Towards a unified theory of emotional contagion in rodents—A meta-analysis

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ABSTRACT

Here we leverage 80 years of emotional contagion research in rodents and perform the first meta-analysis on this topic. Using 457 effect sizes, we show that, while both rats and mice are capable of emotional contagion, there are differences in how various factors modulate empathy in these species: 1) only mice show strain-specific differences in emotional contagion response; 2) although rats and mice have equivalent contagion response to familiar and unfamiliar individuals, our results show that familiarity length is negatively correlated with level of contagion in rats only; 3) prior experience with emotional stimuli almost doubles fear contagion response in rats while no changes are detected in pre-exposed mice; 4) both mice and rats tested alone show comparable reduced contagion compared to animals tested in a group; 5) emotional contagion is reduced in animals from both species missing one sensory modality compared to situations where all sensory modalities are recruited during emotional contagion. Lastly, we report similar patterns of brain activation during emotional contagion in rats and mice.

1. Introduction

In humans, witnessing the emotions of others is related to specific brain activation patterns (see (Lamm et al., 2011) for a meta-analysis). However, a range of studies demonstrate that empathy is not ubiquitous, and that a subset of the population is impaired in detecting distress in other individuals (Dolan and Fullam, 2006), showing an incongruent empathic response to other’s emotions (Dawel et al., 2012; Marsh and Blair, 2008). Such individuals show deficits in the recognition of social signals (Marsch and Blair, 2008; Blair et al., 2005; Muñoz, 2009) but display intact emotional responses to unconditioned stimuli (Birbaumer et al., 2005), suggesting a social domain-specific impairment. While several theories (deficits in stimulus-reinforcement learning (Blair, 2007) or attention (Moul et al., 2012), and spontaneous vicarious perception (Meffert et al., 2013)) have been proposed to account for such social impairments, these theories have remained mostly speculative due to limited strategies for empirical testing. Indeed, while imaging techniques in humans can detect correlation links between processes, they do not enable researchers to influence neuronal activity (hence limiting causal link analysis) and have a poor spatial resolution (hence limiting accurate quantification of the neural networks involved).

Here, animal models, and rodents in particular (Panksepp and Panksepp, 2013a; Keysers and Gazzola, 2016), provide a powerful mean to put theories of empathy to the test by mapping and manipulating the neural networks involved in the perception of others’ emotions (Keysers and Gazzola, 2016). Published literature on social behavior in rodents is quite extensive and ranges from the late 1940’s (Anderson, 1939; Rice and Gainer, 1962; Riess, 1972; Greene, 1969; Daniel, 1942, 1943; Church, 1959; Korman and Loeb, 1961; Laverty and Foley, 1963; Baum, 1969a; Latané, 1969; Krebs, 1971) to recent influential pieces unifying the building blocks of empathy across species (Preston and De Waal, 2002; De Waal and Preston, 2017).

However, the flourishing field of animal empathy in the last decades has come with a cost, namely a wide variability in the behavioral paradigms and experimental parameters used, as well as in empathy-related definitions adopted by different studies performed in rodents (West et al., 2007; Vasconcelos et al., 2012). As a result, the published literature on this topic is often contradictory and confusing. For instance, while several recent reviews suggest that rodents should be put at the center of empathy research (Meyza et al., 2016; Keum and Shin, 2016; Sivaselvachandran et al., 2016; Panksepp and Panksepp, 2013b; Mogil, 2012), other research groups have suggested more parsimonious explanations for reported behaviors (Vasconcelos et al., 2012; Schwartz et al., 2016; Silberberg et al., 2014). A wide variety of factors (e.g. gender, relatedness between individuals, prior experience) can influence behavioral outcome measures and these are likely responsible for the...
inconsistent results in the field. It is therefore crucial to extract quantitative and qualitative data computed from a large range of studies to provide guidance for future research and assess the generalizability of behavioral essays (Gurevitch et al., 2018; Leenaars et al., 2012; Moher et al., 2015).

In this article, we leverage the large body of evidence published in the last 80 years to perform a meta-analytic review on emotional contagion in rodents. Our results provide the first rodent meta-analytic quantitative estimation of 1) emotional contagion, 2) a range of factors that influence how rodents react to other’s emotions and 3) brain activation patterns during emotional contagion.

2. Methods

We followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines (PRISMA, http://www.prisma-statement.org/) (Moher et al., 2015; Liberati et al., 2009; Moher et al., 2009), as well as search strategies suggested by other authors (Leenaars et al., 2012) for the screening and analysis of the relevant literature.

2.1. Information source and search strategy

This meta-analysis asked the following questions: 1) what is the effect size of emotional contagion in rats and mice and 2) what are the main factors modulating emotional contagion in these species? To identify the relevant articles, we defined emotional contagion as a behavioral response triggered by (indirect -in absence of- and direct -in presence of others-) the emotional cues of other individuals.

We used two databases to search for the relevant literature: PubMed and Web of Science. For each database, we constructed filters which included the same words (see supplementary materials, “filters”), but adapted to each database’s search syntax. For both databases, a time and language filter were applied, to only include research articles published in English between 01/01/1945 and 01/01/2019. The output from each database was exported in separate tables, the tables were then combined into a single list and any duplicated article (article present in both databases) was removed from the final list of articles of interest. Each article in this combined database was reviewed to select studies that met the inclusion criteria:

1. Article written in English language (already included in search filter, but false negatives were detected manually).
2. Study performed on rat or mice models. We decided to limit this meta-analysis to rat and mice models because most studies were performed on these two species.
3. Article containing original research (i.e., not review, opinions, etc...).
4. Study reporting emotional contagion-related measures that could be extracted to measure an effect size.

As a result of our definition of emotional contagion, the screened studies featured contagion carried between a test animal (emotional recipient) and a demonstrator animal (animal that experiences an emotion and transmits it), although in some cases the emotion transfer was performed offline (i.e., in absence of the demonstrator, such as playback of ultrasonic vocalizations). When a study made it through the fourth criteria, we devised a strategy to limit selection bias and to make our study selection process as objective as possible. To do so, we followed a set of rules based on the definition of emotion contagion described above, to decide whether the results reported in a screened article met the inclusion criteria. Per this definition, there were multiple points that had to be met: 1) the study measured a behavioral output originating in a rat or mice; 2) the measured behavioral output was triggered by an emotional cue originating from another conspecific (e.g., distressed foot-shocked animal); 3) the emotional cue could be direct (e.g. the presence of a stressed animal) or indirect (e.g. presentation of the urine of a stressed animal, playback of vocalizations); 4) an emotional cue could be of a positive (food intake), negative (electric foot-shock) or of neutral valence (e.g., social buffering, where the conspecific is in a neutral state and the measured subject is distressed). In a few studies (n = 9) where all the criteria were met, except behavioral measures could not be extracted but physiological measurements such as c-fos, cortisol were reported, this were included in the physiology analysis.

2.2. Data coding and management

A custom coding sheet was created to extract all the relevant information with regards to animal related parameters, experimental design and risk of quantification bias. MC and JHL read and coded each selected article. To ensure that the coding was done correctly a third check was performed by PGS. Because of the large amount of data extracted from each study, we selected what we considered to be key parameters to be included and analyzed in this meta-analysis (Table 1), which encompassed potential modulators of emotional contagion, and the actual measures of emotional contagion. These dependent variables were used to compute independent effect sizes.

To ensure consistency in data extraction between all the studies, each variable described in Table 1 followed the properties described below.

Species: defined whether the study was conducted using in rats or mice.

Age: defined the age, in days, of the animals used in the study. In cases where a range was given, the average of the range provided was used.

Housing: defined the number of individuals housed together (until the first day of the experimental manipulation) with the animals from which the effect size was computed (“test animals”, Fig. 1). Possible categories were: 1 single housed (animal was alone in cage), 2 (animal was housed together with another individual), 3 (animal was housed with additional two individuals) and 4 or more (animal was housed with 3 or more individuals).

Sex: defined whether the animals used were males or females. In cases where mixed-sex dyads were used, we categorized them as ‘both’, but due to low sample size, these studies were not included in analysis looking at sex effect.

Familiarity: defined the level of familiarity of the test animal with the animal demonstrating the emotion transferred (only in cases where the origin was another animal, and not a simple social stimuli such as USV playbacks or odors). This variable was coded as categorical and continuous. Possible categories were 1) unfamiliar pairs (animals had never encountered prior to the test), 2) familiar cagemates, 3) familiar sexual couples and 4) familiar siblings. The number of days that animals knew each other was used as the continuous value. The value for...
unfamiliar animals was 0.

Strain: defined the strain of the animals.

Pre-exposure: defined (yes or no) whether the test animal had undergone emotional experience prior to the test. Emotional experience was defined as any prior encounter with the stimulus causing the emotional transfer during the test.

Time of measurement (relative to interaction): defined the delay, in minutes, between the interaction of animals (i.e., emotional transfer) and measurements of dependent variables. For experiments featuring a direct emotional transfer (e.g., observers witnessing the pain or fear of others), a delay of 0 min was used. When the test animal was measured alone after witnessing the emotions of others, the delay was reported in minutes.

Emotion transferred: the emotion transferred was categorized according to the nomenclature proposed by (Panksepp, 2011). Of the seven categories proposed by (Panksepp, 2011), only four were used in the emotional contagion literature: seeking, aggression, fear/anxiety and pain/panic. Seeking was selected as transferred emotion when the witnessed animal initiated approach behavior towards the source of the emotion. Aggression was selected when the witnessed animal initiated an aggressive behavior towards the source of the emotion. Fear and anxiety were selected when the witness animal displayed typical affective states such as freezing or defecating. Finally, pain and panic were selected when the witness animal showed typical pain-related behavior, such as writhing or mechanical pain.

Sensory modality during emotional transfer: defined which sensory modality or combination of sensory modalities were used during emotion transfer: vision, olfaction and/or audition. Generally, the essential contribution of a sensory modality was tested by either removing it from the emotional contagion test by using experimental constraints, such as adding an opaque partition (blocked vision) or chemically induced manipulations (e.g., ZnSO4-induced anosmia) or by only using the sensory modality of interest (e.g., USV playback, urine-soaked cotton balls or pictures).

Testing being done in isolation: defined whether (yes or no) the animal was tested alone or together with another individual.

In addition to these study characteristics, we assessed the quality and the risks of each screened article. For each study, we indicated whether 1) blinding, 2) randomization, 3) prior calculation of required sample size and 4) declaration of conflict of interest was included in the article (Table 2).

2.3. Extraction of data of interest and computation of effect sizes

While statistics were reported in most studies, the comparisons often did not directly test emotional contagion. In such cases, descriptive statistics (typically mean and standard error of the mean) were manually extracted from graphical representation of data. Due to the lack of descriptive data in most manuscripts, manual extraction was performed in 86% of the articles scrutinized (N = 106). Manual extraction was highly accurate, as confirmed by the high correlation between manual and software-based (WebPlotDigitizer) data extraction (8 randomly selected figures from 8 different papers were used: r = 0.99, p < 0.0001). When standard error of the mean (SEM) was provided in the graphical representation of data, we computed the standard deviation (SD) by using the following formula:

\[ SD = \text{SEM} \times \sqrt{n} \]  

Where \( n \) is the number of data points (e.g., number of subjects).

Data obtained from the studies were then used to compute the effect size (\( r \)). For categorical variables where group comparisons were performed, we created a convention in which we assigned a positive sign for one direction and a negative sign for the opposite direction. The distance from 0 in either direction quantified the strength of the effect reported. For each effect size computed, we assigned positive values to effect sizes larger than 0.0001, as confirmed by the high correlation between manual and software-based data extraction (8 randomly selected figures from 8 different papers were used: \( r = 0.99, p < 0.0001 \)). When standard error of the mean (SEM) was provided in the graphical representation of data, we computed the standard deviation (SD) by using the following formula:

\[ SD = \text{SEM} \times \sqrt{n} \]  

Where \( n \) is the number of data points (e.g., number of subjects).

Data obtained from the studies were then used to compute the effect size (\( r \)). For categorical variables where group comparisons were performed, we created a convention in which we assigned a positive sign for one direction and a negative sign for the opposite direction. The distance from 0 in either direction quantified the strength of the effect reported. For each effect size computed, we assigned positive values to effect sizes that were in line with the following:

1. Witnessing negative emotions in others increases fear-related responses such as freezing and startle responses. By the same token, witnessing pain in others increases hyperalgesia, i.e.,

**Fig. 1. Timeline of events of a typical emotional contagion experiment.** The timeline depicts the variables reported for each study. Stable variables (sex, species, strain) are reported at the animal’s arrival. From that point until emotional transfer occurs, a series of variables (age, familiarity and housing) are quantified. Whether pre-exposure happened before emotional transfer is also noted. During emotional transfer, variables such as emotion transferred and sensory modality channeling the transfer are reported. Finally, the dependent variable reflecting emotional contagion is reported at the time of measurement. Note that the time of measurement can happen simultaneously to emotional transfer (not depicted on figure).
decreases pain-related measures such as mechanical thresholds (pressure tests), paw withdrawal latencies (thermic tests) and other pain measures.

(2) Being put in presence of another individual in a neutral affective states (social buffering) decreases fear and anxiety responses.

(3) Witnessing positive emotions in others increases seeking-related behavior, such as locomotion and approach behavior.

(4) Witnessing emotions of a familiar individual triggers higher emotional contagion than for unfamiliar individuals.

(5) Females show higher emotional contagion than males.

(6) Pre-exposed animals show higher emotional contagion response compared to non-pre-exposed ones.

(7) Group-housed animals show increased emotional contagion in comparison with single-housed ones.

(8) Animals presented with an emotional stimulus that triggered all their sensory modalities (i.e., audition, olfaction and vision) show stronger emotional contagion response compared to animals presented with an emotional stimulus recruiting a subset of these modalities (e.g., blinded by an opaque partition) or only one of these sensory modalities (e.g., smell of a fear conditioned animal).

In this meta-analysis, effect sizes were calculated as a standardized mean difference (ES; (Lipsey and Wilson, 2001; Leichsenring, 2001)). When comparisons used two independent groups (i.e., between-subjects comparison, typically experimental vs control), we used the following computation for calculating the effect size:

$$ES = \frac{M_1 - M_2}{\sqrt{\frac{SD_{M_1}^2 + SD_{M_2}^2}{(n_1 + n_2)}}}$$  \hspace{1cm} (2)$$

where $M_i$, $SD_i$ and $n_i$ represent the mean, standard deviation and sample size for experimental and control group $i$, respectively.

When comparisons used two measures from the same group (i.e., within-subjects comparison, typically baseline vs test time point), we used the following computation for calculating the effect size:

$$ES = \frac{M_{t} - M_{i}}{SD_{M_t} + SD_{M_i}}$$  \hspace{1cm} (3)$$

where $M_i$ is the mean initial measurement (usually baseline), $M_t$ is the measurement at a second time point, $SD_i$ is the standard deviation of the initial measurement, $SD_{M_t}$ is the standard deviation of the distribution at the second measurement point, and $N$ represents the sample size of the group.

In order to bring all measures to the same metric and to ease the interpretation, effect sizes were transformed into correlation coefficients ($r$). The effect size estimation was done using procedures thoroughly described elsewhere (Hedges and Olkin, 1985). To convert the standardized mean difference to $r$, the following equation was used:

$$r = \frac{ES}{\sqrt{ES^2 + 4}}$$  \hspace{1cm} (4)$$

When the relevant statistics were provided in the article, effect sizes were computed using the adequate formula:

$$r = \frac{t}{\sqrt{t^2 + df}}$$  \hspace{1cm} (5)$$

where $t$ is the $t$ value, and $df$ is the degrees of freedom.

$$r = \sqrt{\frac{F}{F + df}}$$  \hspace{1cm} (6)$$

where $F$ is the $F$ value, and $df$ is the degrees of freedom.

Finally, in the rare cases where no data was displayed graphically and only p-values were available, the p-values were used to determine $z$-scores. When p values were reported as greater or lower than alpha level ($< \alpha$ or $> \alpha$; alpha typically $= .05$), the p-values used to determine z-score was set at $p = 0.1$. These studies ($N = 6$) were all published between 1955 and 1981.

$$r = \frac{Z}{\sqrt{N}}$$  \hspace{1cm} (7)$$

where $Z$ is the z score value and $N$ is the sample size.

2.4. Combining effect sizes and comparisons

Since the value of $r$ becomes increasingly skewed as it gets further from 0, we normalized effect sizes using Fisher transformation (Hedges and Olkin, 1985), applied to $r$ as follows:

$$z_r = 0.5 \ln \left[ \frac{1 + r}{1 - r} \right]$$  \hspace{1cm} (8)$$

where $r$ is the effect size computed through the methods described above. By convention, $z_r$ was converted back to $r$ for ease of interpretation (Lipsey and Wilson, 2001).

In order to correct for biases caused by low sample size ($< 20$ or $10$ in each group, see (Nakagawa and Cuthill, 2007)), we computed the unbiased $z_r$ ($z_{ru}$) value using the equation proposed by (Hedges and Olkin, 1985; Nakagawa and Cuthill, 2007):

$$z_{ru} = z_r \left[ 1 - \frac{3}{4(n_1 + n_2) - 9} \right]$$  \hspace{1cm} (9)$$

where $n_1$ and $n_2$ are sample sizes of two comparison groups, and the $z_r$ is the biased effect size estimated in eq. 8.

2.5. Random effect model

When conducting meta-analytic approaches, it is necessary to use either a fixed effect or a random effects statistical model. A fixed effect model assumes that all effect sizes are estimating the same effect, whereas a random effects model accounts for differences in the between-studies effect. Since the chosen model affects the interpretation of the summary estimates, we tested which model to use by conducting a heterogeneity test that generates the Q-statistic described in eq. 14. The Q value is a measure of the dispersion of the effect sizes. This measure follows the chi square distribution with $k-1$ degrees of freedom, where $k$ is the total number of effect sizes. In this meta-analysis, the Q value was highly significant ($\chi^2(350) = 954.63, p < 0.001$), supporting the use of a random effects model. This model assumes that the variance of each effect size ($\nu_i$, eq. 10) is composed of variance due to intrinsic sampling errors ($\nu_r$, eq. 11 & 12) plus other sources of randomly distributed variability ($\nu_v$, eq. 10). To estimate these values, we used formulas 10 through 15 thoroughly described by (Lipsey and Wilson, 2001; Nakagawa and Cuthill, 2007):

$$\nu_i = \nu_h + \nu_r$$  \hspace{1cm} (10)$$

$$\nu_r = SE^2$$  \hspace{1cm} (11)$$

$$SE = \frac{1}{\sqrt{n - 3}}$$  \hspace{1cm} (12)$$

$$\nu_v = \frac{Q - (k - 1)}{\sum w_i - (\sum w_i^2 / \sum w_i)}$$  \hspace{1cm} (13)$$

$$Q = \sum w_i(z_{ru_i})^2 - (\sum w_i Z_{ru_i})^2$$  \hspace{1cm} (14)$$
where Q is calculated using Eq. 14 and df is the number of effect sizes minus one, with higher percent values indicating higher heterogeneity. For this meta-analysis, the $I^2 = 63.3\%$, $p < 0.001$, indicating substantial amount of heterogeneity and giving further support for a random model analysis.

For each variable and its different levels, we calculated the mean effect size, 95% confidence intervals (CI) and z score value using Eqs. 16–19.

$$Z_{ru} = \frac{\sum w_i z_{ru,i} }{ \sum w_i }$$

95% CI = $Z_{ru} \pm 1.96(SE_{ru})$

$$SE_{ru} = \sqrt{\frac{1}{\sum w_i}}$$

$$z = \frac{Z_{ru}}{SE_{ru}}$$

2.6. Physiology data: corticosterone and c-fos

In addition to behavioral data, we extracted corticosterone levels (17 studies) and c-fos activation patterns (16 studies) from a subset of studies. For c-fos analysis, no meta-analytics procedures could be performed for some structures given the low number of effect sizes associated with these brain areas (see results). Effect sizes were extracted and analyzed using Python, and color coded effect sizes were overlapped on the rat brain atlas (Paxinos and Watson, 1998), and the Allen mouse brain atlas (https://mouse.brain-map.org/static/atlas). All effect sizes in the corticosterone and c-fos dataset were subjected to the same transformations and benchmarking as behavioral effect sizes.

2.7. General analysis

It is worthwhile noting that some studies used the same animals to measure emotional contagion and the effect of a given modulator on emotional contagion, and thus resulted in 2 non-independent effect sizes extracted from the same group of animals (N = 23 studies). For these scenarios, the relevant effect size was used for either analysis of emotional contagion or modulator effect. However, since we present separate analysis for emotional contagion and modulators of emotional contagion (see results), the effect sizes used in each analysis remain independent. Moreover, because of consistent differences in the paradigms and measurements used between rats and mice, as an a priori decision, all the analysis conducted were performed separately for rats and mice.

For statistical comparison of the levels within modulators we used the meta-analysis module of JASP (JASP Team 2019, Version 0.10.2) and ran a random effects model (restricted ML). Given that for some modulators (i.e., familiarity, memory, sex, sensory modality) there were studies that conducted experiments to specifically test the role of a given modulator, we used these studies to run an additional separate analysis where we only include studies doing this type of analysis (e.g., studies that only looked at familiarity effect).

To assess publication bias, asymmetry in a funnel plot showing study precision (1/standard error) against observed effect sizes was tested using a non-parametric rank test. Also, to estimate the number studies with an average null result needed to bring the significance of the meta-analysis to a significant level of $\alpha = 0.05$, a fail-safe N was estimated (i.e., file drawer analysis). Both the funnel plot and fail-safe N tests were conducted using JASP 0.10.2.0.

3. Results

3.1. Main findings

An exhaustive search (Fig. 2A) of the rodent emotional contagion literature yielded a final count of 124 studies, 457 studies measuring behavior and 174 effect sizes measuring physiological markers. (Table 3). From the 457 behavioral effect sizes, a subset (N = 350) directly measured emotional contagion and 107 effect sizes examined modulators of emotional contagion (e.g., familiarity) (Fig. 2F).

Quality control check of all the studies showed a suboptimal number of papers reporting blinding (45%) and randomization (61%) procedures and only 4% of studies reporting sample size calculations (Fig. 2B). Noticeably, no study reported any conflict of interest.

Each paper was scrutinized to identify experimental details related to emotional contagion processes. The literature on emotional contagion, which has witnessed a drastic surge in number in the last decades (Fig. 2C), is quite heterogeneous in types and nature of experimental manipulations. Typically, studies on rodent emotional contagion featured an individual experiencing a specific emotional state while another individual witnessed the emotional display (Atsak et al., 2011b). Although, the emotional display was generally produced by a conspecific, in some cases only odors (Kiyokawa et al., 2009), auditory (Wöhr and Schwarting, 2007) or visual cues (Nakashima et al., 2015) from other emotionally-stimulated conspecifics were presented to the witness.

We also identified a wide range of dependent variables reported as proxy measures of emotional contagion. Overall, most effect sizes (54%) used freezing as a dependent variable (Fig. 2D), believed to reflect anxiety and fearful states in rodents. Among the remaining effect sizes, more than a fourth (27%) used pain-related dependent variables, typically paw withdrawal latencies, mechanical pain threshold, writhing and tail pinch tests. The remaining effect sizes (18%) used other, diverse dependent variables, such as defecation rate, latency to move or licking behavior.

For each effect size computed, we characterized the type of emotion that was transferred to the measured animal and thus elicited the emotional contagion response. We followed the classification of emotions proposed by (Panksepp, 2011) (Fig. 2E) which distinguished between positive (care, lust and play) and negative emotions (aggression, pain/panic and fear/anxiety). Using this classification, we found a profound lack of studies investigating emotional contagion of positive emotions. Among these, no studies were found to use lust or care emotional categories. A subset of studies used emotional stimuli classified as seeking (n = 28), which represented studies that measured approach to ultrasonic vocalizations playback, see (Wöhr and Schwarting, 2007)). Most experiments investigated emotional contagion using negative emotions (fear/anxiety: n = 293, pain: n = 134, aggression: n = 2). Within the negative emotion category, 64% of total studies used freezing as a dependent variable (fear/anxiety) and 29% used pain-related measures (Fig. 2E). For the negative emotions, we clustered studies into three pools: 1) fear/anxiety, 2) pain and 3) other category, which included studies that used a variety of dependent variables. This ensured that the analysis of fear and pain emotions was based on similar dependent variables. Overall, because of the substantially larger number of studies investigating fear and pain, we focused on these two categories in this meta-analysis.
3.2. Rats and mice show comparable levels of emotional contagion

This meta-analysis estimated an overall positive medium effect size for the emotional contagion of rats and mice with a grand mean of $r = 0.4$ ($z = 15.0$ [0.35 to 0.44], $p < 0.0001$, CI: [0.35 to 0.44], Fig. 2G). The robustness of these results was confirmed with a file drawer analysis ($r = 0.48$, CI: [0.4 to 0.54]) and a lower magnitude ($r = 0.89$, CI: [0.74 to 0.94]). This suggests that: 1) either this measure is a poor indicator of the level of emotional contagion or 2) the paradigms used to extract these measures do not reflect emotional contagion.

3.3. Strain modulates emotional contagion in mice but not in rats

We explored whether certain strains show stronger emotional contagion than others, by clustering effect sizes according to strain (Fig. 3B, C). In mice, we identified four major strains, which accounted for 90% of the studies: C57BL/6 ($N = 120$), CD1 ($N = 49$), 129S1/S4 ($N = 12$) and CF1 ($N = 16$). We found a large unbalance of the emotion scores (Fig. 3A), while rats show a similar effect of this category to that measured in fear (rat: $r = 0.33$, CI: [0.22 to 0.44]). However, mice were the preferred species to investigate emotional contagion of both fear (mice: $N = 111$, rat: $N = 74$) and pain (mice: $N = 82$, rat: $N = 22$).

For the other emotional dimensions (“other” sublevel in Fig. 3A), while rats show a similar effect of this category to that measured in fear and pain ($r = 0.35$, CI: [0.19 to 0.51]), the average effect was close to 0 and non-significant in mice ($r = 0.08$, CI: [-0.17 to 0.32]). This difference could be driven by the fact that a larger number of studies in mice (71% in mice vs 15% in rats) in the “other” category measured emotional contagion by quantifying approach to a negative stimulus. This suggests that: 1) either this measure is a poor indicator of the level of emotional contagion or 2) the paradigms used to extract these measures do not reflect emotional contagion.
Table 3
List of included studies (reference), together with publication year, number of effect sizes extracted and that were used for behavioral analysis (ES-Behavior) and number of effect sizes extracted and that were used for physiology analysis (ES-Physiology: c-fos and corticosterone).

| Study                         | Year | ES Behavior | ES Physiology |
|-------------------------------|------|-------------|---------------|
| (Anderson, 1939)             | 1939 | 1           | 0             |
| (Davitz and Mason, 1955)     | 1955 | 2           | 0             |
| (Church, 1959)               | 1959 | 1           | 0             |
| (Corman and Loeb, 1961)      | 1961 | 1           | 0             |
| (Baum, 1969a)                | 1969 | 2           | 0             |
| (Uno et al., 1973)           | 1973 | 2           | 0             |
| (Armario et al., 1982)       | 1982 | 1           | 1             |
| (Armario et al., 1983)       | 1983 | 9           | 3             |
| (Coles, 1991)                |      | 1           | 0             |
| (White and Galef, 1998)      | 1998 | 1           | 0             |
| (Livio Terranova et al., 1999) | 1999 | 0           | 2             |
| (Kavaliers et al., 2001a)    | 2001 | 2           | 0             |
| (Kavaliers et al., 2001b)    | 2001 | 9           | 0             |
| (Kiyokawa et al., 2004a)     | 2004 | 1           | 1             |
| (Kavaliers et al., 2005)     | 2005 | 6           | 0             |
| (Langford, 2006)             | 2006 | 17          | 0             |
| (Kinapska et al., 2006a)     | 2006 | 1           | 6             |
| (Kiyokawa et al., 2007)      | 2007 | 6           | 15            |
| (Wohr and Schwarting, 2007)  |      | 7           | 0             |
| (Wohr and Schwarting, 2008)  | 2008 | 1           | 0             |
| (Sadananda et al., 2008)     |      | 0           | 22            |
| (Bredy and Barad, 2009)      | 2009 | 5           | 0             |
| (Chen et al., 2009)          | 2009 | 6           | 0             |
| (Kiyokawa et al., 2009)      | 2009 | 3           | 2             |
| (Guzman et al., 2009)        | 2009 | 7           | 0             |
| (Masuda and Aou, 2009)       | 2009 | 2           | 0             |
| (Fikennerschmidt et al., 2009) | 2009 | 1           | 0             |
| (Wohr and Schwarding, 2009)  |      | 2           | 0             |
| (Gioiosa et al., 2009)       | 2009 | 3           | 0             |
| (Kim et al., 2010)           | 2010 | 2           | 0             |
| (Jeon et al., 2010)          | 2010 | 28          | 0             |
| (Kinapska et al., 2010)      | 2010 | 7           | 0             |
| (Langford et al., 2010a)     | 2010 | 3           | 0             |
| (Brechtz et al., 2010)       | 2010 | 1           | 0             |
| (Nakayasu and Kato, 2011)    | 2011 | 1           | 0             |
| (Kodama et al., 2011)        | 2011 | 1           | 0             |
| (Atsuk et al., 2011a)        | 2011 | 2           | 0             |
| (Langford et al., 2011)      | 2011 | 9           | 1             |
| (Watanabe, 2012)             | 2012 | 4           | 0             |
| (Kiyokawa et al., 2012)      | 2012 | 1           | 0             |
| (Parsana et al., 2012a)      | 2012 | 1           | 0             |
| (Parsana et al., 2012b)      | 2012 | 2           | 0             |
| (Kim et al., 2012)           | 2012 | 1           | 0             |
| (Sanders et al., 2013)       | 2013 | 4           | 0             |
| (Takahashi et al., 2013)     | 2013 | 1           | 5             |
| (Kiyokawa et al., 2015)      | 2015 | 1           | 11            |
| (Younusifshah and Rosenkrantz, 2017) | 2017 | 2           | 0             |
| (Nowak et al., 2013)         | 2013 | 3           | 0             |
| (Masuda et al., 2013)        | 2013 | 3           | 0             |
| (Bowen et al., 2013)         | 2013 | 1           | 12            |
| (Jung et al., 2013)          |      | 1           | 0             |
| (Kashieky et al., 2014a)     | 2014 | 0           | 1             |
| (Kim et al., 2014)           | 2014 | 2           | 0             |
| (Gonzalez-Lienares et al., 2014a) | 2014 | 3           | 0             |
| (Kiyokawa et al., 2014a)     | 2014 | 1           | 4             |
| (Jones et al., 2014)         | 2014 | 1           | 0             |
| (Li et al., 2014a)           | 2014 | 6           | 1             |
| (Hunter, 2014)               |      | 1           | 0             |
| (Debiec and Sullivan, 2014)  | 2014 | 4           | 6             |
| (Kiyokawa et al., 2014b)     | 2014 | 2           | 2             |
| (Willemsen et al., 2014)     | 2014 | 5           | 0             |
| (Hodges et al., 2014)        | 2014 | 0           | 2             |
| (Nakahina et al., 2015)      | 2015 | 2           | 0             |
| (Meyza et al., 2015)         | 2015 | 2           | 18            |
| (Pizzato et al., 2015)       | 2015 | 1           | 0             |
| (Irish and Taylor, 2015)     | 2015 | 5           | 0             |
| (Hishihora et al., 2015)     | 2015 | 1           | 0             |
| (Suzuki and Lucas, 2015)     | 2015 | 2           | 0             |
| (Lee and Nob, 2015)          | 2015 | 2           | 0             |

(ES-Behavior: r = 0.48, CI: [0.32 to 0.61]; ES-Physiology: r = 0.51, CI: [0.43 to 0.51]), while differences were found for emotional contagion of pain for different strains (CF1: F = 0.76, CI: [0.61 to 0.86]; CD1: F = 0.15, CI: [0.02 to 0.27]; C57BL/6: F = 0.28, CI: [0.13 to 0.44]). We found significant differences in the emotional contagion of pain (Fig. 3C) between C57BL6, CD1 and CF1 (Q = 57.7, p < 0.001), with CF1 strain showing higher emotional contagion for pain compared to C57BL6 (Q = 15.03, p < 0.001) and CD1 (Q = 23.59, p < 0.001). In addition to being used for researching a specific emotion, same strains were also exposed to comparable experimental designs (Fig. 3D). For instance, most studies that used C57BL/6 as experimental model
investigated fear processes, while CD1 and CF1 strains were used exclusively for pain research. Moreover, we also observed a misbalance in the dependent variables used to quantify emotional contagion for pain. While fear and anxiety were in great majority measured using freezing, pain was quantified using variables such as mechanical pain or thermal threshold, writhing or licking. It is worthwhile noting that all studies of emotional contagion of pain that used CF1 animals measured thermal sensitivity (e.g., latency to react to hot plate), while studies that used C57BL/6 used paw withdrawal or writhing as an experimental measurement. Thus, the observed strain differences could be due to the type of measurement used, rather than differences in intrinsic characteristics of a given strain. Altogether, these results highlight potential between-strain differences, but also emphasize the need to populate each strain’s published data with additional, so far absent experimental variables. More research directly comparing different species and/or strains is needed, although such findings are starting to gather attention in the recent literature (Chen et al., 2009; Keum et al., 2016; Han et al., 2019).

Rats: In rats, we identified three major strains used in the literature: Wistar (N = 68), Sprague Dawley (N = 54) and Long Evans (N = 12).
remaining 12 studies used a range of unconventional strains (Fig. 3A). As observed in mice, there was a strong association between emotion tested and strain used in rats (Fig. 3D). The majority of studies investigating fear processes used Wistar (fear: N = 43; pain: N = 4), while most studies addressing pain processes used Sprague Dawley (fear: N = 23; pain: N = 20). Using the same caution as for the results obtained in mice, our data suggest that all three main strains (SD: $\tau = 0.42$, CI: [0.28 – 0.54], Wistar: $\tau = 0.55$, CI: [0.38 – 0.67], LE: $\tau = 0.49$, CI: [0.25 – 0.68]) showed a positive comparable effect size for emotional contagion of fear (Fig. 3B), with no observable strain differences ($Q = 0.017$, $p = 0.895$). This finding matches the results of recent studies (not included in this meta-analysis) that have directly compared multiple strains (Han et al., 2019), and found no significant difference.

Between strains comparison for emotional contagion of pain was not possible (Fig. 3C), because all pain studies were conducted in SD. Within SDs, emotional contagion of pain showed a medium effect size ($\tau = 0.4$, CI: [0.17 – 0.65]). The majority of these studies used mechanical threshold as a measure of pain contagion (Fig. 3D). Another interesting observation was that, overall, there was a clear preference for albino rat strains such as Wistar and Sprague Dawley, over Long Evan rats. This might be due to the general belief that albino rats are calmer and easier to handle than Long Evan rats, or historical preferences for albino strains in the literature. In fact, the first study in our meta-analysis that uses Long Evans to quantify emotional contagion was published in 1998, that is 59 years after the first study using an albino rat (Anderson, 1939). While the number of effect sizes collected in Long Evans is low for emotional contagion of fear and anxiety ($N = 6$) and no effect sizes could be computed for pain studies, the average effect size of studies performed in Long Evans is high and comparable to the ones observed in the two albino strains (Table 4).

### Table 4

Summary of results for species and strains. Table shows the name of the modulator (Species and Strain), levels examined for each modulator (Levels), the sublevels investigated (fear, pain, and others), the mean effect size value ($\tau$) and the confidence interval (CI), the z score value, heterogeneity value as measured by $I^2$ and sample size (n). Red values indicate non-significant z scores. 

| Modulator | Levels | Sublevels | $\tau$ mean-CI (low-high) | z | $I^2$ % | n |
|-----------|--------|-----------|--------------------------|---|---------|---|
| Fear      | Rat    | Pain      | 0.39 (0.17 – 0.62)       | 3.4 | 51.2 | 22|
|           |        | Other     | 0.35 (0.19 – 0.51)       | 4.3 | 73.3 | 50|
|           |        | Species   |                          |    |        |   |
|           |        | Species   |                          |    |        |   |
|           |        | Wistar    | 0.48 (0.24 – 0.54)       | 12.9 | 32.4 | 111|
|           |        | Mice      | 0.33 (0.22 – 0.44)       | 5.83 | 76.5 | 82|
|           |        | Other     | 0.08 (0.17 – 0.32)       | 0.61 | 59.1 | 25|
|           |        | Strain    |                          |    |        |   |
|           |        | C57BL/6   | 0.55 (0.38 – 0.67)       | 6.1 | 80.4 | 43|
|           |        | Sprague   | 0.42 (0.28 – 0.54)       | 5.6 | 52.9 | 23|
|           |        | Dawley    | 0.4 (0.17 – 0.65)        | 3.23 | 55  | 20|
|           |        | Long      | 0.49 (0.25 – 0.68)       | 3.85 | 30.8 | 6|
|           |        | Evans     |                          |    |        |   |
|           |        | Fear      | 0.51 (0.43 – 0.51)       | 12.33 | 33 | 87|
|           |        | Pain      | 0.28 (0.13 – 0.44)       | 3.6  | 0    | 18|
|           |        | CD1       | 0.15 (0.02 – 0.27)       | 2.34 | 78.8 | 46|
|           |        | CF1       | 0.76 (0.61 – 0.86)       | 6.6 | 44.9 | 11|
|           |        | 129S1/ S4 | 0.48 (0.32 – 0.61)       | 5.8  | 0    | 12|

3.4. **Familiarity effect is dependent on the type of emotional stimulus**

How familiarity between two animals influences the contagion of an emotion has been one of the most investigated variables in this type of paradigms (Kavaliros et al., 2005; Knapska et al., 2010; Jones et al., 2014; Chen et al., 2017; Pisansky et al., 2017; Pitcher et al., 2017; Zhou et al., 2018; Gonzalez-Liencres et al., 2014b; Langford et al., 2006, 2010b; Li et al., 2014b). The accepted hypothesis in the field is that animals that are familiar with each other will have a stronger emotional contagion response (here coded as a positive effect size). Interestingly, when grouping all studies, we found no consistent differences in transfer of emotions of familiar and unfamiliar cage mates for mice or rats (familiar vs unfamiliar; mice: fear: $Q = 0.794$, $p = 0.373$; mice pain: $Q = 0.19$, $p = 0.663$; rat fear: $Q = 0.642$, $p = 0.423$; rat pain: $Q = 0.029$, $p = 0.865$, Table 5, Fig. 4A). One possibility for this negative finding is the large between-study differences in familiarity length (number of days animals were together prior to test, total range: [1 to 196] days, $\bar{x} = 17.9$). We thus ran an additional analysis where we only included studies where dyads were familiar for at least 6 days (median familiarity value of the total range). This analysis yielded similar non-significant results (rat fear: $Q = 1.778$, $p = 0.182$; rat pain: $Q = 0.029$, $p = 0.865$; mice fear: $Q = 0.257$, $p = 0.612$; mice pain: $Q = 2.014$; $p = 0.156$). To further examine the role of familiarity in emotional contagion, we looked at how the relationship length (cutoff at 100 days to exclude extreme values) correlated with the contagion response for fear (Fig. 4B). No enough data was available to run the equivalent analysis for pain contagion. While mice showed a trend in a positive relationship between time spent together and fear contagion levels ($\tau = 0.29$, $p = 0.07$), rats showed a strong negative correlation between familiarity length and emotional contagion response ($\tau = -0.49$, $p = 0.02$). However, it should be noted, that there was a difference in the range of relationship days used for studies done in rats vs mice (Fig. 4C), with studies in mice using a much more extensive range of relationship days. That familiarity might modulate emotional contagion differently in mice and rats requires additional scrutiny, with experiments specifically designed to test this parameter.

In line with this idea, we conducted a separate analysis using studies which specifically tested the role of familiarity in rats (Armario et al., 1982; Knapska et al., 2010; Jones et al., 2014; Rogers-Carter et al., 2018; Li et al., 2014b) and mice (Kavaliros et al., 2005; Langford, 2006; Martin et al., 2015; Gonzalez-Liencres et al., 2016; Pisansky et al., 2017; Pitcher et al., 2017; Zhou et al., 2018; Ueno et al., 2018; Langford et al., 2010b). These studies showed that while mice have a stronger pain contagion response to a familiar animal compared to an unfamiliar one ($Q = 20.425$, $p < 0.001$), this familiarity effect was extinguished for fear contagion ($Q = 16.7$, $p = 0.164$). Interestingly, except for one, studies that found increased pain contagion used abdominal pain as the dependent variable, indicating that perhaps increased response to a familiar in distress depends on the type of pain stimulus. To test this idea, we repeated the familiarity analysis with studies that investigated pain contagion in mice (not enough studies in rats), dividing the response based on the type of pain. Confirming our hypothesis, we found that only in studies using contagion to abdominal pain (i.e., writhing) mice showed an increased response to familiar compared to unfamiliar conspecific ($Q = 13.557$, $p < 0.001$), while there was no difference in the response to familiar vs unfamiliar conspecifics in other types of pain. This differential effect based on the type of emotional stimulus could be driven by differences in the ecological validity of the stimulus (i.e., mice are more likely to witness another with abdominal pain than being fearful due to footshocks).

3.5. **Age modulates differentially fear contagion in rats and mice**

The age of animals used in the emotional contagion literature had a large range for both rats (total range [28 – 275] days, $\bar{x} = 66.13$) and mice (total range [21 – 330] days, $\bar{x} = 77.7$) (Fig. S1). A linear regression
analysis (Fig. 4D) showed that while in rats age is negatively correlated with the amount of fear contagion ($r = -0.32, p = 0.02$), the opposite is true in mice ($r = 0.37, p = 0.0001$). This effect could reflect species specific age-related changes in additional factors such as animal size and weight (as animals get older, they gain more weight), animal cognition and behavior.

3.6. Sex does not modulate emotional contagion in rats and mice

Given the low number of effect sizes for females, we kept the analysis investigating an effect of sex on emotional contagion at the species level. We find no evidence for an effect of sex on emotional contagion of pain or fear in rats or mice (Fig. 4E, Table 5; all $p > 0.05$). In addition, qualitative examination (not enough effect sizes for a quantitative analysis) of studies that specifically looked at sex effects on contagion, revealed no clear effect of sex on contagion of fear nor pain. This is in agreement with findings from a recent study showing that although female rats freeze less compared to males when experiencing shock, the fear contagion response is comparable between males and females (Han et al., 2019b). It is important to note that overall, only 3.5 % of all the studies used females, 10.1 % used both females and males and 86.4 % used males, which highlights how underrepresented is the use of females in studies investigating emotional contagion in rodents. Although, this bias is not specific to empathy research, it is worth underscoring the severity of the problem and highlighting the importance of using both females and males, which recent studies have highlighted (Plesnay et al., 2017). Hence, our results on sex should be taken with caution, since we could not dwell deeply into the role of this effects due to lack of data points.

3.7. Single housing potentiates emotional contagion in rats and mice

In behavioral paradigms investigating social phenomena, whether animals are single or group-housed before or during the experimental measures is often seen as a relevant factor and reported in the method section. However, this variable has not received much attention in studies investigating emotional contagion and was included as a potential modulating factor in this meta-analysis (Table 5, Fig. 4F). We found that compared to group-housed rats, single-housed rats displayed higher levels of emotional contagion of fear (rat alone: $r = 0.65, CI: [0.47 to 0.77]$; rat group: $r = 0.41, CI: [0.29 to 0.52]$; rat alone vs group $Q = 5.906, p = 0.015$). In mice, although grouped-house animals showed higher levels of emotional contagion of fear compared to single-housed mice, this difference did not reach statistical significance (mice alone: $r = 0.57, CI: [0.35 to 0.79]$; mice group: $r = 0.43, CI: [0.36 to 0.49]$; mice alone vs group $Q = 0.724, p = 0.395$).

In paradigms measuring emotional contagion for pain, we found that effects in single-housed mice more than tripled compared to group-housed mice (mice alone: $r = 0.62, CI: [0.5 to 0.73]$; mice group: $r = 0.17, CI: [0.05 – 0.27]$; $Q = 24.247, p < 0.001$) (Table 5, Fig. 4F). This increased contagion could be due to the fact that social isolation triggers a series of physiological changes that increase sensitivity to anxiety and fear-related behaviors (Lukkes et al., 2009). Also, social isolation might make conspecifics more salient, thereby boosting the reaction to other’s emotions.

3.8. Differences in testing related parameters can affect emotional contagion

**Pre-exposure**: It is a common view that first-hand experience with a distress-causing stimulus, can potentiate the emotional contagion response to that stimulus. To take this aspect into account, the behavioral design of paradigms testing emotional contagion sometimes include a pre-exposure session, in which the animal that will witness the emotion of another, experiences itself the stimulus inducing that emotion (Fig. 5A, Table 6). In rats, we found that pre-exposure almost doubles the emotional contagion response to fear (Fig. 5B; not pre-exposed: $r = 0.29, CI: [0.12 to 0.45]$; pre-exposed: $r = 0.55, CI: [0.43 to 0.64]$; comparison: $Q = 4.058, p = 0.044$). For pain contagion, not pre-exposed animals had a slightly higher emotional contagion response than pre-exposed animals ($r = 0.32, CI: [-0.8 to 0.94]$; pre-exposed: $r = 0.42, CI: [0.27 to 0.55]$), but the low number of published studies that used pre-exposure in pain paradigms prevented us from performing statistical comparisons. In contrast, pre-exposure in mice had no effect on contagion to fear (not pre-exposed: $r = -0.44, CI: [0.37 to 0.5]$; pre-exposed: $r = -0.48, CI: [0.35 to 0.58]$; comparison: $Q = 0.177, p = 0.674$) or pain (not pre-exposed: $r = 0.32, CI: [0.2 to 0.43]$; pre-exposed: $r = 0.23, CI: [0.14 to 0.54]$; comparison: $Q = 0.988, p = 0.754$). This lack of pre-exposure effect in mice might explain why this session is rarely included in mice studies (13 % of studies), in comparison to rat studies (66 % of studies). The effect of pre-exposure in contagion of fear we find in rats, matches the finding of studies that explicitly tested for this effect

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Table 5
Summary of results for familiarity, sex and housing. Table shows the name of the modulator (e.g., Familiarity), Species (Rat and mice), levels examined for each modulator (Levels), the sublevels investigated (e.g. fear), the mean effect size value $r$ with the confidence interval (CI), the z score value, heterogeneity value as measured by $I^2$ and sample size (n). Red values indicate non-significant z scores, or modulators with a sample size (n) lower than 5.

| Modulator | Species | Levels | Sublevels | $r_{\text{mean}}$ CI (low-high) | $z$ | $I^2$ % | n |
|-----------|---------|--------|-----------|-------------------------------|-----|--------|----|
| Familiarity | Rat | Unfamiliar | Fear | 0.58 (0.41–0.71) | 5.75 | 81.2 | 35 |
| | | Cagemates | Fear | 0.42 (0.27–0.55) | 5.18 | 51.7 | 19 |
| | Mice | Unfamiliar | Pain | 0.41 (0.001–0.71) | 1.97 | 14.1 | 3 |
| | | Cagemates | Pain | 0.39 (0.16–0.57) | 3.29 | 54.1 | 19 |
| | | Unfamiliar | Pain | 0.41 (0.3–0.49) | 2.1 | 81.9 | 14 |
| | | Cagemates | Pain | 0.42 (0.33–0.51) | 5.66 | 62.1 | 36 |
| | | Unfamiliar | Fear | 0.29 (0.11–0.45) | 7.48 | 27.3 | 39 |
| | | Cagemates | Fear | 0.32 (0.22–0.42) | 8.3 | 32.7 | 57 |
| | | Couples | Fear | 0.52 (0.26–0.64) | 3.5 | 45.9 | 6 |
| | Sex | Rat | Female | Fear & Pain | 0.43 (0.25–0.59) | 4.2 | 17.4 | 6 |
| | | Male | Fear & Pain | 0.48 (0.37–0.57) | 8.3 | 72.2 | 88 |
| | | Mice | Female | Fear & Pain | 0.57 (0.39–0.79) | 5.52 | 0 | 4 |
| | | Male | Fear & Pain | 0.42 (0.35–0.49) | 10.6 | 65.3 | 160 |
| | | Rat | Alone | Fear | 0.65 (0.47–0.77) | 5.7 | 80 | 25 |
| | | Group | Fear | 0.41 (0.29–0.52) | 6.2 | 66.2 | 47 |
| | | Alone | Pain | – | – | – | 0 |
| | Housing | Mice | Group | Pain | 0.38 (0.17–0.55) | 3.4 | 51.2 | 22 |
| | | Alone | Fear | 0.57 (0.35–0.79) | 5.1 | 27.9 | 7 |
| | | Group | Fear | 0.43 (0.36–0.49) | 1 | 34.7 | 96 |
| | | Alone | Pain | 0.62 (0.5–0.73) | 7.7 | 43.3 | 21 |
| | | Group | Pain | 0.17 (0.05–0.27) | 2.7 | 77.9 | 51 |
In contrast, in mice the effect of pre-exposure is not clear, as some studies that explicitly examined the role of pre-exposure find that it is necessary to pre-expose animals (Sanders et al., 2013), while other studies, in agreement with our results, find that it is not required in mice (Kavaliers et al., 2001b, 2005).

One possibility that might account for the between-species difference in pre-exposure effect is a systematic difference in experimental procedures. For instance, if the paradigms used to test emotional contagion had differences in the timing of pre-exposure (exposure to stimuli alone) relative to interaction (transfer of emotion) and test (measure of dependent variable). Although, there were a few studies with a substantial delay between pre-exposure and test, the majority of studies in both rats and mice conducted pre-exposure and test on the same day (Table 6, “PreExp Day”). Moreover, there was no effect of delay between pre-exposure and test in mice or rat (Fig. 5C), suggesting that additional underlying variables might drive the between species difference.

(Atsak et al., 2011b; Han et al., 2019). In contrast, in mice the effect of pre-exposure is not clear, as some studies that explicitly examined the role of pre-exposure find that it is necessary to pre-expose animals (Sanders et al., 2013), while other studies, in agreement with our results, find that it is not required in mice (Kavaliers et al., 2001b, 2005).

One possibility that might account for the between-species difference in pre-exposure effect is a systematic difference in experimental procedures. For instance, if the paradigms used to test emotional contagion had differences in the timing of pre-exposure (exposure to stimuli alone) relative to interaction (transfer of emotion) and test (measure of dependent variable). Although, there were a few studies with a substantial delay between pre-exposure and test, the majority of studies in both rats and mice conducted pre-exposure and test on the same day (Table 6, “PreExp Day”). Moreover, there was no effect of delay between pre-exposure and test in mice or rat (Fig. 5C), suggesting that additional underlying variables might drive the between species difference.
Fig. 5. Pre-exposure and testing conditions influence emotional contagion in rats and mice. (A) Diagram summarizing the timing of different experimental events. In some studies test animals were pre-exposed (PreExp) to the emotion eliciting stimuli prior to emotion transfer (ET). During the ET, the target animal witnessed the response of another animal to an emotional eliciting stimulus. The measurement of emotional contagion was done online during ET or offline after ET. (B) Box plot showing the distribution of effect sizes (r) for pre-exposed and not pre-exposed rats and during contagion of fear (blue) and pain (red). (C) Box plot showing the distribution of effect sizes (r) for rats that had the pre-exposure procedure on the same day (Same) and different day (Different) as the emotion (fear) transfer session. (D) Box plot showing the distribution of effect sizes (r) for rats and mice that were tested alone and not alone during contagion of fear (blue) and pain (red). (E) Box plots showing the distribution of effect sizes (r) for rats and mice that were measured during (online) or after the emotion transfer (offline). (F) Box plot showing the distribution of effect sizes (r) for rats and mice that witnessed demonstrators experience fear or pain emotions when the dependent variable measured was fear (blue colouring). For the box plots: 1) outliers are indicated by black circles, 2) black line indicates the mean effect size value (r) and 4) green line indicates median effect size value (r_m). For comparisons: *p<0.05, NS=not significant and nt=not tested (for comparisons in which one of the groups had less than 5 studies).
Table 6
Summary of results for test related factors. Table contains the name of the modulator: 1) whether an animal experienced pre exposure or not (PreExp), 2) whether an animal was tested alone or not (Testing condition), 3) emotion transferred during interaction (emotion transferred), 4) time of the pre-exposure relative to emotional transfer (PreExp time), and 5) time of measurement relative to emotional transfer (measure time). In addition, the table contains information about the Species (Rat and mice), levels examined for each modulator (Levels), the sublevels investigated (e.g. fear), the mean effect size value for the species differences in shock parameters during emotion transfer, with mice having a significantly higher number of shocks (mice: \( n = 37 \)), rats having a significantly higher number of shocks (rats: \( n = 50 \)), and mice tested in group vs alone-tested animals, with mice tested in group: \( r = 0.31, CI: [0.09;0.53] \), comparison: \( Q = 0.08, p = 0.014 \). In rats, we observed increased fear contagion in group vs alone-tested animals, with rats tested in group: \( r = 0.55, CI: [0.41 to 0.67] \), comparison: \( Q = 3.98, p = 0.022 \). Indeed, we found that during pre-exposure, while there were no differences in the shock intensity, inter-stimulus intervals or the time thresholds or anxiety levels (Smith et al., 2016). We found that mice had a contagion response without the need of a pre-exposure.

| Modulator | Species | Levels | Sublevels | \( t \) (mean-Cl (low-high)) | \( z \) | \( \% \) | \( n \) |
|-----------|---------|--------|-----------|-----------------------------|-------|-------|------|
| PreExp    | Rat     | Pre-exp| Fear      | 0.55 (0.43 – 0.64)          | 8.1   | 75    | 59   |
|           |         | No pre exp| Fear | 0.29 (0.12 – 0.45)         | 3.2   | 43    | 15   |
|           |         | Pre-exp Pain| Pain | 0.32 (0.27 – 0.55)         | 5.22  | 0     | 18   |
|           | Mice    | Pre-exp Fear      | 0.48 (0.35 – 0.58)         | 6.9   | 19    | 20   |
|           |         | No pre-exp Fear | 0.44 (0.37 – 0.5)         | 11.2  | 34.7  | 91   |
|           |         | Pre-exp Pain      | 0.23 (0.14 – 0.54)         | 1.21  | 67    | 3    |
|           |         | No pre-exp Pain   | 0.32 (0.2 – 0.43)         | 4.99  | 81    | 64   |
| PreExp Day| Rat     | Same day Fear | 0.52 (0.4 – 0.64)         | 6.8   | 75.5  | 49   |
|           |         | Diff day Fear     | 0.47 (0.17 – 0.69)         | 2.97  | 75.6  | 9    |
|           | Mice    | Same day Pain     | 0.32 (-0.8 – 0.94)        | 0.45  | 90.1  | 4    |
|           |         | Diff day Pain     | –                     | –     | –     | 0    |
| Testing condition | Mice    | Alone Fear | 0.39 (0.26 – 0.5) | 5.8   | 46.8  | 26   |
|           |         | Not alone Fear   | 0.55 (0.41 – 0.67)        | 6.7   | 78.3  | 48   |
|           |         | Alone Pain | 0.36 (0.11 – 0.6) | 2.86  | 52.8  | 20   |
|           | Mice    | Not alone Pain | 0.62 (0.24 – 0.85) | 0     | 2.88  | 0    |
| Transferred | Mice    | Alone Fear | 0.31 (0.09 – 0.53) | 2.72  | 73.5  | 16   |
|           |         | Not alone Fear   | 0.48 (0.43 – 0.53)        | 15.3  | 0     | 95   |
|           |         | Alone Pain | 0.37 (0.21 – 0.52) | 4.6   | 14.5  | 21   |
|           | Mice    | Not alone Pain | 0.32 (0.19 – 0.45) | 4.8   | 81.2  | 61   |
| Measurement Time | Mice    | Online Fear | 0.55 (0.41 – 0.65) | 7.34  | 76.9  | 56   |
|           |         | Offline Fear | 0.41 (0.26 – 0.52) | 5.5   | 30.1  | 15   |
|           |         | Offline Pain | 0.44 (0.36 – 0.51) | 10.3  | 0     | 11   |
|           | Mice    | Offline Fear | 0.48 (0.43 – 0.53) | 15.3  | 0     | 95   |
|           |         | Offline Pain | 0.3 (0.19 – 0.4) | 5.19  | 77.1  | 74   |
| Sensory   | Rat     | All Fear | 0.51 (0.4 – 0.6) | 7.76  | 75.35 | 62   |
| Modality  | All Pain | Not all Fear | 0.41 (0.22 – 0.57) | 4     | 18.8  | 10   |
|           |         | All Pain | 0.39 (0.17 – 0.57) | 3.57  | 53.15 | 21   |
|           | Mice    | Not all Fear | 0.45 (0.39 – 0.5) | 12.8  | 32.7  | 109  |
|           | All Pain | 0.37 (0.32 – 0.8) | 1.06 | 47.8  | 2    |
|           | Mice    | All Pain | 0.32 (0.2 – 0.43) | 5.01  | 81.2  | 62   |

Social testing situation: While in some experiments the measurement of contagion was performed when the animal was alone (rat: \( N = 46 \); mice: \( N = 37 \)), in the majority of studies the measurement was performed when the animal was in a social context (rat: \( N = 50 \); mice: \( N = 156 \); Table 6, 'Testing condition'). One example of such paradigm was exposing a target animal to emotions of a conspecific, and then separating the target animal and testing the emotional contagion response in a socially isolated situation (alone), to extract measures such as pain threshold or anxiety levels (Smith et al., 2016). We found that mice tested alone showed significantly reduced fear contagion compared to animals that were tested in together with a demonstrator animal (Fig. 5D; mice alone: \( r = 0.31, CI: [0.09;0.53] \), mice tested in group: \( r = 0.55, CI: [0.43 to 0.53] \), comparison: \( Q = 5.98, p = 0.014 \)). In rats, we also observed increased fear contagion in group vs alone-tested animals, however this difference did not reach statistical significance (rat alone: \( r = 0.39, CI: [0.26 to 0.5] \), rat tested in group, \( r = 0.55, CI: [0.41 to 0.67] \), comparison: \( Q = 3.023, p = 0.082 \). However, being alone or in group during testing procedures seemed to be only important for contagion of fear, since the social testing conditions had no effect in paradigms probing the contagion of pain (mice alone: \( r = 0.37, CI: [0.21 to 0.52] \),
mice tested in group: \( \tau = 0.32, CI: [0.19 to 0.45]; \) comparison: \( Q = 0.180, p = 0.671; \) not enough data in rats).

Further, we considered whether the “alone” testing might be homologous to measurements that happened after emotional transfer. It that were true, that mice tested in an isolated situation show a reduced contagion response could be driven not by the social situation, but by the timing of the contagion measure relative to emotion transfer. We categorized this timing as online, when the contagion measure was during the emotional transfer and offline, when the contagion measurement happened after the emotion transfer (Fig. S2). Overall, in most studies emotional contagion was measured during emotional transfer (i.e., online measure; 70 % of rat studies, and 88 % of mice studies; Table 6). We find that mice show stronger fear contagion when the contagion measure happens during emotional transfer (\( Q = 6, p = 0.014 \)). This effect was not dependent on the emotion experienced by the demonstrator (Fig. S2).

**Sensory Modalities:** Emotional contagion depends on an effective communication of the affective state from the source of the emotion to the receiver. The receiver gathers all information about the source through its sensorial system but are all sensory modalities equally effective is a question that remains unclear.

We found that emotional contagion was higher when all sensory modalities were recruited during emotional transfer, compared to studies in which the measured animal was missing one or more sensory modalities (e.g., anosmic animals), although this difference did not reach statistical significance in rats (fear-all: \( \tau = 0.51, CI: [0.4 to 0.6] \), fear not all: \( \tau = 0.41, CI: [0.22 to 0.57] \); not enough data for pain, \( p < 0.05 \) for all) or in mice (fear-all: \( \tau = 0.45, CI: [0.39 to 0.5] \); fear not all: \( \tau = 0.37, CI: [0.32 to 0.8] \); pain-all: \( \tau = 0.32, CI: [0.2 to 0.43] \); pain not all: \( \tau = 0.22, CI: [-0.07 to 0.48] \), \( p < 0.05 \) for all).

Similarly, to other modulators, a significant amount of studies (\( N = 21 \)) were specifically designed to investigate the effect of certain sensory modalities in the transfer of emotions (Fig. 6B). Among those studies, we found that animals with blocked olfaction (rat: \( \tau = -0.65, CI: [-0.94 to 0.21] \); no mice data) or vision (mice: \( \tau = -0.41, CI: [-0.92 to 0.6] \), no rat data) had an overall reduction in the contagion of fear and pain. Given these results we would expect that studies in which a single modality was used to convey information about the emotional level of a conspecific, little or no contagion would be observed. In contrast to our expectations, studies in which emotional transfer was done solely through the olfactory (rat: \( \tau = -0.20, CI: [-0.07 to 0.48] \), mice: \( \tau = -0.69, CI: [0.44 to 0.85] \) or auditory channel (i.e., USV, mice: \( \tau = 0.59, CI: [0.35 to 0.77] \), no rat data) showed increased contagion when compared to controls in which a non-emotional stimulus was used as control. However, because
of the small number of animals and variability in the data, we have to take these results with caution. Together this suggest that emotional contagion is a multi-sensory phenomenon, in which single modalities can suffice in conveying emotional contagion, but where full effect strength is reached by a multi-modality transfer of emotion.

3.9. Physiological measures of emotional contagion

Corticosterone: To examine whether contagion of fear and pain also results in increased levels of stress some studies measured corticosterone levels in the target animals following emotional transfer (Fig. 6C). Together these studies show inconsistent changes in corticosterone levels in mice ($r = -0.005, CI: [-0.06 to 0.07]$) and rats ($r = 0.16, CI: [-0.1 to 0.4]$) following interaction with a distress conspecific. The large variability in the effect sizes suggests that there is no simple relationship in the transfer of emotional distress and fluctuations in corticosterone level.

3.10. C-fos activation patterns reveal a cortico-limbic circuit strongly involved in emotional contagion in the rodent brain

In order to identify which brain structures play a role in emotional contagion, we quantified effect sizes in experiments reporting c-fos in rats and mice collected after emotional transfer (Table 3). The proto-oncogene c-fos is an immediate early gene expressed in neurons in response to various stimuli and is commonly used as a marker of neuronal activation. Given the small amount of c-fos related effect sizes, we limited our analysis to differentiating rats and mice, while not including any other sub-levels (e.g., strain, familiarity). Among the papers selected for this meta-analysis, $N = 16$ papers reported c-fos data, with a majority of them using rats ($N = 13$, mice, $N = 3$). The effect sizes were computed for each brain structure reported in the studies (Fig. 7A). In rats, a large number of effect sizes ($N = 112$) allowed to perform meta-analytics on 22 brain structures, while one brain area (lateral preoptic area), associated with only 1 effect size, was not included in the analysis (Fig. 7A, red marking). In rats, the results highlight a cluster of activation in medial frontal areas, with strong c-fos activation pattern in the anterior cingulate and prelimbic cortices, and to a lesser extend infralimbic cortices (Table 7). A second cluster of activation grouped subcortical areas containing mainly the striatum (nucleus accumbens, NAcc) and specific amygdala nuclei, in particular the basolateral and lateral nuclei (Fig. 7B).

In mice, the limited number of effect sizes ($N = 32$) associated with brain areas precluded us from computing meta-analytics in 10 regions for which only one effect size was computed (Fig. 7A, red marking). In
the case of the ACC, we leveraged a number of studies (n = 9) where comparisons in emotional contagion levels were performed between groups of healthy mice and groups of mice where the function of the anterior cingulate cortex had been altered (Fig. 7C). We found that deactivating the ACC in mice strongly reduced emotional contagion (r = 0.58, CI: [-0.97 to 0.20]), in line with the observation of high c-fos activation levels in the rat ACC during emotional contagion. Regarding this meta-analysis, in order to guide our decisions, we elaborated a clear methodology and procedures in which the emotional state from one individual is contaged to another (measurement time could happen during or after emotional transfer); 4) measurements of emotional contagion had to recruit an emotional observable response; if they failed to do so (such as memory effects), they were not considered direct measurements of emotional contagion but rather secondary processes related to emotional contagion. All the studies included in the current meta-analysis fall under this classification.

4. Conclusion and limitations

4.1. Updating current models of emotional contagion

While a high number of reviews attempting to summarize the literature on emotional contagion in rodents were published in recent years (Keysers and Gazzola, 2016; Meyza et al., 2016; Reum and Shin, 2016; Sivaselvachandran et al., 2016; Mogil, 2012; Lukas and de Jong, 2016; Reum and Shin, 2019), one article in particular went one step further and proposed a classification of experimental approaches used in the field (Panksepp and Panksepp, 2013a). This classification distinguished a variety of phenomenon such as contagion, social analgesia, social buffering, social priming, behavioral matching and social transfer. In the current meta-analysis, we updated and simplified this classification based on our revised inclusion criteria for studies measuring emotional contagion: ‘a study measuring a behavioral response associated with (indirectly - in absence of- and directly - in presence of others-) the emotional cues of other individuals’. This means that all the phenomena mentioned above, per our definition, fall under the emotional contagion umbrella. One illustrative example is the case of social buffering, where a distressed animal shows reduced fear when paired with a neutral non-distressed conspecific. In these cases, we considered the observed phenomenon as emotional contagion from an animal in a neutral emotional state to one in a fearful state. This approach allowed us to unify different paradigms, and seemingly diverse approaches on rodent empathy into a single model. Our classification had additional key differences with the classification proposed by Panskepp & Panskepp (Panksepp and Panksepp, 2013a): 1) contagion can occur without the direct presence of an individual (e.g., through a cotton boll soaked with urine of a fearful animal); 2) emotional contagion paradigms consist of three phases: pre-exposure, emotional transfer and measure of emotional contagion; 3) the term emotional transfer refers to the point in time in which the emotional state from one individual is contaged to another (measurement time could happen during or after emotional transfer); 4) measurements of emotional contagion had to recruit an emotional observable response; if they failed to do so (such as memory effects), they were not considered direct measurements of emotional contagion but rather secondary processes related to emotional contagion. The lack of clear definitions and unity in the field made it challenging in deciding which data was indeed relevant for this meta-analysis. In order to guide our decisions, we elaborated a framework through which each study was pipelined to take a decision on whether the effect size reflected emotional contagion-related data. For instance, research performed on social transmission of taste aversion can be arguably included in the emotional contagion field, since, typically in these paradigms, one animal undergoes an aversive emotion (taste), which is thereafter transmitted to a naïve conspecific through interactions. However, these publications were not included in this meta-analysis due to the fact that the aversive emotion experienced by the demonstrator was often not measured and quantified, nor was the actual transfer of emotion. Similar issues were encountered in studies where emotional contagion was used as a tool, rather than a measure, to study how observing the distress of others affected cognitive abilities later in time, such as memory and learning (Nowak et al., 2013; Ito et al., 2015a). Albeit these are important effects of emotional contagion in...
other neural processes and behaviors, they are not a direct measurement of emotional contagion, and as such were excluded from the main analysis.

However, we find it important to emphasize the caveats of our approach by pointing out other missing aspects of the emotional contagion literature. For instance, the filters used in this study failed to capture articles on mother-pup interaction and the emotional transfer inherent to such social systems (Moriceau and Sullivan, 2006; Barr et al., 2009). Future meta-analytic work on this topic could increase their search filter range to include such studies and encompass even more variability in rodent emotional contagion.

It should also be noted that our filters might have failed to include articles where similar processes were studied but other wording was used. It is notable that rodent emotional contagion is a controversial topic (Balter, 2011) and several studies have framed their results in terms of stress-related processes instead of emotional contagion (Breitfeld et al., 2015; Zalaquett and Thiessen, 1991; Mackay-Sim and Laing, 1981). While we believe that the high number of effect sizes and studies included in this meta-analysis already allow for careful conclusions to be drawn, future endeavors should carefully increase the granularity of their filters to encompass studies that investigated similar processes under a different framework.

Another limitation of our work is the low number of effect sizes present in some distributions. For instance, the low number of effect sizes reported in females makes it difficult to conclude on the results reported here, that is, that sex does not modulate emotional contagion. Similar parsimony should be used when interpreting effect sizes reported in different strains. For instance, the differences reported between CD-1 and CF-1 mice, two very close strains, are quite surprising. One likely explanation for this (and other) differences might lie in the experimental paradigm used, which differed between strains. These disruptive results suggest that additional, more granular variables should be added to future meta-analysis. For instance, an attempt at classifying experimental paradigms to identify contexts and situations where emotional contagion might be more salient would allow to associate differences in effect sizes to experimental manipulations rather than to species, strains or other parameters.

This meta-analysis revealed that, although, emotional contagion can occur in response to both positive and negative emotions, as already noted by (Panksepp and Panksepp, 2013c), to date nearly all studies investigating emotional contagion in rodents use negative stimuli to trigger emotional transfer, which could be due to the fact that in rodent empathy research negative reinforcers are traditionally used. This observation stresses the need to use positive reinforcers to study the other side of rodent empathy, as already performed in some studies (Willuhn et al., 2014b; Kastielyan et al., 2014b; Lichtenberg et al., 2018), and more generally in the field of prosocial behavior (Lichtenberg et al., 2018; Márquez et al., 2015; Hernandez-Lallement et al., 2016b, 2020). A promising avenue would lie in studies that directly compare the effects of positive and negative reinforcers, although we acknowledge that developing comparable positive and negative stimulus is a challenge given the higher saliency and reinforcing power of negative stimuli. On the other hand, it is important to consider the possibility, that the under reporting of studies using positive stimuli could be due to lack of effect of this type of stimuli and bias to report null effects.

A final limitation that we encountered was the incomplete reporting of information, namely, the methods section. We noticed that some variables more likely to not be properly reported such as age and number of days that observers and demonstrators were related to each other, with 13 % and 21 % of overall missing values per category respectively. In addition, our quantitative analysis suggested that randomization, blinding and sample size calculations are seldom reported (and/or done) in studies in the field, which overall reduces the results quality.

4.3. Conclusion

Overall, this is the first meta-analysis and systematic review conducted to date on the field of rodent emotional contagion. In this meta-analysis we develop an umbrella definition of emotional contagion that covers a large rage of studies investigating this response. We also developed a classification model that allowed us to unify a range of existing paradigms used to investigate emotional contagion. Within this model we identified key parameters that have a modulatory effect on emotional contagion and that can be used for optimizing the design of future studies in the field. However, we underscore that many differences reported here should be taken cautiously since the lack of effect sizes and major differences in experimental paradigms could still account for effects we report in this meta-analysis. We also identify a range of brain regions that can be used as targets to further our understanding of the neural mechanisms of emotional contagion. Lastly, this meta-analysis also identifies gaps in knowledge and potential research areas of interest.

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