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Empathic Fear Responses in Mice are Triggered by Recognition of a Shared Experience

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Background: Empathy is an important capacity that involves the ability to recognize and share emotions with others. Empathy for others is facilitated by having had a similar prior experience. It increases with the intensity of distress that observers believe is occurring to others, and is associated with acute emotional responses to witnessing others' distress. We sought to develop a mouse model of human empathy that modeled these characteristics.

Methods: We recorded the freezing of an 'observer' mouse while it witnessed the experience of a 'subject' mouse. We studied four experimental groups: (1) SH_{obs}=observers that received footshocks in context A on day 1, and then observed footshocks given to a subject in context B on day 2. (2) SHN_{obs}=observers that received footshocks in context A on day 1, and then observed a subject in context B, where footshocks were not delivered on day 2. (3) SW_{obs}=observers that underwent forced swim stress on day 1, and then observed footshocks given to a subject in context B on day 2. (4) Naïve=observers that remained in their homecage on day 1, and that observed footshocks given to a subject in context B on day 2. Footshocks were delivered within a contextual fear conditioning session consisting of 120 s of free exploration followed by six non-signaled foot shocks (duration 1 s, intensity 0.7 mA) with an interstimulus interval of 15 s for a total duration of 216 s.

Results: All groups showed low levels of freezing during a 120 s baseline period in context B (~0–6%). SH_{obs} behaved significantly different from all other groups during the subsequent period when they observed cagemates receiving footshocks (main effect for group (F(3, 52)=12.1, $p<0.001$). During footshock observation SH_{obs} froze significantly more than baseline levels and SH_{obs} freezing increased with consecutive shocks delivered to subjects (F(6, 312)=2.97, $p<0.05$), reaching up to 40%. SH_{obs} froze more in the 5 s interval immediately after witnessing subject footshock, with lower freezing during the remaining 10 s ($p<0.05$). In contrast, none of the other groups showed freezing levels different from baseline. Minimal freezing in SHN_{obs} excluded the recognition of contextual cues as a source of observer freezing. Observer freezing was also minimal in SW_{obs}, ruling out a non-specific effect of heightened anxiety from a prior stressful experience. As an added control observers witnessed a subject in context B where shocks were delivered, but where the subject was protected from shock by a thin barrier placed upon the shock grid (SH_{obs}-Block). SH_{obs}-Block did not show freezing different from baseline. Therefore, we also ruled out observer freezing as an artifactual response to cues coming from the footshock equipment.

Conclusions: Our experiments indicate that SH_{obs} freezing was specifically triggered by their recognition of a shared footshock experience with subject mice. Our assay models several aspects of human empathy in mice. These include emotional responses in observer mice that were modulated by a shared life experience with subjects and by the intensity of aversive experience occurring to subjects. These also include acute emotional responses to observing the aversive experience of others. This model may allow for an improved understanding of

neurobiological systems for the ability to recognize and share emotion with others, a core feature of empathy that is oftentimes impaired in clinical disorders.

Keywords: model, empathy, fear, emotion, mouse.

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