

1 **Fellowship of the fin: Fish empathy and oxytocin**

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15 **Summary**

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

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23 **Empathy in fishes**

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

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

39

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

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

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58 **What Akinrinade et al. (2023) found**

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

78

79 **Fear contagion to gather information about predators**

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

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

98

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

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112 **Oxytocin as a social spotlight**

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

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

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