Fellowship of the fin: Fish empathy and oxytocin

Adam R. Reddon* & William T. Swaney

School of Biological and Environmental Sciences
Liverpool John Moores University

*Author for correspondence
a.r.reddon@ljmu.ac.uk
James Parsons Building
Byrom Street
Liverpool, UK
L3 3AF

Summary

Zebrafish exhibit fear contagion, a basic form of empathy, and when observing social fellows that have been exposed to predation cues, will themselves exhibit similar distress behaviours. As in mammals, the nonapeptide hormone oxytocin is essential for this empathic response, and homologous areas of the brain are involved, suggesting that the mechanistic basis of empathy may be conserved among vertebrates.

Empathy in fishes

Empathy is the tendency to enter the same emotional state as another individual despite not directly experiencing the factors that gave rise to that state. Empathic behaviours can strengthen social bonds, improve coordination within groups, and help reinforce complex forms of sociality. There can be key survival advantages to being able to join others in their emotions, for example, if there is unseen danger nearby, being in the right emotional state can prepare an animal to react appropriately. Noticing that another member of your group is afraid may prime an animal to escape from or confront danger.

Empathy is well known among social mammals and is a key aspect of the social lives of our own species but has been seldom examined in non-mammals. However, at least some fish species do appear to show a form of empathy known as fear contagion. For example, when zebrafish (*Danio rerio*) observe other members of the same species showing antipredator behaviours, such as swimming erratically or staying motionless after detecting predator cues, the observing fish will also exhibit these behaviours, despite not having been exposed to the cues of the potential threat themselves (Silva et al. 2019).

While fear contagion may be a relatively rudimentary form of empathy, it is a behaviour seen in many vertebrate taxa and may represent a building block of more complex forms of sociality seen in larger-brained animals. However, it is unknown whether this empathic response is a conserved expression of the same phenomenon, or if different vertebrate taxa have evolved fear contagion by convergence. One way to explore these two distinct options is to examine the degree to which the mechanisms underpinning fear contagion are shared across distantly related species. This approach has been used by Akinrinade et al. (2023) to examine the evolution of empathy and explore the neurobiological basis of fear contagion in zebrafish. In mammals, the nonapeptide hormone oxytocin is essential for the expression of empathic behaviours and has been shown to influence fear contagion and other forms of empathy in different species, including rodents, primates, and humans. Oxytocin is important for social behaviour and decision making in fishes including zebrafish, but its involvement in fear contagion was unknown. In their paper, Akinrinade et al. describe a series of elegant experiments making use of different genetic knockout strains that each lack the ability to produce either oxytocin or oxytocin receptors to determine whether, and to

what extent, the oxytocin system is required for the expression of fear contagion in zebrafish.

What Akinrinade et al. (2023) found

Akinrinade and colleagues showed that zebrafish carrying a knockout of either oxytocin or its receptors do not show the fear contagion response exhibited by wild-type zebrafish. In knockout fish that lacked endogenous oxytocin, the fear contagion response was rescued by administration of exogenous oxytocin, emphasising that oxytocin was both necessary and sufficient to express these empathic behaviours, consistent with previous results in mammals. The hypothesis that the neural basis of this fear contagion response is conserved in vertebrates is further supported by the fact that wild-type zebrafish exposed to distressed conspecifics showed consistent changes in neuronal activity in brain nuclei homologous to the lateral septum and striatum, key areas that regulate empathy in mammals. Akinrinade et al. also showed that oxytocin specifically modulates inhibitory activity in the zebrafish homologue of the lateral septum during fear contagion, just as occurs in mice experiencing social fear. Zebrafish with a knockout of the main oxytocin receptor do not show the same patterns of brain activity and have altered functional connectivity throughout the network of brain areas involved in social decision making, a likely explanation for their inability to show fear contagion. Perhaps surprisingly, wild-type fish, but not those with knockouts of oxytocin or its receptors, preferred to associate with social fellows they earlier observed showing fear, when intuitively you might expect fish to avoid individuals who could be associated in time and space with predators. This result was interpreted by Akinrinade et al. as a potentially prosocial oxytocin-mediated behaviour to console distressed group members.

Fear contagion to gather information about predators

The primary function of empathy in zebrafish could be to gather information about nearby predation risk and then modulate internal state appropriately, thus preparing the observer fish to mount an antipredator response in advance of direct exposure to risk. The perception of damage induced chemical alarm cues, released into the water by injured conspecifics, serves a similar function (Chivers & Smith, 1998) and in either case, socially derived information is used to guide decisions about predator avoidance and evasion. Interestingly, Akinrinade et al. used damage induced alarm cues to induce the fearful behaviour in their

stimulus fish from which the focal animals may experience fear contagion, as these cues serve as potent unconditioned stimuli which inherently evoke antipredator responses. It is possible that the information gathered from conspecifics that leads to fear contagion, i.e., perception of behavioural indicators of distress, has similar effects on the brain to those induced directly by chemical alarm cues. In other species, including humans, there are similarities in brain activity patterns when experiencing fear-evoking stimuli or when observing another individual doing so. It would be intriguing to see to what degree the direct response to chemical alarm cues is also dependent on oxytocin signalling and/or neuronal activity levels in the lateral septum and striatum homologues in zebrafish, and whether there is overlap in the neural mechanisms of fear and the processing of socially derived information about risk.

The potential use of distressed social fellows as a source of information about risk in the environment could also explain why wild-type zebrafish preferred to associate with conspecifics that they had previously observed showing fear. By showing fear responses, distressed fish indicate that they are knowledgeable about such dangers in the environment. Fish that are not showing distress may be naïve to nearby predators and therefore less valuable as shoalmates, as they cannot convey that valuable social information. Many fish engage in other seemingly counterintuitive behaviours when encountering predators, such as approach and inspection to assess the immediate risk. Predator inspection can be a social behaviour performed by pairs of fish and coordination is an important aspect of this behaviour. Social coordination of antipredator responses may have been an important force in the initial emergence of empathy and may have set the stage for the more nuanced forms of emotional coordination between social fellows seen within complex societies.

Oxytocin as a social spotlight

An influential hypothesis for the central function of oxytocin is that it acts as a 'social spotlight', marking the salience and valence of social information in the environment (Shamay-Tsoory & Abu-Akel, 2016). Oxytocin can increase the attention paid to socially derived information, for example, cichlid fish injected with exogenous oxytocin were more sensitive to the relative formidability of potential rivals and more responsive to dominant fish (Reddon et al. 2012). The lack of a functioning oxytocin system, as in the genetic

knockout animals used by Akinrinade et al., may cause socially derived information to be underappreciated or ignored. Indeed, Akinrinade et al. showed that while social brain activity was altered, brain areas thought to process fear remained functional in the oxytocin receptor-knockout fish. If fear contagion in zebrafish represents individuals using social information to guide antipredator behaviours, then interfering with the salience of social information by inactivating oxytocin signalling may disrupt fear contagion by reducing the attention paid to socially derived information. Further evidence that social information perception or weighting is regulated by oxytocin signalling would support the hypothesis that fear contagion among zebrafish, and possibly among other animals, should be considered in the context of social information gathering, and that oxytocin is an ancestral mechanism in this process.

References

Akinrinade, I., Kareklas, K., Teles, M. C., Reis, T. K., Gliksberg, M., Petri, G., Levkowitz, G., & Oliveira, R. F. (2023). Evolutionarily conserved role of oxytocin in social fear contagion in zebrafish. *Science*, *379*, 1232–1237. https://doi.org/10.1126/science.abq5158

Chivers, D. P., & Smith, R. J. F. (1998). Chemical alarm signalling in aquatic predator-prey systems: A review and prospectus. *Écoscience*, *5*, 338–352. https://doi.org/10.1080/11956860.1998.11682471

Reddon, A. R., O'Connor, C. M., Marsh-Rollo, S. E., & Balshine, S. (2012). Effects of isotocin on social responses in a cooperatively breeding fish. *Animal Behaviour*, *84*, 753–760. https://doi.org/10.1016/j.anbehav.2012.07.021

Shamay-Tsoory, S. G., & Abu-Akel, A. (2016). The social salience hypothesis of oxytocin. *Biological Psychiatry*, *79*, 194–202. https://doi.org/10.1016/j.biopsych.2015.07.020

Silva, P. F., Leaniz, C. G. de, & Luchiari, A. C. (2019). Fear contagion in zebrafish: a behaviour affected by familiarity. *Animal Behaviour*, *153*, 95–103. https://doi.org/10.1016/j.anbehav.2019.05.004