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ECR SPOTLIGHT

ECR Spotlight – Sandy Saunders

ECR Spotlight is a series of interviews with early-career authors from a selection of papers published in Journal of Experimental Biology and aims to promote not only the diversity of early-career researchers (ECRs) working in experimental biology during our centenary year but also the huge variety of animals and physiological systems that are essential for the 'comparative' approach. Sandy Saunders is an author on 'Activation of respiratory-related bursting in an isolated medullary section from adult bullfrogs', published in JEB. Sandy is a postdoc in the lab of Joseph Santin at the University of Missouri-Columbia, USA, investigating how breathing is generated, maintained and fails throughout life.

Sandy Saunders

Describe your scientific journey and your current research focus

My research interest in respiratory physiology began as a technician in Erica Levitt's lab at the University of Florida (now at the University of Michigan). I was performing rather difficult experiments as a technician and, frankly, was fascinated by the data I was collecting. I inevitably transitioned into the PhD in her lab shortly after joining. For my PhD work, I was the first to describe how firing of respiratory neurons in the dorsolateral pons of rats changes during fentanyl overdose (i.e. when breathing 'turns off'). For my postdoctoral work, I joined Joseph Santin's laboratory with a goal to better understand cellular neuroscience within the context of respiratory neurobiology. Unlike humans and lab rodents, many animals in nature remain dormant for many months of the year while maintaining functionality of their motor systems, including the motor circuit that controls breathing in American bullfrogs. Bullfrogs do not breath air for months at a time during overwintering when they are submerged in ice-covered ponds, and oxygen demands are met via cutaneous respiration. To complement the pathological nature of my PhD work, this phenomenon provided a physiological context to study how respiratory neurons turn 'off' and back 'on' in a way that is critical for the animal in the wild. My current research project seeks to uncover new aspects of the amphibian respiratory network and how these neurons adapt and compensate for chronic inactivity during hibernation, ultimately protecting the drive to breathe upon emergence.

How would you explain the main finding of your paper to a member of the public?

We breathe continuously throughout our life, most of the time without thinking about it. This automatic and subconscious process is generated in the brainstem by activity of neurons – cells that transmit information throughout the nervous system. Most work investigating this process has occurred in mammals, leaving other vertebrates, including amphibians, in the dark. In mammals, our ability to inspire is driven by rhythmic activity in a specific area of the brainstem called the preBötzinger complex. Although some researchers have identified a similar brainstem region in amphibians, referred to as the lung area, it remains unknown whether this area can produce breathing-like activity in a highly reduced circuit. To resolve this longstanding question, we generated a thick brainstem section that contained the lung area. We found that this region in isolation does not produce activity associated with breathing, which confirmed previous studies. However, we showed that breathing-like activity can be reliably 'kickstarted' by partially blocking inhibitory neurotransmission, which functions as a 'brake' on brain activity. Thus, by reducing the 'brake'. our brainstem section was able to reliably produce rhythmic breathing-like activity. Our results represent the first convincing evidence that an adult vertebrate brainstem section can generate rhythmic respiratory-like activity in a highly reduced brainstem network, which has the possibility to launch a new era of mechanistic work on how breathing is generated across vertebrates.

What are the potential implications of this finding for your field of research?

Most work that investigates the cellular basis of breathing generation uses neonatal rodents under 4 days old. Thus, there is a major gap in our understanding of cellular mechanisms of respiratory rhythm generation in older animals. Unlike our work, where we had to 'cut the brakes' to turn on breathing, 'pushing down the gas pedal' reliably

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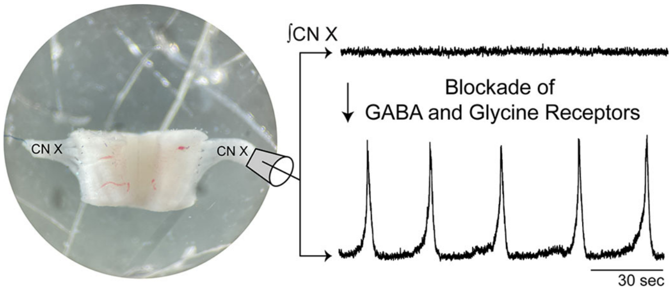
Journal of Experimental Biology (2023) 226, jeb246657. doi:10.1242/jeb.246657



This small section of the brainstem can generate breathing-like rhythmic activity following block of inhibitory neurotransmission.

initiates the rhythm in young animals. It has been a major challenge to initiate rhythmic activity in reduced networks containing the preBötzinger complex in animals greater than 3 weeks old. Work across vertebrates shows that high potassium reliably induces rhythmic activity in reduced respiratory networks of juvenile animals, but perhaps sub-saturating block of inhibitory neurotransmission, as we performed in our experiments, may also initiate respiratory-like activity in reduced preparations from adult animals.

Which part of this research project was the most rewarding/challenging?

When we first sectioned the brain and recorded it, it was silent. We tried a few different approaches to induce rhythmic activity, and nothing really worked. The first time we applied the blockers of inhibitory neurotransmission, we saw beautiful rhythmic bursting emerge from the silence. It was awesome!!!

Why did you choose JEB to publish your paper?

JEB has a strong focus on comparative physiology and is well respected in the field. Many of the papers that informed our experiments and we ultimately built upon were published in JEB. JEB also has an excellent editorial staff that will ensure our paper will be the best it can be. Lastly, JEB plants a tree for every article published in their journal. Overall, an awesome journal to work with!

What do you think experimental biology will look like 50 years from now?

I hope that the wealth of genetic tools we have for mice will become available for non-traditional model organisms, allowing us to combine classic physiology approaches with animals in natural environments. I also hope we get to the point where we can image voltage activity of all neurons, in different parts of the neuron, throughout the brain, at a single-cell resolution, in any freely behaving animal. This is the dream.

If you had unlimited funding, what question in your research field would you most like to address?

Breathing activity is defined in part by the pattern of activity. One question that keeps me up at night is how vertebrates can generate similar patterns of motor activity, in a wide range of contexts. For example, episodic breathing has been reported to occur in all classes of vertebrates and is believed to occur through central mechanisms. What conserved properties of the brainstem, if any, drive this phenomenon? Furthermore, when you block inhibitory neurotransmission at a high enough dose, many motor networks across vertebrates will produce a nearly identical shape of output, i.e. large 'decrementing' bursts. Why? What conserved properties of motor neurons, if any, drive this specific shape of output? How completely different animals, in a wide range of contexts, can generate nearly identical patterns of motor activity is something I hope to investigate in the future.

What's next for you?

In the short term, I will finish up some projects and likely start a few more, all the while collecting beautiful data. In the long term, I hope to start my own lab where I can answer some long-standing questions that I would really like to know the answer to!

What do you like to do in your spare time, when you are not in the lab?

I recently started a local underwater hockey team, named the COMOdo Dragons, in Columbia, MO! I love to get in the pool and play the game with folks in the community. Underwater hockey is a wonderful way to exercise with the respiratory challenge providing me with real-world respiratory neuroplasticity that helps me to keep calm, cool and collected when my experiments don't go as planned.

Reference

Saunders, S. E. and Santin, J. M. (2023). Activation of respiratory-related bursting in an isolated medullary section from adult bullfrogs. *J. Exp. Biol.* **226**, jeb245951. doi:10.1242/jeb.245951