learn to liberate an animal restrained in a small tube. (D) Focal rats (white) prefer opening the door to a side that provides food for themselves and a conspecific (gray) than to one that only provides rewards for themselves. (E) During shaping, rats develop a preference for one of two levers delivering food. If that preferred lever is later made to deliver footshocks to a conspecific, they learn to avoid the now-shock-lever.

(Figure 4B), in which an observer can freely interact with a demonstrator that has been stressed (e.g., previously restrained, defeated, shocked, acid or bee venom injected, or presented with a CS+), the observer not only approaches but also sniffs, licks, touches, and **allogrooms** the stressed demonstrator and does so more often and for longer than when interacting with a nonstressed conspecific [27,49,66,114–119]. The stressed demonstrator, in contrast, engages more in nonsocial behaviors such as self-grooming, digging, rearing, and nesting [115,118,119]. Stressing the observer itself reduces its proximity seeking [12,120–122] (but see [49]). The motive to approach and interact with distressed demonstrators remains somewhat unclear, but such curiosity could have two benefits. Firstly, proximity maximizes the observer's access to the alarm pheromones produced by the demonstrator, which are most effective at close range [123] and trigger physiological and behavioral changes in approachers when direct contact is possible [96,118,124]. The resulting increase in pheromone exposure increases emotional contagion, including changes in pain sensitivity [27,49] and neural plasticity [118,124], thereby increasing the observer's preparedness to deal with similar threats. Proximity seeking can thus be conceived of as a social form of risk assessment that benefits the approaching observer: a propensity that leads to the collection of valuable information about potential dangers [108]. Indeed, also for pups, fear is best transferred from mothers if the mother engages in direct contact with her pups [125]. Secondly, the proximity of, and allogrooming by, the calmer observer provides the demonstrator with calming pheromones [96] and leads to social buffering [24,114–116,118,119,124,126,127]. Proximity seeking can thus also be conceived of as a form of consolation that benefits the approached demonstrator [5,12,49,66,114–116,120,121,128]. Given such benefits for the observer and the demonstrator, it is perhaps not surprising that this propensity to approach and the increased allogrooming, licking, and sniffing are so ubiquitous in rats, mice, and voles and have been documented in males and females [66,114,115,119,120], although more strongly towards familiar conspecifics [27,49,66,114–117]. However, the information benefits for the observer raise the question of whether the primary motivation for observers is to console or to seek information. That allogrooming is reciprocated [129,130] also questions whether approachers do so to benefit the demonstrator or to increase the likelihood of being allogroomed in the future.

Beyond the information benefits for the observer and the social buffering for the demonstrator, this propensity to approach distressed individuals has further implications for prosociality. A number of prosocial behaviors we will discuss later (liberation, harm-aversion, and other-regarding preferences) require that the attention of an agent is directed towards another individual in need; attention that this propensity to approach animals in distress helps ensure. Even if proximity seeking were therefore not primarily motivated by a prosocial motivation to console, it may still increase the likelihood of other prosocial behaviors. This is similar to how stimulus enhancement, the fact that animals will pay more attention to objects manipulated by others, is not true imitation but can still facilitate it [131]. Interestingly, proximity seeking and allogrooming are triggered by brain structures also involved in emotional contagion, including the central [109] and medial amygdala [117,119], area 24 [115,117,120,121,128], and insular cortex [113,117,132], and this activity is often modulated by the oxytocin system [115,117,120]. The social transmission of stress and the buffering effect that result from these behaviors have been shown to increase and decrease, respectively, the hypothalamic and hippocampal plasticity normally associated with stress [116,118,124]. Future research will be needed to integrate the circuits associated with triggering, and resulting from, these behaviors.

Prosocial learning paradigms: liberation, harm aversion, and other-regarding preferences

Following an early wave of seminal experiments in the 1950s and 1960s suggesting that rats can find positive outcomes for others reinforcing [133,134], recent experiments have converged on three types of instrumental learning paradigms to provide evidence that rats and mice can learn

to prefer actions that benefit others and to shed light on the mechanisms through which outcomes for others can become reinforcers.

Liberation

Rats and mice learn to open a door to free a rat that is trapped in a tube [135,136], or a wet compartment [137] (Figure 4C). Although interacting with a liberated conspecific could reinforce such behavior [138], rats also release conspecifics if they cannot interact with them, showing that reducing victim distress is a significant reinforcer [139]. In contrast to vicarious freezing that is shown in response to demonstrators of strains they have not been raised with ('outgroup') [15], rats do not liberate members of this outgroup [140,141]. Rats' area 24 was activated when facing a trapped rat of the ingroup or outgroup, but this activity was transferred through direct connections to the NAcc only for ingroup members. This has implications for the link between emotional contagion and helping: while the former correlates with robust activation in area 24 for ingroup and outgroup members both in this experiment and in those reviewed earlier, the latter requires an added step that depends on an area 24 → NAcc connection regulated by familiarity. Emotional contagion is then necessary but not sufficient for liberation. This causal relation is further borne out by observations that anxiolytics prevent emotional contagion and liberation behavior [142] and manipulations of activity in area 24, through local injection of an oxytocin antagonist, also reduce liberation [137].

Harm aversion

If pressing either of two levers provides food rewards, but one additionally delivers footshocks to a conspecific, rats show a preference for the lever not delivering shocks (Figure 4D). This is true even if the lever delivering the shocks delivers twice as much food reward or requires half as much effort to press as the non-shock lever [56]. However, while all rats pre-exposed to shock show substantial increases in freezing when witnessing demonstrators receive footshocks [15], less than half avoided using the shock lever. Also, none of the rats stopped using the shock lever if it produced thrice the food than the alternative lever. These experiments establish that some rats attribute positive value to preventing the distress of others in the cost/benefit calculations they perform when faced with alternative actions. In line with the idea that emotional contagion is a core motivator for avoiding harm to others, deactivating area 24 abolishes harm aversion in rats [143]. However, they also highlight that for the other half of the rats, such value is too low to alter their decisions, and for all of the rats in that study, that value is smaller than that of two food pellets. Avoiding harm to others is thus a less robust effect than the emotional contagion that may drive it.

Other-regarding preferences

Rats prefer options that also reward others. In two experiments, two rats were face-to-face in a double T-maze [35,36] (Figure 4E). The focal (i.e., decision-making) rat decided whether to go right or left, while the other had to follow to the same side. One side provided food to both (prosocial side), the other only to the focal rat. Results showed that if the focal rat must move first, focal rats develop no preference at all [35] or only a slight one for the prosocial side where they see the follower receive food (55%) [36]. If the focal animal can observe the follower's eagerness for the prosocial side before deciding, the preference increases to 65% [35], in line with rats' foraging strategy to favor arms chosen by others over empty arms [103]. Local enhancement and the fact that witnessing a conspecific receive food triggers a dopamine release in the NAcc [32] could contribute to this preference. Still, there is great variability in prosociality across rats, with about one-third failing to develop any preference and the remaining displaying a prosocial preference varying from 60% to 90%. Such variance may in part be explained by social dominance since dominant rats seem more prosocial than their submissive cagemates [144], but

not by familiarity [144]. Choosing between a lever that delivers food to the focal animal or to both animals also generates a modest preference for the prosocial option in rats [37]. In mice, this preference is absent if the recipient is unfamiliar, but robust if the recipient is familiar [38]. Deactivating the BLA, a region necessary for emotional contagion, abolishes that preference in mice [38] and rats [145], suggesting once more a link between emotional contagion and prosociality.

Summary

Instrumental learning tasks show that benefits for others can act as reinforcers of prosocial behavior and this reinforcement depends on brain structures involved in emotional contagion. Future experiments will need to explore whether the same neural populations in these regions account for emotional contagion and vicarious reinforcement of prosociality. While emotional contagion and approach behaviors towards stressed demonstrators are robust, instrumental learning paradigms suggest that the reinforcing value of benefits for others appears less robust. For instance, other-regarding preferences or harm aversion occurs only in some of the animals and rats only liberate ingroup members [140,141]. Together, this suggests that emotional contagion indeed feeds into prosociality, perhaps by making rodents share the outcomes they cause for others, but it does so through a filter that allows shared distress or rewards to spill into prosociality only under specific conditions. Understanding the causes of the considerable individual differences in prosociality and how they relate to variability in the response to the fear and pain of others is an important question for future research that may speak to the causes of the individual variability within the human population and its extreme in antisocial disorders. Comparing different strains may provide traction on the genetic contributions to such variability [18,146]. It is possible that the competitive nature of foraging [147,148] may counteract other-regarding preferences, as providing food to others makes these limited resources unavailable to the self. Finally, an intriguing philosophical question is whether rodents choose actions that benefit others to selfishly avoid vicarious distress or maximize vicarious rewards, or more altruistically to truly benefit their conspecifics.

Concluding remarks

The past decade has seen dramatic technological and conceptual advances in our understanding of the impact that the emotions of one rodent has on others. Although the field is still young, and many key questions remain poorly understood (see Outstanding questions), behavioral paradigms have revealed that rats and mice show robust emotional contagion: they display increased and flexible defensive and nocifensive behaviors following the interactions with distressed demonstrators that suggest that fear and pain are transmitted across animals. Approach paradigms further suggest that rodents actively seek emotional contagion by approaching individuals in altered states. Instrumental decision-making tasks reveal that some rats and mice can learn to engage in behaviors that benefit others. Such instrumental prosocial behavior is less robust and sometimes biased towards 'ingroup' recipients. Neuroscientific tools unraveling the cellular basis of these processes highlight notable similarities between the circuitry involved in human empathy and that involved in emotional contagion and prosocial behavior in rodents. These homologies speak to the evolutionary continuity of emotional contagion and open a pathway to translationally study the cellular basis of human emotional contagion at a resolution that human neuroscience cannot afford. The demonstration of the existence of emotional mirror neurons has shown that the emotions of others do not alter behavior exclusively through a specialized social brain, but by mapping those emotions onto the neural substrates of the observer's own emotions. We must, however, remain mindful that understanding how emotional states transfer between rodents may not fully explain how complex feeling states transfer across humans in mature empathy. Conceptually, the work on rodents offers a new perspective on the evolutionary value of emotional

Outstanding questions

Do observers experience a negatively valenced state when witnessing a demonstrator exposed to threats or injury?

How similar is the neural and physiological state of the observer to that of the demonstrator?

How much detail about the nature of the threat or injury is contained in the neural activity triggered in the observers?

How and where in the brain does prior experience of threats or injury influence emotional contagion?

Is freezing while witnessing others receive shocks dependent on neural representations of pain or fear in the observer?

Does emotional contagion trigger attributions of the shared emotion to a demonstrator?

Given a choice between helping a distressed conspecific and escaping the situation, would rodents escape (as suggested by self-regarding personal distress) or help (as suggested by other-regarding empathic concern)?

Are interactions with stressed demonstrators primarily intended to seek information or console the demonstrator?

Does a demonstrator emit more or different signals when close to a kin or familiar conspecifics, or is the observer more sensitive to them when coming from kin or familiar demonstrators?

What causes the substantial individual differences observed in prosocial behavior? Do these differences correlate with individual differences in emotional contagion?

Would modulating activity in neurons involved in emotional contagion alter prosocial behavior?

contagion: sharing fear and pain with others increases our preparedness to deal with threats and injuries by harnessing others as sentinels. This provides a fresh, more selfish but evolutionarily powerful perspective on emotional contagion that differs from the often-held notion that emotional contagion serves to nurture pups.

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Declaration of interests

No interests are declared.

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