The Neural Bases of Empathy in Humans

Chapter · March 2018

DOI: 10.1016/B978-0-12-805397-3.00003-6

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The neural bases of empathy in humans

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Definitions: empathy and related terms

While numerous definitions exist (Batson, 2009), there is wide agreement that empathy is a multi-faceted construct that involves intricate interactions of bottom-up and top-down components (Decety & Jackson, 2004; Singer & Lamm, 2009; Zaki & Ochsner, 2012, for review). Before discussing these components and their neural underpinnings in humans in more detail, we need to elaborate on definition issues that will allow us to distinguish empathy from concepts that are related to, yet distinct from the term. The distinction between emotion contagion, empathy, sympathy and compassion, and prosocial and altruistic behavior seems particularly vital in a book on empathy in non-human animals. In fact, much of previous reports on empathy in non-human animals pertains more to the domains of emotion contagion or prosocial behavior, rather than empathy in the sense that it is defined in the human social psychological and social neuroscience literature. In that literature, empathy is usually conceptualized as the ability to re-experience ("to share") the feelings of another person, with full awareness that the other person is that source of one's affect (see, e.g., de Vignemont & Singer, 2006). This view allows a clear distinction from emotion contagion, which denotes the tendency to "catch" or "be contaged" by other people's emotions and has also been labeled

"primitive empathy" (Hatfield, Rapson, & Le, 2008). For example, babies start crying when they hear other babies crying, but they do so long before they develop a sense of self separate from others. On a conceptual level, emotion contagion can only contribute to the full-blown experience of empathy, as it lacks the defining component of self-awareness and self/other distinction. The necessity of self-other distinction has important practical implications, too, as without it, witnessing someone else's emotions might result in personal distress and a self-centered response in the observer (Decety & Lamm, 2011, for review). Moreover, definitions in the human literature stress that empathy can be triggered both by direct observation, but also the imagination of the other's affective state. Taken together, this view proposes to regard emotion contagion as an important, yet distinct and neither necessary nor sufficient processes for the experience of empathy. Putting self-awareness and self-other distinction as a requisite for "true, full-blown empathy" (in the sense the term is used in humans) does not imply, though, that non-human animals cannot experience empathy. While for quite some time many scholars would have agreed with such a conclusion, recent experimental evidence in e.g. ravens as well as canines (Bugnyar, Reber, & Buckner, 2016; Muller, Schmitt, Barber, & Huber, 2015), two species known for their advanced social skills, suggest that we should not be so quick in dismissing animals to possess skills that for a long time we have thought to be uniquely human.

Apart from emotion contagion and the related bottom-up, sensory driven processes, we also need to distinguish empathy from higher-level and top-down regulated processes such as empathic concern, sympathy or compassion (Singer & Klimecki, 2014; for review). These three terms usually describe experiences that do not only encompass but require sharing another's affect, in the sense of "feeling as" the other person, but also to "feel for" and care for that person, and becoming motivated to alleviate their distress or suffering. This distinction also implies that the "feeling for" aspect, when responding to the emotions of others resulting in prosocial and altruistic behavior - i.e., behavior that benefits others, such as helping or

supporting them, usually is associated with a cost to oneself. This is not to say, though, that empathy (in the sense of "feeling as") plays no role in prosocial behavior and "feeling for" another person – because while being distinct on a conceptual level, these phenomena are usually highly interrelated in their everyday occurrences. For instance, emotion contagion triggered by seeing a portrait of a desperate refugee can result in empathy in the sense of sharing that person's affect, which in turn might trigger sympathy, and prompt prosocial actions (such as donating money or goods, or engagement in volunteer work). However, this example also serves to illustrate that prosocial action and the associated prosocial feelings and motivations are by no means an automatism. This can be shown by how many people respond now, in the second year of an ongoing "refugee crisis", to very similar portraits – i.e., with quite radically changed emotions and behaviors. From a scientific perspective, several factors can explain this shift in public and individual responses to similar stimuli. This includes bottom-up processes, such as habituation – i.e., seeing similar stimuli over and over again results in blunted affective responses. Top-down processes also play a role, such as when political messages playing with our fears result in refugees not being perceived any more as people in need, but as economic refugees who are threatening our welfare. Importantly, such modulations of empathy are additionally influenced by stress, an aspect that we will focus on in a later part of this chapter.

Mirror neurons, shared representations, and self-other distinction

The fact that empathy "doesn't happen in a vacuum" brings us to the next part of this chapter, which is a brief review of how neuroscience research of the last 15 years or so has provided increasingly detailed insights into the neural underpinnings of empathy. Three aspects deserve particular attention in the context of the present book: what is the role of "mirror neurons" in empathy; is affect sharing implemented by shared representations; and what is the role of self-other distinction ?

Ever since the exciting discovery of mirror neurons in the early 90ies (di Pellegrino, Fadiga, Fogassi, Gallese, & Rizzolatti, 1992), this special class of neurons which respond both to executed and perceived actions has been heavily linked to interpersonal phenomena. This went from simple processes, such as action coordination, to more elaborate ones, including empathy, up to high-level phenomena such as aesthetic appreciation (Freedberg & Gallese, 2007). Notwithstanding recent criticism that some of these interpretations might have been overstretched (Hickok, 2009), mirror neurons certainly play an important role in many cases of empathy-like responses in non-human and human animals alike. It is, however, important to keep in mind that mirror neurons are neither a necessary, nor a sufficient condition for empathy to arise (Lamm & Majdandzic, 2015). This is so because empathy, as outlined above, can also be evoked without direct action observation (e.g., by imagining how refugees described in a newspaper article without photos must feel like). Moreover, mirroring of actions does not necessarily lead to correct mirroring of the associated affective response - such as when being exposed to people whose sensorimotor affective mappings differ from our own. This has been illustrated by experiments in which participants were exposed to situations that would be painful for themselves, but in reality were not painful for the observed other. The consistent finding of these studies was that mechanisms other than motor resonance alone mediate the empathic response and its regulation (Lamm, Meltzoff, & Decety, 2010; Lamm, Nusbaum, Meltzoff, & Decety, 2007). More specifically, areas involved in self-other distinction and cognitive control, such as the temporo-parietal junction and prefrontal areas, were recruited when participants had to control their automatic yet inaccurate vicarious emotional responses (see also below, for effects of stress on similar experimental manipulations). Hence, for the translation of these findings to the animal literature, it is important to keep in mind that conclusions such as that a species has mirror neurons is insufficient to show that this species also possesses empathy, or even emotion contagion.

Regarding the exact neural mechanisms enabling affect sharing, there is an ongoing debate whether this can be accounted for by so-called "shared representations" (Krishnan et al., 2016; Rutgen, Seidel, Riecansky, & Lamm, 2015; Rütgen, Seidel, Silani, et al., 2015; Zaki, Wager, Singer, Keysers, & Gazzola, 2016). The concept of shared representations builds up on the observation that empathy for a certain emotion recruits similar brain areas as the first-hand experience of that emotion. This has not only been observed very consistently, but also using a variety of neuroscience methods, such as functional magnetic resonance imaging (fMRI) (e.g., Lamm, Decety, & Singer, 2011), electroencephalography (EEG) (e.g., Bufalari, Aprile, Avenanti, Di Russo, & Aglioti, 2007), and transcranial magnetic stimulation (e.g., Avenanti, Bueti, Galati, & Aglioti, 2005). For instance, fMRI research has consistently shown that parts of the network that are activated during self-experienced pain are also activated during empathy for pain, such as the mid-cingulate cortex and the anterior insular cortex (Lamm et al., 2011, for meta-analysis). The crucial question is what conclusions can be drawn from this activation overlap, as fMRI basically only provides information on "neural correlates", with limited spatial resolution. Hence, similarity in activation maps between two conditions (i.e., self- and other-related pain responses) might stem from different underlying neural populations, and hence different brain functions. While some recent evidence using more refined multivariate fMRI analyses suggests that this seems the case (Krishnan et al., 2016), psychopharmacological methods and variations in experimental design allowing more causal conclusions support a partially specific sharing of brain functions and representations (Rütgen, Seidel, Riecansky, & Lamm, 2015; Rütgen, Seidel, Silani, et al., 2015). More specifically, these studies indirectly suggest an involvement of the opioid system in empathy for pain. Future studies will thus need to resolve this controversy, and to show whether affect sharing indeed relies on a specific sharing of affective experiences and their underlying neural computations, or whether previous neuroscience evidence only indicates rather-domain general processes such as vicarious arousal or engagement of the so-called salience network (though see (Lamm, Silani, & Singer, 2015), in which sharing of pleasant affect

activated areas outside the “salience network”). Resolving this debate is important both for reasons of scientific curiosity and rigor, but also because of its implications for subsequent processes such as sympathy and prosocial behavior - as models relying on genuine and specific affect would make slightly different predictions as a more domain general “salience account”. Ultimately, the truth might very much lie in between the two explanations, with some parts of the activation overlap being specific, and others being domain-general.

The fact that empathy activates neural networks related to affective processing and regulation explains the necessity of self-other distinction, which, as outlined above, is a defining feature of empathy. Recent progress in neuroimaging, lesion and TMS research has tied this ability to a specific sub region in the human brain, the temporo-parietal junction (Carter & Huettel, 2013; Donaldson, Rinehart, & Enticott, 2015; Lamm, Bukowski, & Silani, 2016, for review). In empathy, this area seems to be particularly important when disentangling one’s own, often aversive, responses to the plight of another person, from the actual emotions experienced by that person. Being a multi-modal association area, some scholars have even argued that this area might be at the root of seemingly unique human social-cognitive abilities (Saxe, 2006). Hence, with the recent advent of neuroimaging in a variety of non-human animal species - including e.g. dogs and birds (Andics, Gacsi, Farago, Kis, & Miklosi, 2014; De Groof et al., 2013), it will be very interesting to test such claims.

Modulations of empathy – the case of stress

Intriguingly, recent research has shown that shared emotions of self and other can be profoundly modulated by situational factors. One ostensive example of this plasticity is shown by documentation of the effects of acute stress on empathy. Although this line of research is still in its infancy, there is evidence that acute stress might affect shared representations of self and other in profound ways. On a physiological level, stress is known to trigger adaptive responses in the body in order to reallocate resources (mainly modulated by the release of catecholamines

and cortisol (Lovallo & Thomas, 2000; Sapolsky, Romero, & Munck, 2000). The physiological changes modulated by these adaptive responses have been shown to also profoundly affect cognition. Stress effects on cognition are particularly prevalent in attention (e.g., Elling et al., 2011; Vedhara, Hyde, Gilchrist, Tytherleigh, & Plummer, 2000), memory (e.g., Vedhara et al., 2000; Wolf, 2009) and decision making (e.g., Starcke & Brand, 2012). Crucially, the underlying level of experienced anxiety has been shown to modulate the effect of stress on cognitive functioning (Bishop, Duncan, Brett, & Lawrence, 2004; Hood, Pulvers, Spady, Kliebenstein, & Bachand, 2015). Research so far has shown that cognitive processes associated with „higher-order“ cognition, such as strategic reasoning and self-control seem to be impaired under stress (Maier, Makwana, & Hare, 2015; Starcke & Brand, 2012). However, other cognitive processes, such as focused attention and general alertness (Plessow, Fischer, Kirschbaum, & Goschke, 2011), learning and memory consolidation (Henckens, Hermans, Pu, Joels, & Fernandez, 2009) and working memory (Yuen et al., 2011; Yuen et al., 2009) have been shown to improve under stress. This discrepancy has led to the view that stress selectively enhances cognitive and affective abilities that are beneficial for survival, at the expense of other mental abilities (Hermans et al., 2014).

Intriguingly, stress has also been shown to profoundly affect social behavior and social emotions, such as empathy. However, the direction of these effects is much less clear, as empirical research has shown both, improvements, and impairments in social interactions under stress. For example, several behavioral experiments have shown that acute stress and anxiety appear to decrease affect sharing (Buruck, Wendsche, Melzer, Strobel, & Dorfel, 2014; Martin et al., 2015; Negd, Mallan, & Lipp, 2011). Intriguingly, one of these contributions was able to show these effects in both humans as well as in mice, with a surprisingly direct translation of magnitude and direction of the effects between species (Martin et al., 2015). However, other studies found the opposite – i.e., that stress can improve certain aspects of empathy. For

example, in a behavioral study it was shown that across different processing levels, self-other distinction was profoundly modulated during acute stress (Tomova, von Dawans, Heinrichs, Silani, & Lamm, 2014). However, the effects were modulated by sex/gender - while men showed decreased self-other distinction under stress, women displayed the opposite pattern, and increased their self-other distinction across different domains (Tomova et al., 2014). More specifically, stressed women showed reduced emotional egocentricity, improved cognitive perspective-taking and a reduction of automatic imitative tendencies. In contrast, men exposed to acute stress showed diminished self-other distinction on all three levels. Their emotional egocentricity bias increased, they showed lower perspective-taking abilities, and reduced ability to overcome automatic imitation tendencies. These results are in line with the tend-and-befriend hypothesis by Taylor and colleagues, which suggests that women show increased affiliative behavior when stressed (Taylor et al., 2000). As appropriate self-other distinction is a prerequisite for crucial social interaction skills such as empathy (Singer & Klimecki, 2014; Singer & Lamm, 2009) and perspective taking (Epley, Keysar, Van Boven, & Gilovich, 2004) these findings might represent empirical evidence for the tend-and-befriend hypothesis.

Contradictory to these findings, several behavioral experiments with male participants also found increased prosocial behavior under stress (Buchanan & Preston, 2014; Margittai et al., 2015; Takahashi, Ikeda, & Hasegawa, 2007; von Dawans, Fischbacher, Kirschbaum, Fehr, & Heinrichs, 2012) and prosocial decision making under time pressure (Rand, Greene, & Nowak, 2012), indicating that automatic responses can produce prosocial outcomes in both, men and women. Viewed from a bio-evolutionary point of view, these modulations in automatic reflexive responding to others' pain might represent adaptive modulations to increase prosociality which overall might improve the survival of the group. However, it is not entirely clear how these findings of increased prosocial behavior under stress relate to evidence on decreased self-other distinction in men. A possible mechanism might have been identified in a recent fMRI study

which has shown stress-induced enhancements in magnitude of neural responding in the empathy for pain network in response to seeing someone else in pain (Tomova et al., 2016). This finding indicates that automatic bottom-up empathic responses to painful situations of others increase under stress. Thus, a possible underlying mechanism might be that decreased self-other distinction leads to increased self-other merging which ultimately leads to higher affect sharing when confronted with emotions of others. Intriguingly, for one, these modulations have been shown in a male sample and for the other, were found to be associated with increased prosocial behavior.

Hence, these findings might provide further insights into the potential mechanisms of how stress, empathy and prosocial behavior are connected. As increased self-other resonance has been proposed as an underlying mechanism driving prosocial behavior (Christov-Moore & Iacoboni, 2016), stress-induced decreases in self-other distinction (i.e., increased self-other resonance) might present an underlying mechanism why individuals exhibit increased prosocial behavior under stress.

This does not yet explain, though, how women, who show increased self-other distinction under stress, could become more prosocial under stress. An alternative path, mainly based on a model proposed by Singer and Klimecki (Singer & Klimecki, 2014), might be that increases in self-other distinction lead to increased compassion and by this increase prosocial behavior. Compassion, as defined by Singer and Klimecki, in contrast to empathy, would not mean sharing the suffering of the other, but is characterized by feelings of warmth, concern and care for the other, as well as a strong motivation to improve the other's wellbeing (Singer & Klimecki, 2014). Thus, from this reasoning, both increased as well as decreased self-other distinction could lead to higher prosocial behavior, although based on different underlying motivations (i.e., affect sharing versus compassion).

Oxytocin as a potential moderator of stress effects on empathy?

It remains unclear though why exactly sex/gender differences appear to be so profound in the effects of stress on social emotions. One possible candidate to explain the effects might be the oxytocin system. The neuropeptide oxytocin is synthesized in the hypothalamus (Swaab, Pool, & Nijveldt, 1975; Vandesande & Dierickx, 1975) and then projected to the posterior pituitary, from which it is secreted into the systemic circulation (Brownstein, Russell, & Gainer, 1980). Oxytocin plays a crucial role in parturition and lactation (Gimpl & Fahrenholz, 2001) but also has been shown to function as a central regulator in social attachment and prosocial behaviors (Heinrichs, von Dawans, & Domes, 2009). For a number of reasons, oxytocin might be a strong candidate to explain these sex/gender differences on a physiological level (Heinrichs et al., 2009; Meyer-Lindenberg et al., 2011). First, women are known to show higher oxytocin release under stress than men (Carter, 2007; Jezova et al., 1996; Sanders et al., 1990). Furthermore, oxytocin has been shown to improve mind reading (Domes, Heinrichs, Michel, Berger, & Herpertz, 2007) - although see: (Lane et al., 2015) - and enhance emotional empathy (Hurlemann et al., 2010). Most importantly, two recent studies found that administration of oxytocin leads to sharpened self-other perception (Colonnello, Chen, Panksepp, & Heinrichs, 2013) and improved self-other distinction on a cognitive level (Tomova et al., 2014). Thus, the gender differences in self-other distinction under stress might be explained by gender differences in oxytocin release under stress, and the neuropeptide's positive effects on coping with stress (Heinrichs & Domes, 2008).

Crucially, though, more empirical evidence is needed to support these ideas and predictions. For example, the proposed mechanism suggesting increased compassion rather than affect sharing under stress in women has not been empirically supported so far. Due to the fact that women show different cortisol responding to stressors depending on their menstrual cycle phase and hormonal contraceptive-usage (Kirschbaum, Kudielka, Gaab, Schommer, & Hellhammer, 1999), most stress studies exclude women from participation. Thus, also the

empirical evidence of increased prosociality under stress so far is restricted to male participants (although, ironically, the original tend-and-befriend hypothesis stated these increases in prosociality to be a specifically female stress response (Taylor et al., 2000)). Therefore a very important next step in this line of research is to empirically investigate prosocial behavior under stress in women. In addition, future empirical research should address whether women in fact show increased compassion under stress which would suggest that there is in fact a dissociation in the underlying mechanisms of how stress affects prosociality between the two genders.

In conclusion, future research on empathy should consider the factors sex/gender and stress, as most neuroscience experiments in humans and non-human animals involve stressful procedures whose effects should thus be taken into account when interpreting such research. Furthermore, adding experimentally endocrinological measures or manipulating them in neuroscience research might enable a more mechanistic understanding of these modulations, and the resulting sex/gender differences.

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