Social anxiety isn't just for mammals anymore

A new study, "Social harassment induces anxiety-like behaviour in crayfish", shows a novel crayfish model for acute anxiety in response to harassment that responds well to pharmacological treatment.

Percy Atwell

In humans, anxiety is often brought about by social stressors and acute harassment[1]. Social stress can also increase the risk of depression, heart disease, or substance abuse[2,3,4]. In order to model this form of anxiety accurately, animal models focus on the use of rats and mice, or sometimes hamsters, to create situations of "social defeat" or harassment[5]. These harassed animals may then be administered anxiolytics such as diazepam to attenuate the anxiety-like behavior[6]. Oddly enough, in certain mice strains, instead of displaying anxiety-like activity in a dark/light plus maze the mice show "catatonic-like immobility"[7]. While there exists a range of murine models for examining the efficacy of anxiolytics on attenuating anxiety-like behavior, there is room for improvement. In a study published in *Nature,* Bacqué-Cazenave Cattaert, Delbecque, and Fossat set out to find another possible model for anxiety. Their paper shows how social harassment in crayfish induces anxiety-like behavior that is analogous to human anxiety. Examining crayfish in 2014, Bacqué-Cazenave and his colleagues found that the crayfish acted anxious after a physical stressor, but the existing body of research on crayfish had only established their use in models of aggression[8,9]. Returning to crayfish once again, the authors set out this time to determine if social harassment would elicit anxiety-like behaviors; if so, would the crayfish respond to anti-anxiety drugs.

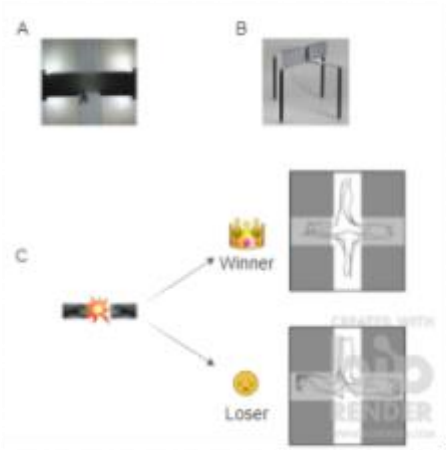

Fig. 1 **Light/dark plus maze. A)** Image of crayfish within the light/dark maze. **B)** Image of mouse within analogous maze. **C)** After social harassment period, crayfish routes within maze tracked with Ethovision software showed winning crayfish exploring the whole maze while losing crayfish stayed within dark arms. Images modified from Bacqué-Cazenave et al. 2017 and Linton Instrumentation.

When two crayfish males are placed together within a small aquarium, once they come face to face, they'll have a fight. These fights always end by one crayfish backflipping away, similar to the fight and defeat that murine models use. Also similar to murine models, the winner will continue to follow around the loser, attacking randomly. These repetitive hostile attacks are considered similar to harassment in humans. After 20 minutes paired together, allowing time for harassment to occur, both winner and loser crayfish were placed in an underwater dark/light plus maze (Fig. 1). The more a crayfish sticks to the dark, the more anxious it is. The crayfish were split into three

groups for the dark/light maze. One group was isolated without social contact to serve as a control, one group was the fight winners, and one group was all the losers. Both isolated and winner crayfish explored the entire maze, but loser crayfish stuck to the dark arms. Then, the losing crayfish were injected with Chlordiazepoxide, an antianxiety drug commonly used due to its low rate of intolerable side effects[10]. The drug-treated crayfish explored the entire maze, no longer showing an anxious preference for the dark arms. Compared to both saline-injected losers and untreated losers, this was a significant reduction of anxiety-like behavior.

These findings display the validity of crayfish as a model for studying anxiety or psychological harassment, examining either the losing or the winning crayfish in a pair respectively. Not only are crayfish useful for examining the underlying neurological pathways that allow both crustacean and human brains to experience anxiety, but they're sensitive to the same pharmacological treatments. Anxiety-like behavior in crayfish reacted to anxiolytic drugs in the same way that anxiety in humans, allowing for the use of crayfish in drug development research. Finally, while animal models of social stress show a great variety of behavioral changes that can be quantified and linked to anxiety-like activity, it is known that stressors may also affect the brain. Net changes in the amount of various neurotransmitters, especially serotonin, have been observed, and chronic social stress has shown shrinkage of dendritic arbors within the hippocampus in mammalian models[11,12]. In the future, robust examinations of the effects of stress on serotonin or the hippocampal-like structures within the crayfish brain may provide an even stronger case for the use of crayfish models in the study of stress.

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