Neuroscience and Biobehavioral Reviews 76 (2017) 216–234

Contents lists available at ScienceDirect

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

Review article

The roots of empathy: Through the lens of rodent models☆

K.Z. Meyza[a,*], I. Ben-Ami Bartal[b], M.H. Monfils[c], J.B. Panksepp[d], E. Knapska[a,*]

[a] Laboratory of Emotions' Neurobiology, Nencki Institute of Experimental Biology, Warsaw, Poland
[b] Helen Wills Neuroscience Institute, University of California Berkeley, Berkeley, CA, USA
[c] Department of Psychology, University of Texas, Austin, TX, USA
[d] Department of Behavioral Neuroscience, Oregon Health and Science University, Portland, OR, USA

ARTICLE INFO

Article history:
Received 15 December 2015
Received in revised form 18 October 2016
Accepted 28 October 2016
Available online 4 November 2016

Keywords:
Neuronal correlates
Animal empathy
Emotional contagion
Vicarious experience
Rodent
Rat
Mouse

ABSTRACT

Empathy is a phenomenon often considered dependent on higher-order emotional control and an ability to relate to the emotional state of others. It is, by many, attributed only to species having well-developed cortical circuits capable of performing such complex tasks. However, over the years, a wealth of data has been accumulated showing that rodents are capable not only of sharing emotional states of their conspecifics, but also of prosocial behavior driven by such shared experiences. The study of rodent empathic behaviors is only now becoming an independent research field. Relevant animal models allow precise manipulation of neural networks, thereby offering insight into the foundations of empathy in the mammalian brains. Here we review the data on empathic behaviors in rat and mouse models, their neurobiological and neurophysiological correlates, and the factors influencing these behaviors. We discuss how simple rodent models of empathy enhance our understanding of how brain controls empathic behaviors.

Contents

☆ Review based on the symposium "Neuronal correlates of rodent empathy", held at the 24th Annual Meeting of the International Behavioral Neuroscience Society, June 2–7, 2015 in Victoria, BC, Canada.

* Corresponding authors at: Laboratory of Emotions' Neurobiology, Nencki Institute of Experimental Biology PAS, Department of Neurophysiology, Pasteur 3, Warsaw, 02–093, Poland.
E-mail addresses: k.meyza@nencki.gov.pl (K.Z. Meyza), e.knapska@nencki.gov.pl (E. Knapska).

http://dx.doi.org/10.1016/j.neubiorev.2016.10.028
0149-7634/

1. Introduction

By motivating prosocial behavior, inhibiting aggression and providing a basis for moral development empathy plays a fundamental role in human life and society. Human empathy is a very complex social phenomenon, which has been defined in different ways. Most definitions, however, have common elements including the ability to experience and share feelings of others and to respond with care to the distress in others (de Waal, 2008). For a long time, empathy received much attention from philosophers and psychologists rather than neuroscientists. More recently, vigorous development of human brain imaging techniques (especially fMRI) encouraged systematic neuropsychological studies of empathy that provided many correlates of higher psychological functions (Bernhardt and Singer, 2012; Stanley and Adolphs, 2013). These studies identified brain regions activated during processing of complex social stimuli involved in advanced forms of empathic behaviors observed in humans. However, since neuroimaging studies are correlative in nature and their resolution is limited, neural mechanisms of empathy are largely unknown. Studies employing animal models provide mechanistic insights into the exquisite organization of the neuronal circuitry underlying emotional behaviors such as fear (Tovote et al., 2015), suggesting that these complex neural mechanisms may also control social emotions. To date, however, methods allowing detailed (at the level of neuronal circuits) insight into the mechanism of such control have not been developed for human studies.

Empathy is considered by many to be a uniquely human trait. The possibility of emphatic behaviors in non-human animals has been largely ignored. However, accumulating data show pro-social behaviors in multiple species including primates and rodents, suggesting that some forms of empathy are phylogenetically older than humans. Such findings strongly support the hypothesis about evolutionary continuity of empathic behaviors. Taking such a perspective offers an experimental insight into simpler forms of empathy and gives a chance to understand neuronal processes underlying empathic behaviors. Several theories of empathy that adopted an evolutionary perspective and widened the scope of research have been proposed. One of the most influential ones is de Waal's *multi-level conceptualization of empathy*. It puts the simplest forms of empathy, involving adoption of another's emotional state (*emotional contagion*) at the core of all empathic behaviors, followed by more complex level of the continuum involving concern about another's state and attempts to ameliorate this state by, e.g., consolation (*sympathetic concern*), and the most elaborate level – attributing emotional state to another instead of self (*empathetic perspective taking*) (de Waal, 2008, also see Preston and de Waal, 2002). Emotional contagion has been observed in many animal species (Darwin, 1871; Panksepp and Panksepp, 2013), sympathetic concern and consolation has been described in non-human primates (de Wall and Aureli, 1997) and canines (Custance and Mayer, 2012), whereas the highest level of empathy in the de Waal's model, including targeted helping coming from cognitive appreciation of the other animal's situation (perspective taking), characterize mainly humans and apes (Hare et al., 2006, 2001; Hirata, 2009). Some levels of cognitive empathy, however, involving an understanding of what caused the distress in another animal (and subsequent active inhibition of that behavior in order to minimize the distress of another individual) was also observed in Rhesus monkeys and rats (Church, 1959; Masserman et al., 1964).

The evolutionary roots of empathy, and thus the existence of many levels of empathic complexity, has been also acknowledged by Decety and Lamm, who postulated that empathy encompasses both emotion sharing and cognitive control. According to their definition, affective representations in the brain are automatically activated by perceptual input, whereas cognitive control is mediated by cortical structures, mainly the prefrontal cortex (Decety and Lamm, 2006).

More recently, another model emphasizing the complex, multilayered character of empathy based on brain circuits involved in the control of empathic behaviors has been proposed (Panksepp and Panksepp, 2013). It recognizes three levels: the *deeply subcortical primary level* responsible for *emotional contagion*; the *secondary level based on basal ganglia and limbic structures* involved in *learning and memory*; and the *tertiary process governed largely by cortical and limbic structures* required for *cognitive empathy*. Several of these brain circuits may be crucial for more than one level of empathy and their specific actions are dependent on the given emotion. At the primary level, emotions such as seeking, rage, fear, lust, care, panic or play (Panksepp et al., 1997), could theoretically be shared through so-called emotional empathy. Top-down control exerted by cortical and limbic structures is required for both the formation of conditioned reflexes based on information from other conspecifics (*i.e.*, secondary empathy: the learning and memory formation), and for cognitive regulation of behavioral responses to these stimuli (*i.e.*, tertiary process). This elegant definition is uniform for many species, including humans.

The theories proposed by de Waal and Panksepp and Panksepp form a frame for studying primal emotional foundations of empathy in mammalian brains. Acknowledging the existence of empathy in other animals allows the design of relevant animal models. Here, we will describe the relevant rodent models and review the data, gathered with the use of such models, on the neurobiological and neurophysiological correlates and the factors influencing empathic behaviors. In order to gain insight into animal empathic behaviors, in line with Tinbergen's four questions (Tinbergen, 1963), besides the mechanisms we will also discuss their ontogeny, phylogeny and adaptative value. The reviewed models involve different levels of empathy (emotional contagion, social modulation of learning and empathic concern), thus providing an opportunity to model complex human disorders characterized with impairments of different aspects of empathy. Such models may shed some light on neural mechanisms of empathy, which are still largely unknown. One of the most interesting hypotheses on neural basis of emotional sharing proposed so far is mirroring mechanism, which we discuss in the next section.

2. Do mirror neurons control social emotions?

The discovery of mirror neurons, originally found in macaque premotor cortex (Gallese et al., 1996; Rizzolatti et al., 1996; Umiltà et al., 2001), fueled speculations about neuronal mechanisms of imitation and mimicry. Their involvement was hypothesized in the wide range of abilities and diagnoses, including empathy and autism spectrum disorder (Baird et al., 2011). In the social domain, mirroring occurs when the same neurons are activated by the emotions experienced directly and by observing/interacting with others who are experiencing emotions. Such vicarious activation would