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Animal Behaviour: Learning Social Distancing

Elena Dreosti[1] **and Hernán López-Schier**[2,*]
[1]Wolfson Institute for Biomedical Research, University College of London, The Cruciform Building, Gower Street, London WC1 6BT, UK
[2]Sensory Biology and Organogenesis, Helmholtz Zentrum München, Munich, Germany
*Correspondence: hernan.lopez-schier@helmholtz-muenchen.de
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Early-life experience has a long-lasting influence on social behaviour. A new study has revealed a role for mechanosensation in shaping social avoidance responses in zebrafish.

Interpersonal relationships are a major part of everyday life. We are a thoroughly social species and our brains are hardwired to connect with others. Although this drive is innate, social interactions are also strongly shaped by our early social experiences. Because experience has a strong stochastic component, studying its protracted influence on social behaviour has long been challenging. As they report in this issue of *Current Biology*, Groneberg *et al.* [1] have overcome the technical barriers in their new study with larval zebrafish. By controlling social experience and sensory manipulation, the authors have found that lateral-line mediated mechanosensation during early life underlies the development of social avoidance reactions.

Studies in humans and other social species have shown that social deprivation during critical periods of development has profound and long-lasting effects on social behaviour [2,3]. For many species, two discrete and important critical periods are found during post-embryonic growth and during the transition from infancy to adulthood. Social experience within these periods modulates the acquisition of cognitive skills that animals will need upon gaining full independence, and can have a significant impact on their position within social hierarchies and reproductive success. For instance, episodic rewarding or stressful consequences of inter-individual interactions may lead to the production of neuromodulatory factors that modify neuronal circuits which, in turn, reinforce or inhibit innate behaviours over periods that far exceed the ‘teaching’ experience [4]. One type of social interactions that is amenable to quantification is that involved in the collective movement of animals, which requires that individuals constantly keep an optimal distance from one another. The ‘rule of avoidance’ has been put forward as a framework that typifies individuals’ spatial distribution within a group [5]. One pressing question is whether the rule of avoidance is deterministically hard-wired, or develops from a combination of innate and experience-based mechanisms.

The recent establishment of zebrafish as a model for studying the development of social circuits and behaviour is allowing light to be shed on some of the mysteries surrounding social behavior [6–8]. One advantage of zebrafish is that they do not require parental care, which enormously facilitates the manipulation of early social experience. Zebrafish exhibit complex social behaviours that develop gradually during larval stages and consolidate as juveniles [9]. They are amenable to well-controlled interventions via pharmacology, gene mutagenesis, ablation of defined neuronal classes, and optogenetic control of neural activity. Importantly, the onset of inter-individual avoidance in zebrafish occurs within the first week of life, when animals are small and translucent, respectively simplifying complete anatomical description of neuronal circuits and allowing non-invasive whole-brain neuronal activity imaging at high resolution. Finally, larval zebrafish behave in sequences of discrete swim bouts, which can be quantified automatically and classified into well-defined events that can be statistically compared between individuals and experimental conditions.

To study the effect of deprivation of social interactions during early life, Groneberg *et al.* [1] leveraged high-speed video tracking and classification of swim-bout types in freely interacting zebrafish larvae. Using unsupervised clustering, they found that animals raised in isolation expressed a higher avoidance to conspecifics as manifested by larger inter-individual distances and higher probability of avoidance manoeuvres (Figure 1). Surprisingly, they found that the mechanosensory lateral line is

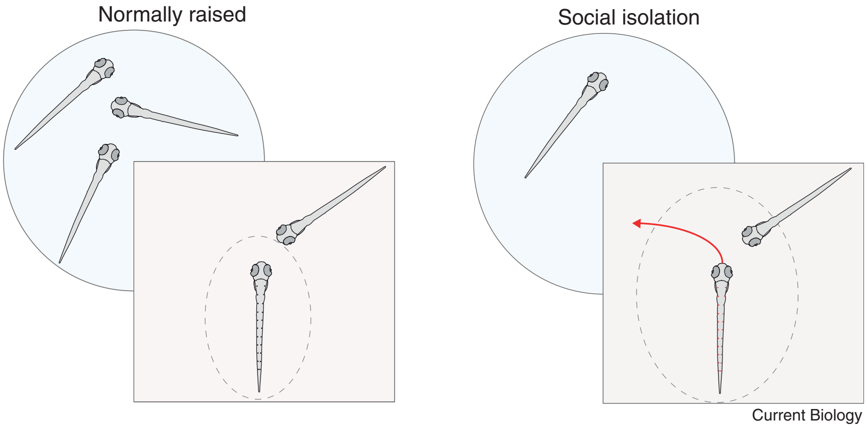

Figure 1. Enhanced social avoidance in isolated zebrafish.
Socially isolated animals show an increase in the distance at which they react to one another, as well as in short-latency escape responses.

necessary and sufficient to mediate avoidance reactions [10]. The authors further dissected the contribution of vision and lateral-line mechanosensation by selectively eliminating each sensory modality. Social avoidance in darkness strongly affected avoidance distance without modifying the choice or motor reactions, suggesting that fish use vision to gauge distance but not how to respond to the physical proximity of conspecifics. This result supports previous findings showing that vision is crucial for social interactions [9], and Groneberg *et al.* [1] further provide the first evidence that the lateral line is required for the development of social behaviour.

One aspect of the work of Groneberg *et al.* [1] that is particularly interesting is how mechanosensation impacts neuronal circuits during early life and leads to long-term changes in social interactions. This cannot happen via modification of the sensory elements or their first synapse because hair cells in the lateral line are constantly replaced via regeneration through the life of the fish, suggesting that any possible alterations of mechanoreception of mechanotransduction are short lived. Long-term modifications of the intrinsic activity of lateralis afferent (ascending) neurons are also unlikely to account for the observations because these neurons are not known to express spontaneous activity. One possibility is that early-life experience underlies the establishment of a set point for internal brain states that would make the fish more or less prone to be near other conspecifics. Lateral-line information reaches the brain at the first output in the medial octavolateralis nucleus in the hindbrain and is then relayed through a still unknown number of synapses to the optic tectum. Therefore, there is ample opportunity for mechanosensation to impact the formation of circuits in several areas of the brain.

Previous studies across many species, including humans, have shown that a surprising consequence of being socially deprived is an increase in social avoidance. This seems counterintuitive since one would expect that not seeing conspecifics would increase an individual's desire to remain close to others. More recent work in humans and in zebrafish has shown that social isolation causes hypersensitivity to visual stimuli, which leads to increased anxiety and, in turn, social avoidance. The work by Groneberg *et al.* [1] supports this idea and expands the scope of early-life experience on other sensory modalities, by demonstrating that mechanosensation is hypersensitive following social isolation. Specifically, the lateral line mediated short-latency escape responses (fast avoidance manoeuvres) are increased in isolated fish, even in the dark, but these stereotyped responses are abolished after ablating the lateral line. Therefore, this work is a big step forward in better understanding why early-life social deprivation increases later-life social avoidance.

There may be a lesson for us currently living through a massive social deprivation experiment after being isolated from our relatives and friends due to COVID-19. After weeks or months of lockdown, we have all experienced to different degrees a sense of anxiety as we try to go back to normal social life. As we move forward, handshaking and hugging might initially be overwhelming, but they will be crucial to help us restore our pre-coronavirus life.

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