

## OUTSIDE JEB

## Oestrogens encode love for female mice



Timing is everything when trying to land a mate. In many species, female receptivity to male sexual advances is synchronized to fertility and is mediated by steroid hormones produced in the gonads, such as oestrogens. How these hormones tune neural circuits to transition females to mate-seeking mode is unclear. In a series of elegant experiments, neuroscientist Jenna McHenry and colleagues in Garret Stuber's laboratory at the University of North Carolina at Chapel Hill, USA, investigated a hormone-responsive neural circuit important for mate attraction in female mice.

The medial preoptic area in the brain controls a range of social and sexual behaviours. McHenry focused on cells containing the reward-associated peptide neurotensin. Neurotensin-expressing cells make up nearly one-third of all input to the ventral tegmental area of the brain, which produces the pleasure-associated neurotransmitter dopamine, making it likely that the neurotensin-expressing cells mediate reinforcement of social behaviour.

To determine the sensory input that activates neurotensin-producing neurones, McHenry constructed mice that emit light in the medial preoptic area every time  $Ca^{2+}$  is released as an indicator of neural activity. McHenry then 'perfumed' female mice with male or female urine while measuring the amount of light emitted by the neurotensin-producing cells. They discovered that a large group of neurones was excited by the male scent (37%), while only a small number of cells responded to female odours (8%). Neurotensin-

producing cells in the medial preoptic area of the brain are turned on by social cues and the team also showed that social excitement is amplified by steroid hormones. But the behavioural consequences of activating these cells were still not clear.

To get at the behavioural function, McHenry developed a new set of mice with special light-gated neurotensin neurones. Unlike the mice used previously that emitted light from active neurones, these mice had light-activated neurones. Specifically, McHenry expressed light-gated  $Na^+$  channels in neurotensin-expressing cells, so that every time she artificially flashed a light pulse in the brain, these photoreceptive neurones perceived the light and  $Na^+$  channels rapidly opened, leading to neural activation. McHenry implanted fibre optic cables into the medial preoptic area to provide a light source, and monitored how rewarding it was for mice to stimulate these light-sensitive neurotensin-producing cells by seeing how often mice chose to activate these cells. McHenry found that mice activated these cells across all phases of the female's fertility cycle, but activated them the most when oestradiol levels were highest, suggesting that natural rises in oestradiol activate oestrogen receptors in neurotensin-producing neurones, leading to an increase in mate seeking coincident with peak fertility. However, McHenry was still in the dark about how medial preoptic activation changed the brain.

The team posited that the medial preoptic area controls dopamine release in the downstream ventral tegmental area of the brain. As most of the neurotensin-producing cells in the medial preoptic area that signal to the ventral tegmental area of the brain inhibit neural activity, the team suspected that they may silence cells in the ventral tegmental area and release the brakes on dopamine production, making the experience pleasurable. To test this, McHenry activated the medial preoptic area cells and simultaneously measured dopamine levels in the downstream nucleus accumbens brain region. She found that activating the medial preoptic area ramped

up dopamine levels in the nucleus accumbens, especially in oestradiol-primed mice. Thus, the medial preoptic area enables mate seeking by increasing dopamine in reward-related brain regions such as the nucleus accumbens.

In short, McHenry and colleagues' study has illuminated the role of a specific brain circuit that enables mate seeking and sheds mood-light on how these hormone-sensitive cells scent the stage for finding love at the right time.

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McHenry, J. A., Otis, J. M., Rossi, M. A., Robinson, J. E., Kosyk, O., Miller, N. W., McElligott, Z. A., Budygin, E. A., Rubinow, D. R. and Stuber, G. D. (2017). Hormonal gain control of a medial preoptic area social reward circuit. *Nat. Neurosci.* **20**, 449-458.

Dan Vahaba

University of Massachusetts Amherst

[dvahaba@umass.edu](mailto:dvahaba@umass.edu)

## Message in a sperm cell



Animals face stressful environments in the wild. When the going gets rough, parents can prepare their developing offspring for life in a tough world. They can alter gene expression patterns in their young to best 'match' their babies' physical characteristics to their new home. For example, in a habitat with little food, parents may influence gene expression to produce smaller offspring that would require fewer meals and be more likely to survive to adulthood. They may also affect their offspring's characteristics in other ways, including selecting the sex, or even altering behaviour. Together, these parent-induced changes are called parental effects.

Outside JEB is a monthly feature that reports the most exciting developments in experimental biology. Articles that have been selected and written by a team of active research scientists highlight the papers that JEB readers can't afford to miss.

But which parent causes these changes? So far, the maternal effects that mothers exert through signalling in their eggs have received the most research attention; but, what about fathers? Might they also signal to their future young about the environment that they are experiencing through sperm cells?

Jonathan Evans and his colleagues from the Centre for Evolutionary Biology at the University of Western Australia wanted to investigate the potential for paternal effects. The research team placed soon-to-be father guppies on an abundant or restricted diet for one month, mimicking the fathers' experiences of an environment with plentiful or scarce food resources.

Next, Evans and colleagues tested whether the sperm would inform the offspring of the harsh or plentiful conditions that the fathers experienced. To do this, the team artificially inseminated female guppies with sperm from males in either diet treatment (the females were fed normally). The researchers found that the juvenile guppies sired by males on a restricted diet were smaller, while those sired by males on a plentiful diet were larger. The researchers showed that fathers could in fact change their offspring's growth and size through the contribution of sperm alone.

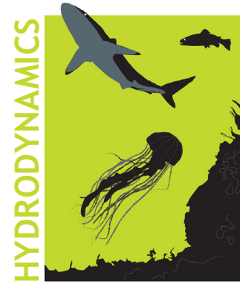
The team underscored the important effects that smaller or larger body size might have on the survival of young guppies in the wild. For instance, larger newly hatched guppies are better at avoiding predators than smaller guppies, and larger juvenile guppies grow faster, out-competing their smaller counterparts in a dense population. The group's tantalizing finding that a father's sperm can influence their offspring's development opens up many exciting avenues for future research. It will be intriguing to understand exactly how sperm transmit their message to developing offspring and also whether sperm signal in other species of the animal kingdom.

10.1242/jeb.147512

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Erin McCallum  
Umeå University  
erin.mccallum@umu.se

## Fish larvae feed in the danger zone



About 99% of fish larvae die within weeks of hatching, but what causes this extreme death toll? Disease, predation, lack of food and inhospitable habitats are possible culprits, but most larvae die even when raised with plenty of food and safety. Recently, Roi Holzman and colleagues at Tel Aviv University and Afeka College of Engineering, Israel, explored this paradox of 'starvation despite food abundance' through the lens of biomechanics. Whereas most theories of larval mortality have focused primarily on ecological factors, Holzman and colleagues tested whether feeding success was influenced by the hydrodynamic forces acting upon larvae. In a previous study, they found that recently hatched larvae experienced 'hydrodynamic starvation' whereby strong viscous forces in water make many larvae physically incapable of capturing prey. In a new study led by Victor China working with colleagues at Tel Aviv University and the Inter-University Institute for Marine Sciences, Israel, they continue to delve into the mechanisms that drive hydrodynamic starvation by evaluating how suction feeding is affected by the development of physical traits and the associated hydrodynamic forces that work with, or against, them.

Larval fishes primarily use suction feeding, where they rapidly expand their mouth cavity to create a pressure gradient that draws water (and the prey within it) into the mouth. How water moves can be described by its Reynold's number ( $Re$ ), which is a ratio of the viscous forces that resist movement and the inertial forces that keep the fluid moving. Small organisms experience a low  $Re$  environment, where viscous forces predominate and water feels as thick as molasses. By the end of the larval period,  $Re$  increases 100-fold and prey capture improves 4-fold. This improvement could be due to changes in the hydrodynamic

regime that make it easier to move water, or developing anatomical traits that make larvae better predators (e.g. better vision). To disentangle the contributions of hydrodynamics and development, the team used high-speed videos to compare the feeding manoeuvres of gilt-head bream (*Sparus aurata*) ranging between 8 and 23 days old in hydrodynamic environments that were experimentally manipulated to have higher viscosities.

They found that increased feeding success was not necessarily a matter of being older and more developed, but instead depended on the correct combination of physical traits that allowed individuals to escape the danger zone of low  $Re$  and high viscosity. Larger body sizes associated with older individuals and decreased viscosities improved feeding success, but only indirectly through the alteration of physical characteristics that conferred higher  $Re$ , such as larger body/mouth sizes and faster attacks. At low  $Re$ , the team also observed events in which the prey was engulfed but then inadvertently spat out as the fish closed its mouth. These 'in&out' events suggest that timing is of the essence and that larvae face unique challenges in the viscous world compared with adult fish living in a higher  $Re$  environment. Consequently, high larval mortality may be due not to intense predation but to being too small and slow to eat properly.

The discovery that feeding success depends on escaping the danger zone of low  $Re$  brings us closer to solving the mystery of massive larval die-offs and helps inform wildlife management decisions. The team suggests that selection for larger larvae at hatching could increase survival rates because bigger individuals feed better, faster and on a greater range of prey by bypassing low  $Re$ . With many fishes decreasing in size as a result of over-fishing, these results also serve as a cautionary note that being smaller can be big trouble for fishes.

10.1242/jeb.147496

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Sandy Kawano  
Royal Veterinary College  
smkawano@rvc.ac.uk

## To be or not to be ... male or female?



Whether one is genetically born as male or female is decided when the sperm meets the egg. It is only under unique conditions that Mother Nature would divert from such a rule in mammals. This is not the case in fish, where the environment can influence the sex that an animal assumes later in life. Working with sea lamprey (*Petromyzon marinus*), Nicholas Johnson from the US Geological Survey at Hammond Bay Biological Station in Michigan and colleagues from the Department of Fisheries and Wildlife at Michigan State University serendipitously identified additional factors that influence whether a fish becomes male or female in the wild.

Sea lampreys – which have retained most of their ancestral characteristics from over 500 million years ago – undergo a complex life cycle. Most of a lamprey's life is spent as an earthworm-like larva in rivers and streams, where it resides in sediments, feeding on algae and

decomposing material for 3–7 years. Once it reaches a certain size, it stops feeding and goes through a restructuring of its body, in a process called metamorphosis, before migrating to the Great Lakes or the ocean, where it feeds on large fishes and matures. Once maturation is complete, it then migrates to upstream rivers to spawn. Whether a lamprey becomes male or female is determined before it undergoes metamorphosis, but little is known about what influences sex assignment in this ancient fish.

While examining sea lamprey populations in the Great Lakes as part of a larger study to investigate rates of lamprey metamorphosis and survival in the Great Lakes tributaries, Johnson and colleagues collected larvae from the streams, tagged them and released them either directly into Great Lakes tributaries (nutrient-rich stream environment) or at the river mouth (nutrient-poor sluggish water environment). In the following years, the authors recaptured some of the larvae that had grown in those habitats, as well as the ones that had metamorphosed, matured and returned to spawn in the rivers. Johnson's team then compared the sex ratios of sea lampreys between the stream and slowly moving environments and found that in the nutrient-rich stream, the ratio of males to females was much lower than in the in nutrient-poor slow-moving water areas. In addition, the authors found that for sea lamprey that had metamorphosed 3 years after stocking, 56% of the population was male in the

stream habitat and 78% was male in the poor-quality estuary habitat, suggesting that the level of nutrition in that habitat may influence sex assignment in this fish.

Using a probability model, Johnson and colleagues then calculated how likely it was that the animals reared in the nutrient-poor environment would become males and found that over 6 years, more than 90% of these lampreys would be male. To add to this observation, the authors reported that the animals reared in the nutrient-rich stream environment grew 2–4 times faster than those in the sluggish areas, making this the first study to link growth rate to sex determination in fish.

The effects of the environment, particularly those of temperature and social context (such as density) on sex ratios in fish have been well established, but it appears now that there are other players: nutrient level in the water and growth rate. It seems to me that when it comes to sex assignment in fishes, the Shakespearean phrase 'To be or not to be' gains a whole new meaning when you add the environment into the mix.

10.1242/jeb.147520

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**Oana Birceanu**  
**Wilfrid Laurier University**  
 obirceanu@gmail.com