Figures and figure supplements

Rat behavior and dopamine release are modulated by conspecific distress

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Figure 1. Pavlovian Social Distress Paradigm. (A) Rats were placed side by side, separated by a divider, during ‘together’ trial blocks. The conspecific was removed during ‘alone’ trial blocks. (B–D) Trial types. All trials started with illumination of a houselight. Five seconds later an auditory cue was presented. A 5-second directional light was presented, followed by a 5-second outcome cue, and finally a 5-second outcome light. (E) Lichtenberg et al. eLife 2018;7:e38090. DOI: https://doi.org/10.7554/eLife.38090
Figure 1 continued

presented indicating the outcome that would occur at the end of the trial (i.e., outcome cue). Five seconds after the ‘outcome cue’, the ‘directional cue’ was presented for 5 s, indicating which rat would receive the reward (i.e., reward trials; blue, B), nothing (i.e., neutral trials; green, C), or a shock (i.e., shock trials; red, D). (E) Placement of chronic recording electrodes within the NAc core based on histology.

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Outcomes delivered to recording rat (self)  

Outcomes delivered to conspecific (other)  

Figure 2. Beam breaks in food cup. An infrared beam was placed above the recording rat’s food cup. (A) and (B) illustrate percent beam breaks over trial time during ‘self’ and ‘other’ trials, respectively (n = 40 sessions; 8 rats). (C–J) During the directional cue epoch (gray) of each session indices were computed by subtracting percent beam breaks during neutral trials from percent beam breaks on shock (red) and reward (blue) trials during ‘self’ (C–F; left panels) and ‘other’ trials (G–J; right panels) when rats were ‘alone’ (C,D,G,H) or ‘together’ (E,F,I,J). (K–P) During the directional cue epoch of each session indices were computed by subtracting percent beam breaks during ‘together’ trials from ‘alone’ trials for reward (blue), neutral (green), and shock (red) trials when the outcome was to be delivered to ‘self’ (left panels) or ‘other’ (right panels). Distributions of indices were deemed significantly shifted from zero via Wilcoxon (insets provide mean (µ) and p value).

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Figure 3. Freezing and Approach. (A–D) Percent freezing over 12 trial types for ‘self’ (A,B; solid) and ‘other’ (C,D; open) trials during the 5 s directional cue epoch (A,C) and the 5 s outcome epoch (B,D) when rats were ‘alone’ (left) and ‘together’ (right). Blue = Reward; Green = Neutral; Red = Shock. (E–G) Contingencies same as A–D except for percent approach. Note that n = 34 instead to 40 due to technical issues during video recording. *Wilcoxon; p < 0.05.

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Figure 4. Dopamine release when the outcome was delivered to the recording rat (i.e., self). (A) Average DA release over trial time (n = 40 sessions, 8 rats). See Figure 4—figure supplements 1 and 2 for example sessions. Shock trials (red) are truncated due to shock artifact. (B–D) During the directional cue epoch (i.e., 5 s after directional cue) of each session indices were computed by subtracting average DA release during ‘together’ trials from ‘alone’ trials (Alone minus Together) for reward (blue; B), neutral (green; C), and shock (red; D) during ‘self’ trials. (E) Distributions of the same indices as in B–D (Alone – Together for reward, neutral and shock trials) shown by session (small dots) and rat (large dots) color coded by rat identity. See Figure 4—figure supplement 3 for regressions between behavior and DA release by session and rat. (F–I) Reward (reward – neutral) and shock (shock – neutral) indices taken during the directional cue epoch when rats were alone (F and G) or together (H and I). Distributions of indices were deemed significantly shifted from zero via Wilcoxon (insets provide mean (μ) and p value).

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Figure 4—figure supplement 1. Example false-color plots for reward-self, reward-other, and shock-other trial-types. In the main text we show average DA release over all rats and sessions on ‘other’ trials during performance of the Pavlovian social distress paradigm to make the point that DA release was reduced when the conspecific received reward on reward-other trials and that DA was released upon conspecific foot shock on shock-other trials. Here we show false-color plots that indicate voltammetric current (z-axis) plotted against applied scan potential (y-axis) and time (x-axis) averaged across one session for reward-self (A), reward-other (B), and shock-other (C) trials when the rat was with the conspecific (i.e., together) to make the same points. (A) On together-reward-self trials, DA release was observed at the time of the outcome cue and reward. (B) On together-reward-other trials, DA was released only at the time of the outcome cue, but declined after the directional cue. (C) On together-shock-other trials, DA release was observed at the time of conspecific foot shock.

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Figure 4—figure supplement 2. Example false-color plots for shock-self and shock-other trial-types when together and alone. In the main text we show average DA release over all rats and sessions during performance of the Pavlovian social distress paradigm on shock-self trials to make the point that DA release was not reduced during presentation of shock cues when rats were together as opposed to alone. Here we show false-color plots that indicate voltammetric current (z-axis) plotted against applied scan potential (y-axis) and time (x-axis) averaged across one session for shock-self trials when the rat was alone (A) and together (B) to further illustrate this finding.

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Figure 4—figure supplement 3. Regressions between alone and together for beam breaks and DA release during shock-self trials. In the main text we show that DA release is less inhibited on self-shock trials when rats are together during the Pavlovian conspecific distress paradigm. We interpret this result as a consolation effect, whereby the threat of shock is not as aversive in the presence of the conspecific. We found that during the directional cue period rats tend to show less of suppression in the food well (Figure 2). In Figure 4—figure supplement 3 we now correlate differences in beam breaks and DA release observed on alone and together trials for sessions and rat averages, color coded as the DA figures were in the main text.

**Figure 4—figure supplement 3 (A)** shows that in the majority of sessions there was reduced DA release during the direction cue epoch on shock trials relative to neutral (as in Figure 4) and there was a near significant correlation between the two ($p = 0.066; r^2 = 0.086$). **(B)** Likewise, for beam breaks into the food cup, there was a reduction in beam breaks on both alone and together trials, with effects being more pronounced when rats were alone (as in Figure 4—figure supplement 3 continued on next page).
Figure 2. Here, we show that there was a significant correlation between the two (p < 0.05; $r^2 = 0.11$). (C,D) Lastly, we asked if DA and beam breaks were correlated for alone (C) and together (D) trials. Neither were significant (alone: p = 0.58; $r^2 = 0.008$; together: p = 0.39; $r^2 = 0.02$).

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Figure 5. Dopamine release when the outcome was delivered to the conspecific (i.e., other). (A) Average DA release over trial time (n = 40 sessions, 8 rats). See Figure 4—figure supplements 1 and 2 for example sessions. (B–D) During the directional cue epoch of each session indices were computed by subtracting average DA release during ‘together’ trials from ‘alone’ trials (Alone minus Together) for reward (blue; B), neutral (green; C), and shock (red; D) during ‘other’ trials. (E) Distributions of the same indices as in B–D (Alone – Together for reward, neutral and shock trials) except shown by session (small dots) and rat (large dots) color coded by rat identity. Figure 5—figure supplement 1 for regressions between behavior and DA release by session and rat. (F–I) Reward (reward – neutral) and shock (shock – neutral) indices taken during the directional cue epoch when rats were alone (F and G) or together (H and I). Distributions of indices were deemed significantly shifted from zero via Wilcoxon (insets provide mean (μ) and p-value).

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Figure 5—figure supplement 1. Regressions between alone and together for beam breaks and DA release during shock-other trials. In the main text we show that DA release increased at the time of conspecific shock during the Pavlovian conspecific distress paradigm. As in Figure 5—figure supplement 1 we explored correlations between alone and together for both DA release and beam breaks, except here the analysis was performed during the outcome epoch (as in Figure 5). As in the main text, we see higher DA release on together-shock-other trials. Figure 5—figure supplement 1 (A) illustrates the correlation between alone and together (p < 0.05; $r^2 = 0.11$). (B) During shock-other trials the suppression in beam breaks was weaker when together than when alone, but there was no correlation between the two (p = 0.95; $r^2 = 0.0001$). (C,D) Finally, there was no correlation between DA and beam breaks when alone (C: p = 0.18; $r^2 = 0.05$) nor together (D: p = 0.26; $r^2 = 0.03$).

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Figure 6. Instrumental Social Distress Task. (A–D). Rats performed a task during which three independent auditory stimuli predicted three different trial-types. All lever presses led to one sucrose pellet delivery. One stimulus signaled that a subsequent lever press would result in reward with no shock (A, B, ‘no-shock’, blue). The second auditory stimulus signaled that the lever press would produce shock to oneself along with delivery of reward (A,C, ‘shock-self’, red). The third stimulus predicted shock to the conspecific upon lever press and reward delivery to the lever-presser (A,D, ‘shock-other’; orange). (E and F) Percent lever press and reaction time (lever out to lever press) over 24 sessions (n = 8 rats). (G) Percent approach by the recording rat toward the conspecific after extension of the lever to offset of lights. (H) Placement of chronic recording electrodes based on histology. *Wilcoxon; p < 0.05.

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Figure 7. DA release during performance of the Instrumental Social Distress Task. (A) Average DA release (n = 24 sessions, 9 rats) over time for no-shock press trials (blue), shock-self no press trials (red), shock-other no press trials (orange), and no-shock non-press trials (light blue dashed). See Figure 7—figure supplement 1 for an example session. Note that trials during which the recording rats were shocked could not be shown due to significant noise in the signal and that there were no significant differences between shock-other press and no-shock press trials during the reward epoch (ttest; p = 0.08). (B-D) During the outcome cue epoch (5 s after cue onset) indices comparing DA release between trial-types were computed for each session. Distributions of these indices are shown in B-D. B = Shk self no press minus Shk-other no press; C = Shk self no press minus No-shock press; D = Shk other no press minus No-shock press. (E) Distributions of the same indices as in B-D except shown by session (small dots) and rat (large dots) color coded by rat identity. See Figure 7—figure supplement 2 for regression between behavior and DA release by sessions and rat. Distributions of indices were deemed significantly shifted from zero via Wilcoxon (insets provide mean (μ) and p-value).

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Figure 7—figure supplement 1. Example false-color plots for no-shock press, shock-self no press, and shock-other no press trial-types. In the main text we show average DA release over all rats and sessions during performance of the instrumental social distress task to show high DA release during no-shock press trials and shock-self no press trials. DA release was also present on shock-other no press trials but attenuated compared to the other two trial-types. Here we show false-color plots that indicate voltammetric current (z-axis) plotted against applied scan potential (y-axis) and time (x-axis) averaged across one session for no-shock press (A), shock-self no press (B), and shock-other no-press (C) trials to further illustrate these findings.

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Regressions between ‘self’ and ‘other’ for behavior and DA release. In the main text we show that during performance of the Instrumental conspecific distress paradigm that on shock-self and shock-other trials where shock was avoided (i.e., non-press trials) that DA release was present during the cue and during the period after the lever was extended but not pressed. In the main text we report that the increase in DA during the cue period was not significantly different between self-shock-avoid trials and no-shock reward-press trials. This suggests that rats similarly value avoiding the shock and obtaining reward as we have shown in a previous publication (Gentry et al., 2016). Although DA release is also present on trials when the conspecific is spared, it is at significantly lower levels (as in Figure 7). Figure 7—figure supplement 2 (A) shows DA release on the shock-self and shock-other trials were correlated (p < 0.05; r² = 0.59). This correlation was also present in the behavior (Figure 7—figure supplement 2 continued on next page)
supplement 2B). (B) To quantify the degree that the rats valued the reward relative to the avoiding the shock we subtracted percent lever pressing on shock trials from no-shock trials and subtracted the reaction times on shock trials from no-shock trials and then averaged them together, after dividing by the sum for each. This gave us one measure (i.e., ‘behavioral index’) of the how much the recording rat valued saving themselves and the conspecific based on two behavior measures. The majority of the points fell above zero consistent with the Figure 6E and F showing that rats chose to press less often and were slower to press on shock-self and shock-other trials. Figure 7—figure supplement 2B shows that two were correlated (p < 0.05; \( r^2 = 0.25 \)). Thus, DA release and behavior reflect the value the rats place on avoiding shock. (C,D) Although DA release was high when rats avoided shock, we found no significant correlation between behavior and DA release on self (C: \( p = 0.81; \ r^2 = 0.003 \)) and other (D: \( p = 0.36; \ r^2 = 0.038 \)) shock trials.

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