The Physiology of Kindness

Empathy is one of the traits that make us human. In exploring the origins of empathy disorders, however, we can learn a lot by studying animals.

KAPA65/WWW.PIXABAY.COM

The word "empathy" comes from the Greek word *έμπάθεια* (*empatheia*), a composite of the prefix *ἐν* (*en*) and the word *πάθος* (*pathos*), which stands for "passion" and "suffering." The term was brought into English through Edward Bradford Titchener's translation of the German coinage *Einfühlung*, which faithfully renders the composition of the Greek word.

Dr. Ksenia Meyza

Nencki Institute of Experimental Biology
Polish Academy of Sciences, Warsaw

In the popular understanding, empathy is a trait attributable only to humans and our closest evolutionary relatives. However, this anthropocentric approach is contradicted by research seeking the sources of empathy in parental care commonly displayed by birds and mammals. This discrepancy is visible in the academic debates over how empathy should be defined. Some scientists believe that empathy merely reflects the ability to feel another's emotional state, which later gives rise to a prosocial change in behavior. When considered from this perspective, empathy boils down to what is known as emotional contagion, a phenomenon that occurs both in humans and in other animals. For example, ravens have been observed to console other ravens who were victims of antagonistic interactions. Rats have been shown to voluntarily free other rats from small containers despite being simultaneously offered the opportunity to receive a sweet reward in another corner of the cage. After freeing the trapped rat, the liberator would often reach for the reward and share it with its cagemate. Such behavior is an example of "other-oriented motivation" in line with the definition of empathy proposed by Daniel Batson.

Likewise, empathetic behaviors in animals may assume the form of acts of omission. Rhesus monkeys and rats subjected to instrumental conditioning

in which their own receipt of a reward (food) was linked to an unpleasant stimulus being delivered to another animal in a neighboring cage refrained from performing the rewarded action.

Under an alternative definition, Frans de Waal's perception-action model, empathy is a complex behavior that corresponds to three levels of imitation. The most basic level is motor mimicry, which corresponds to emotional contagion. The next level comprises coordination and shared goals, which are reflected in sympathetic concern and consolation. The highest level of complexity comprises perspective-taking and targeted helping, which correlate with true imitation and emulation on the imitation side. According to de Waal, the first two levels of empathy can be found in different animals, whereas the highest level is limited to humans, apes, dolphins, and elephants – in other words, to species whose brains, more specifically the anterior cingulate cortex and the anterior insular cortex, are characterized by the presence of spindle neurons, which are responsible for complex emotions, cooperation, and deception.

Another hierarchical model of empathy has been proposed by Jaak and Jules Panksepp, who link degrees of empathy to the activity in the corresponding areas of the brain. According to this model, a range of subcortical structures of the brain are responsible for emotional contagion. These structures are involved in the initiation of simple behavioral responses such as fear, panic, rage, lust, care, or the urge to play. Emotions related to these responses then transferred upward through emotional empathy, with the basal ganglia and the limbic system being responsible for learning and the formation of memory traces based on the transferred emotions. The same structures of the brain together with higher-level cortical regions are responsible for cognitive empathy, which represents the highest and, from the phylogenetic perspective, the youngest level of empathy complexity. Like in de Waal's model, its role is to facilitate perspective-taking.

Human imperfections

Studies that use neuroimaging techniques show that the aforementioned parts of the brain, namely the anterior insular cortex as well as the anterior cingulate and midcingulate cortices, are the main structures involved in the sharing of both pain and positive emotions in humans. When subjects were shown abstract cues suggesting the infliction of pain to a loved one, their brains exhibited strong activity in the structures responsible for dealing with representations of other people's emotions, such as the prefrontal cortex, the superior temporal cortex, the inferior frontal gyrus, and the temporoparietal junction.

Empathy disorders in humans can have a range of causes and should be considered in four categories: cognitive empathy deficit disorder (CEDD), emotional empathy deficit disorder (EEDD), general empathy deficit disorder (GEDD), and general empathy surfeit disorder (GESD). The first, cognitive empathy deficit disorder, is characteristic of neurodevelopmental disorders such as autism spectrum disorders, Asperger's syndrome, or the agenesis of the corpus callosum, whereas emotional empathy deficit disorder is typical of psychopathy and behavioral disorders of an asocial nature (e.g. aggression). Individuals that show deficits in cognitive empathy lack the capacity to fully identify other people's emotional states, despite declaring that they share their feelings. By contrast, individuals with emotional empathy deficit disorder are aware of other people's feelings, but these do not affect them or cause them to feel and behave in a compassionate manner. If also characterized by a lack of scruples, such individuals may have a tendency to abuse and hurt others. The third category, general empathy deficit disorder occurs, in patients who suffer from schizophrenia. Such people have a tendency to isolate themselves from society, which additionally intensifies their symptoms. Lastly, general empathy surfeit disorder is exhibited by patients with Williams syndrome, in whose case it is difficult to determine to what extent they understand other people's emotions due to coexisting cognitive disorders.

Cognitive and emotional empathy disorders are reflected in low activity of the brain structures that are responsible for imagining other people's feelings. In children and adults with diagnosed autism spectrum disorders, the insular cortex is characterized by decreased activity and is functionally less connected to the limbic structures, which may cause insufficient stimulation. Curiously enough, autistic individuals show greater empathy towards other autistics, which is attributable to increased activity of the ventral prefrontal cortex (responsible for the detection of similarities). In addition to lower empathy levels related to the inability to differentiate between fear and disgust, individuals with congenital agenesis of the corpus callosum (which is involved in the exchange of information between the left and right

The argument that empathy is a uniquely human trait is contradicted by research seeking the sources of empathy in the **parental care commonly displayed by birds and mammals**.

Dr. Ksenia Meyza is an Assistant Professor in the Laboratory of Emotions Neurobiology at the Department of Neurophysiology, Nencki Institute of Experimental Biology, Polish Academy of Sciences (PAS). Her research focuses on explaining the molecular mechanisms underlying autism spectrum disorders by determining the level and activity of proteins involved in neuronal plasticity and examining their influence on social behavior in mouse models of autism.

k.meyza@nencki.gov.pl

hemisphere) have a reduced population of spindle neurons in the anterior cingulate cortex and the anterior insular cortex.

Individuals with psychopathic inclinations are characterized by decreased activity of the parts of the brain responsible for the recognition of facial expressions as well as the regions responsible for impulsiveness, emotional stability, and the making of emotional decisions. However, in response to faces expressing fear, sadness, and pain, such individuals also show increased activity in the dorsal part of the insula as compared to the control group. Studies on prisoners showed that individuals with strong psychopathic traits subjected to pain stimuli showed correct activation in the anterior insula, the anterior cingulate cortex, the supplementary motor area, the inferior frontal gyrus, the sensory cortex, and the right amygdala. When they were asked to imagine the pain of another person, however, these parts of their brain showed impaired activity. Schizophrenia patients show decreased activity in the anterior insular cortex and the anterior cingulate cortex during tasks that require self–other differentiation whereas other–self differentiation led to increased activity in these parts of the brain as compared to the control group. In turn, the brains of Williams syndrome patients, who have general empathy surfeit disorder, exhibit decreased activity of the visual structures responsible for the recognition of facial expressions, no activation of the right inferior occipital lobe, and decreased deactivation in the right temporal operculum in response to pictures of faces displaying different emotions.

Confirming the occurrence of emotional contagion in mice opened up **new avenues of research into the underpinnings of empathy disorders in humans**.

The help of rats

All these studies help us piece together which regions of the brain are involved in processes related to empathy. Even so, they fail to explain the mechanisms, especially at the cellular and molecular level, that are responsible for the ability to share the feelings of others. Understanding these mechanisms is vital for the development of adequate therapies for empathy disorders. Determining whether it is possible to create reliable animal models to study empathetic behavior is therefore crucial.

For several years, the Laboratory of Emotions Neurobiology at the Nencki Institute has been studying the exchange of emotional information between subjects of the same species. Initially, we looked at pairs of rats. In each pair, one rat (the demonstrator) was subjected to fear conditioning, while the other (the observer) was waiting in the homecage. After the return of the demonstrator, the interaction between the rats was recorded and compared to the behavior of pairs of rats in which the demonstrator had not undergone aversive training. After that, the brains of the rats were removed and analyzed using immunohistochemical tests. The observers paired with the demonstrators that were subjected to aversive conditioning were a lot more interested in the return of their cagemates, which was accompanied by strong activation of the amygdala, for example in the cells of the central nucleus of the amygdala. However, this part of the brain was not activated in the demonstrators that were subjected to conditioning. This part of the brain is involved not only in learning pleasant experiences but also in aversive learning. Further behavioral experiments showed that following contact with the demonstrators subjected to conditioning, the observers were more agitated (enhanced startle responses to acoustic stimuli) and were better at learning the avoidance response in the shuttlebox. Similar results were obtained in mice: the placement of a mouse subjected to conditioning in the cage led to the renewal of the fear response in animals in which the extinction of that response had been already observed.

The confirmation that emotional contagion occurs in mice opened up new avenues of research into the underpinnings of empathy disorders in humans. This is thanks to numerous mouse models of social interaction disorders. In the most recent study, we demonstrated that the transfer of fear between two mice was impaired in BTBR $T^{+}Itpr3^{tf}/J$ mice, characterized by the absence of the corpus callosum. This strain is considered the most extensively studied mouse model of idiopathic autism. Moreover, these animals exhibit not only impaired reception of information from distressed individuals but also impaired neuronal plasticity in response to the same stress stimulus. Combined with data indicating the impairment of functional neuronal plasticity in the amygdala of these animals and the elevated levels of enzymes involved in synaptic plasticity in the amygdala of these mice, this model allows for the identification of a possible mechanisms responsible for impaired emotional contagion. This offers a starting point for further studies using local interventions in the level of proteins regulating neuronal plasticity. Their findings should bring answers to questions related to the molecular mechanisms of empathy disorders.

Ksenia Meyza

Further reading:

Decety J., Bartal I.B., Uzefovsky F., Knafo-Noam A. (2016). Empathy as a driver of prosocial behaviour: highly conserved neurobehavioural mechanisms across species. *Philos Trans R Soc Lond B Biol Sci. 371* (1686), 20150077.

Knapska E., Nikolaev E., Boguszewski P., Walasek G., Blaszczyk J., Kaczmarek L., Werka T. (2006). Between-subject transfer of emotional information evokes specific pattern of amygdala activation. *Proc Natl Acad Sci U S A. 103* (10), 3858–62.

Meyza K., Nikolaev T., Kondrakiewicz K., Blanchard D.C., Blanchard R.J., Knapska E. (2015). Neuronal correlates of asocial behavior in a BTBR T (+) Itpr3 (tf)/J mouse model of autism. *Front Behav Neurosci. 9*, 199.