The Journal of Undergraduate Neuroscience Education (JUNE), Spring 2021, 19(2):R35-R38

AMAZING PAPERS IN NEUROSCIENCE
Examining Empathy Through Consolation Behavior in Prairie Voles

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Empathy is an affective and cognitive event in which an organism experiences an approximation of the physical or psychological state of another organism. The phenomenon has been well-studied in humans but is not as widely researched in other animals. Burkett and colleagues in a 2016 article published in *Science* measured empathy in prairie voles (*Microtus ochrogaster*) and meadow voles (*Microtus pennsylvanicus*) by observing consolation behavior between non-stressed and stressed individuals. Their data from behavioral analyses and histochemistry support their hypothesis that consolation behavior in prairie voles shares similar behavioral characteristics and conserved biological mechanisms with human empathy. Prairie voles match anxiety and fear states as well as groom stressed familiar conspecifics to lessen their stress. An oxytocin receptor antagonist abolished this empathetic response. This research impacted the field of neuroscience by demonstrating human-like empathy in rodents, and thereby supporting the value of animal models to investigations of higher order human experiences. The paper is also a valuable and accessible resource to undergraduate neuroscience students—from introductory courses to advanced seminars. In the classroom, this research provides a foundational look at the expanding field of social neuroscience. Empathy in prairie voles raises thought-provoking discussion concerning emotions, social behavior, and human nature.

Key words: empathy; social neuroscience; Microtus ochrogaster; Microtus pennsylvanicus; *consolation behavior; allogrooming; Pavlovian fear conditioning; immunohistochemistry; oxytocin receptor antagonist*

A person may experience a flash of pain or even wince at the observation of someone stubbing their toe. It is even possible to feel another's pain or sadness without witnessing its cause. This affective reaction to another person's distress is an empathetic response and is observable through consolation behavior (Fraser et al., 2008; Singer and Lamm, 2009). Consolation behavior is affiliative contact toward a stressed individual in order to mitigate their negative experience (Zahn-Waxler et al., 1992; Fraser et al., 2008). Empathy and consolation behavior have been studied in both humans and non-human primates, which is why, until recently, it was believed only primates with complex cognitive systems were capable of empathy (de Waal and van Roosmalen, 1979; Preston and de Waal, 2002). However, empathy is now thought to be present in rodents and other animals as well (Bartal et al., 2011; de Waal, 2019).

In 2016, Burkett and colleagues published a study in the journal *Science* investigating consolation behavior in prairie voles (*Microtus spp.*) which demonstrated these animals' capacity for empathetic behavior. They characterized allogrooming, or the grooming of one vole by another, as a consolation behavior. Through multiple assays, Burkett et al. (2016) showed that consolation behavior in prairie voles possesses four similar characteristics as exhibited in human empathy: state matching, emotional contagion, familiarity bias, and self-other differentiation. First, the researchers tested for state matching, and verified that prairie voles experience the physical and psychological distress of their conspecific. Second, the researchers showed that prairie voles emotionally experience the distress of their conspecific, demonstrating emotional contagion. Third, the familiarity bias assay showed that the consolation behavior is only performed toward familiar stressed individuals and not toward strangers. Finally, the prairie voles demonstrated self-other differentiation behavior, in that only the non-stressed individuals increased allogrooming, signifying that voles are knowledgeable of their conspecific's experience varying from their own. Prairie voles also share similar neurobiological mechanisms of empathy with humans as demonstrated by the inhibitory effects of oxytocin receptor antagonists (OTA) in the anterior cingulate cortex (ACC) (Burkett et al., 2016).

This research provides evidence that allogrooming in prairie voles is an empathetic response. In addition to its impact on how social neuroscientists will investigate the evolutionary development and causal mechanisms of empathetic behavior, this paper is also a valuable resource for the classroom. Burkett et al. (2016) present their research in a way that is accessible to all undergraduate students, from introductory neuroscience courses or research methodology, to more advanced seminars concerning comparative studies or animal behavior. This research examines a relevant topic that reflects the growing field of social neuroscience, which uses multi-level approaches and integrates different disciplines to examine the neurobiological processes underlying psychosocial phenomena (Cacciopo and Bernston, 1992). This paper can be used in the classroom to facilitate learning and thoughtful discussion among undergraduate neuroscience students.

RESEARCH SUMMARY

Burkett et al. (2016) hypothesized that prairie voles would exhibit consolation behavior in reproducible conditions and that this behavior would be based on empathy mechanisms—behavioral characteristics and neural processes—as exemplified in humans. In order to test this hypothesis, consolation testing was performed in vole pairs. As shown in Figure 1 of the paper, vole pairs were separated for a period of time in which the "demonstrator" vole was either subjected to a Pavlovian fear conditioning paradigm, which induced stress by low-intensity foot-shocks after a series of tones, or sat alone in a home cage. The demonstrator was then reunited with the "observer" vole that was unaware of the other's experience and was not stressed. Once the voles were reunited, allogrooming of the demonstrator by the observer vole commenced. In situations in which the demonstrator was stressed, observer voles were quicker to begin allogrooming and did so for longer than with the control that had not been stressed. Meadow voles (*Microtus pennsylvanicus*), a closely related but promiscuous breed that was also tested, did not change their behavior based on the stress of their conspecific in the aforementioned assays. The elevated plus maze test was used as an assay for anxiety, in which less time spent on the open arms demonstrates greater anxiety-like behavior. Stressed demonstrators that remained alone after fear conditioning displayed more anxiety-like behavior than the stressed demonstrators that were reunited with and groomed by the observer. Thus, consolation by allogrooming serves as a type of social buffer which reduces stress or anxiety-like behavior.

After demonstrating the reproducibility of consolation behavior, the next assays determined whether allogrooming is based on human empathy mechanisms as demonstrated through certain behavioral characteristics: emotional contagion, state matching, familiarity bias, and self-other differentiation. Figure 2 demonstrates emotional contagion as observer voles mimicked the anxiety-related behavior of demonstrator voles through increased self-grooming. The observer voles also showed state matching through behavioral and physiological means as shown in Figure 3. Observer voles matched fear-related behavior by freezing when witnessing the demonstrator freeze in response to a tone stimulus, to which only the demonstrator had been conditioned. Physiologically, observer voles matched heightened plasma corticosterone levels of demonstrator voles that they could see after fear conditioning but could not console because of a clear barrier. Familiarity bias was displayed through observers selectively consoling familiar stressed demonstrators and not stressed strangers. Lastly, because observers increased allogrooming but demonstrators did not, allogrooming must be dependent upon the specific source of stress from the demonstrator rather than stress more generally, which reveals self-other differentiation.

By demonstrating these four behavioral characteristics of empathy in prairie vole consolation, Burkett et al. (2016) provide convincing evidence for the expression of empathy similar to humans in a mammal perceived as less cognitively advanced. The authors also argue that their use of unconditioned responses strengthens their findings compared to previous empathy-related studies. In other words, because the observer voles in this paradigm are not familiar with the stress by observation or experience, they solely responded to the observed stress of the demonstrator vole upon reunion. By providing convincing evidence and excluding other possibilities, Burkett et al. (2016) strengthen their results and conclusions.

Following the experiments supporting behavioral empathy mechanisms, Burkett et al. (2016) investigated the neural mechanisms involved. Figure 4 shows that the prelimbic cortex (PLC), anterior cingulate cortex (ACC), and nucleus accumbens shells (NACS) contain high amounts of oxytocin receptors, which have been linked to empathy in humans (Domes et al., 2007; Modi and Young, 2012). Observers administered an OTA in their cerebral ventricle showed no increase in allogrooming, and therefore no consolation response, compared to observers administered a control vehicle. Immunohistochemistry assays of the FOS protein revealed that the ACC was activated more in observers interacting with stressed demonstrators compared to unstressed ones as shown by an increase in FOS protein. This was not the case for the PLC or NACS brain areas, which showed no difference in activation between the stressed and unstressed groups. Thus, it is likely that oxytocin receptor activation specifically in the ACC may be necessary for consolation behavior. Burkett et al. (2016) confirmed this by abolishing consolation behavior through the administration of an OTA directly into the ACC. Therefore, humans and prairie voles may share an underlying neurobiological mechanism of empathy: oxytocin receptor activation in the ACC.

Overall, this research presents an account of consolation behavior in prairie voles that is mediated by oxytocin and behaviorally and physiologically similar to human empathy. This conclusion entails a variety of consequences and applications. Firstly, it further supports that mammals with less demonstrated cognitive ability, such as rodents, are capable of consolation and perhaps empathy. Secondly, the development of consolation behavior or empathy may depend upon certain genetically determined social conditions since the closely related meadow vole differs in behavior. Thirdly, oxytocin may be a viable tool to investigate psychiatric disorders involving social and emotional processing. In addition to contributing to the field of neuroscience, this research is valuable for introducing and teaching the field of social neuroscience to undergraduate students.

TEACHING VALUE

This paper is valuable for teaching undergraduate neuroscience students in multiple ways. From a basic writing standpoint, the paper is clear, concise, and accessible. Although educators may need to explain some specific concepts regarding methodological procedures, the paper is free of complex jargon. The paper concisely explains the experiments, presenting only need-to-know information. However, if students are interested in expanding their understanding of the experiments, the supplementary material and previous papers offer further elaboration (Getz, 1972; Getz et al., 1993). The figures fully demonstrate the results and resonate with the conclusions. Overall, the paper logically guides the reader through the experiment as it investigates the hypothesis.

From the classroom perspective, the paper can assist educators with the instruction of research methods and writing or facilitation of thought-provoking discussions. Appropriate for a variety of neuroscience courses—pharmacology, research methodology, behavioral neuroscience, comparative neuroscience, and social neuroscience—this paper can be reviewed in a more general or detailed manner. For example, classroom teaching can focus on big-picture ideas, such as the basic components of research, or target specific methods, such as fear-conditioning or histochemistry. This paper is adaptable to different kinds of teaching. It would best be used in combination with other scientific papers and textbooks (see 'Guidelines and Resources' for details) to provide a foundational understanding of social neuroscience topics, especially empathy and prosocial behavior.

There are a wide number of questions and discussions pertaining to this paper and social neuroscience for students to explore. Emotional and social behavior are at the center of a variety of disciplines, including sociology, psychology, anthropology, and philosophy. As neuroscience delves further into multidisciplinary areas, it would be useful to discuss the many theories and perspectives involved in examining and understanding emotional and social behavior. The following questions can be used to generate discussion and debate: What is empathy? How does empathy relate to altruism? Under what social or evolutionary conditions does empathy develop? How can we study emotions in humans and non-human animals? Can non-human animals have human emotions? This paper demonstrates the value of animal models, while also raising inquiries concerning the limitations of this approach and relevance to complex human behaviors.

AUDIENCE

This research is potentially appropriate for many undergraduate neuroscience courses as it covers a range of fields and ideas. The paper is well-suited for first- and second-year undergraduates as the writing and methodologies are simple and give a foundational introduction to neuroscience research. The topic of empathy should be familiar enough to engage beginner students and the techniques of behavioral observation and neurobiological analysis will demonstrate the range of research available to neuroscientists. Advanced students can use their previous years of experience to ask deeper theoretical questions and learn how to answer them empirically by formulating their own hypotheses and experimental designs.

GUIDELINES AND RESOURCES

Three primary uses for this research in the classroom are in an introductory neuroscience course, a specialized neuroscience course, or a higher-level neuroscience seminar. For an introductory course, educators could use this paper most effectively as supplemental reading to a main textbook. Most general neuroscience textbooks, such as Cognitive Neuroscience: The Biology of Mind (fourth edition), contain chapters addressing emotional or social neuroscience; this paper would help students to understand and apply concepts to research and behavior (Gazzaniga et al., 2013). Although this paper is accessible to students with little neuroscience background, it may be best to use this paper in the latter half of a semester, after covering the fundamentals of neurons, synaptic transmission, and general research methods. Introductory level students, such as first- and second-year undergraduates, may still have questions regarding the specifics of pharmacology and histochemistry techniques, but the basics will be sufficient for understanding the general ideas. Therefore, this paper is better for exploring more complex cognitive capabilities—emotions, social cognition, empathy, theory of mind, and altruism—toward the end of the semester.

This research is also pertinent for specialized neuroscience classes aimed toward second- and third-year undergraduate students that already have general neuroscience experience. Specialized classes may include pharmacology, comparative neuroscience, or social and emotional neuroscience. In a pharmacology course, this paper would be a helpful resource during a unit about neurotransmitters and hormones. This paper would be appropriate for exploring oxytocin and the neural pathways it affects. The course can also focus on the research and treatment of psychiatric disorders using drugs, agonists, and antagonists. As mental health and disorders become increasingly relevant in society, more students will be interested in learning about it, and social neuroscience offers a unique perspective.

Within a comparative neuroscience course, this paper is a useful tool to investigate similar research done in humans, non-human primates, and other mammals (de Waal and Roosmalen, 1979; Clay and de Waal, 2013; Byrne et al., 2008). Through an exploration of the animal behavioral research literature, students will get a glimpse of how research methods vary between animal models and the evolutionary changes that have shaped behavioral and neural mechanisms. After reading this paper, students can search for related research literature that studies empathy in a different animal or utilizes a different method. In a class such as this one, the translational benefits of research can be highlighted through the comparison of experiments with rodents, non-human primates, and humans.

Many academic departments are beginning to offer courses in social neuroscience as research in this area continues to evolve. A social and emotional neuroscience course can use Burkett et al. (2016) as a foundational piece to better understand empathy, altruism, and pro-social behavior. A social neuroscience course could use part of the semester to examine social and emotional research in non-human animal models and the other part to investigate human-specific social cognition and behavior. This allows students to compare social behavior between humans and non-humans more easily. Students in these specialized classes may benefit by first grasping the concepts presented by this paper and then applying and comparing the concepts to other research.

Lastly, this research could be useful for higher-level courses such as seminars. Although many questions can be asked of this paper alone, it would be useful to pair it with a review of the social neuroscience field or an article that supports its results with alternative methods (e.g., de Waal and Preston, 2017; Kiyokawa and Hennessy, 2018; Lee and Beery, 2019). This paper is inspirational for discussions concerning human nature, specifically, the differences in social behavior between humans and non-human animals. Discussions may also arise concerning the best techniques to study empathy and complex social behaviors. For example, empathy can be explored in regard to psychiatric disorders such as sociopathy and autism spectrum disorder (ASD) as this study provides a possibility of pharmacological treatment in the oxytocin system (Modi and Young, 2012; Putnam and Young, 2018).

CONCLUSION

Burkett and colleagues (2016) offer a foundational study that guides exploration in both the laboratory and the classroom. In the laboratory, prairie voles can be considered a valuable animal model to observe empathy mechanisms similar to those in humans. This work also guides translational research addressing psychiatric disorders involving oxytocin. In the classroom, students can learn about the development of social neuroscience as a discipline and learn about the types of questions and techniques common in the field. Overall, this paper provides an ideal platform for combining research innovation and classroom education in social neuroscience.

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Received July 15, 2020; revised September 01, 2020; accepted August 18, 2020.

The author would like to thank Dr. Bruce Johnson, Dr. Stefan Pulver, and her colleagues in the University of St. Andrews MRes in Neuroscience program for their support and feedback.

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