EMPATHY FOR PAIN
And its Neural Correlates

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Abstract

The phenomenon of empathy has been fascinating laymen and scholars for centuries and has recently been an important subject for cognitive neuroscientific study. Empathy refers to the ability to understand and share others’ emotions and a characteristic of this ability is the capacity to empathize with others in pain. This review intends to examine and read up on the current state of the field of the neural and behavioral mechanisms associated with empathy for pain. The neural underpinnings of the first-hand experience of pain have been shown to be activated in a person observing the suffering individual, and this similarity in brain activity has been referred to as shared networks. This phenomenon plays an important role in the study of empathy. However, different factors have been shown to influence empathy for pain, such as age, gender, affective link between observer and sufferer, as well as phylogenetic similarity. This thesis discusses these differences, as well as atypical aspects affecting the empathic ability such as synaesthesia for pain, psychopathy and Asperger’s disease. Further, empathy for pain can be modulated by the individual observing someone in pain. For example, caregivers often down-regulate their empathic response to patients in pain, possibly in order to focus on their treatment and assistance. Also, paying attention to harmful stimuli heightens the perception of pain; therefore, the painful experience can be less remarkable when focusing on something else. The effect of empathy from others directed to oneself when suffering is discussed, as well as the consistency and limitations of presented research.

Keywords: empathy, pain, shared networks, pain matrix, empathy for pain
# Table of Contents

Introduction 5

Empathy 9

- Neural Correlates of Empathy 9
  - Mirror neurons 9
  - The empathy circuit 11

Pain 13

- Theories of Pain 13
  - Gate control theory of pain 15

- Pain Pathways 17

- Neural Correlates of Pain 18

Empathy for Pain 19

- Neural Correlates of Empathy for Pain 19
  - Shared networks 21
  - Somatosensory system 22

Factors Influencing Empathy for Pain 23

- Age 23

- Gender 25

- Empathy for non-human entities 26
Empathy among caregivers 27

Racial bias 28

Atypical Aspects of Empathy for Pain 30

Synaesthesia for pain 30

Psychopathy 31

Huntington’s disease 32

Asperger’s syndrome 33

Post-traumatic stress disorder 34

Regulation of Empathy for Pain 35

Empathy Affects Pain Perception 37

Conclusions 38

References 43
EMPATHY FOR PAIN

Introduction

The term “empathy” derives from the Greek word “empatheia” (passion), composed of “en” (in) and “pathos” (feeling). It was introduced into the English language from the German word “einfühlung” (feeling into), which was then referred to as resonance with works of art, but later on came to describe the resonance between humans (Singer & Klimecki, 2014). The phenomenon of empathy and its many facets have been fascinating laymen and scholars for centuries (Lamm & Majdandžić, 2015). In the late 20th century, researchers began to study this phenomenon on a scientific level. (Singer & Klimecki, 2014)

In order to explain empathy, we first need to clarify how it differs from other related states which also have to do with the sharing of emotions. Empathy is commonly referred to as the ability to understand or feel what another being is experiencing (e.g. Singer & Klimecki, 2014; Fan & Han, 2008; Mu, Fan, Mao, & Han, 2008). According to some researchers, the sharing of emotions is a conscious process in which the other individual is considered the source of the state or the feeling (Betti & Aglioti (2016). However, others support the view that empathy is a multifaceted construct, consisting of several sub-constructs (Preston & de Waal, 2002).

Empathy refers to the ability to understand and share others’ emotional states (Mu et al., 2008). For example, if someone is happy we get happy too, and if someone suffers from pain, we suffer too. Importantly, one does not confuse the feelings of another with one’s own feelings. Empathy is not to be confused with emotion contagion, which is a state in which feelings are shared, but the self-other distinction is not present. Emotion contagion is commonly present in babies, where this distinction is not yet developed (Singer & Klimecki, 2014). It is assumed that emotion contagion is the foundation of empathy, and that its function is on the one hand on a phylogenetic level to provide a link between humans and other
species, and on the other hand on an ontogenetic level between adults and children (de Wall, 2008).

When someone experiences negative emotions, the observer often experiences compassion, or more commonly referred to as *sympathy*. In this state, one does not share the feeling of suffering but rather experiences a warm and caring feeling of concern. This is accompanied by a motivation to help the other, a so called prosocial motivation (Singer & Klimecki, 2014). In sympathy, one feels *for* and not *with* the other. Another reaction to the suffering of others is empathic/personal distress. In this case, the observer perceives the suffering as self-oriented, and reacts with aversion to the situation. The observer has a strong desire to withdraw from the situation in order to avoid this negative feeling (Singer & Klimecki, 2014).

As in the state of sympathy or empathic distress, empathy does not concern only negative feelings. On the other hand, empathy can occur regardless of the valence of the feelings, either positive or negative (Singer & Klimecki, 2014).

The ability to experience empathy is not unique to humans; it seems to derive from antecedents in other species as well as rodents (Panksepp & Panksepp, 2013). There is also compelling evidence that other animals than humans possess the ability to experience sympathy; for example, some animals consolidate each other when losing a fight (de Waal, 2008).

It is of great social importance to possess the ability to feel empathy for others. If we encounter a person who seems to lack this ability, they are usually considered to be either socially impaired or socially deviant (Bruneau, Jacoby, & Saxe, 2015). The ability to experience empathy is one of our most fundamental skills. It requires both emotional and cognitive functioning in the sense that one needs to be able to understand the thought and feelings of another, as well as take part in their emotions (Rameson, Morelli, & Lieberman,
2012). Therefore, many scientists differentiate between affective, or emotional empathy, and cognitive empathy (Ruckmann et al., 2015). Affective empathy refers to the sharing of feelings with others whereas cognitive empathy is the ability to understand others’ emotions, which is strongly connected to theory of mind (Eres & Molenberghs, 2013).

For example, affective empathy is most often associated with activity in the insula, whereas cognitive empathy is, on the other hand, connected to activity in the midcingulate cortex and the adjacent dorsomedial prefrontal cortex (MCC/dmPFC). These findings provide validation for the hypothesis that empathy consists of several components. In other words, affective and cognitive empathy correlate with different neural and structural activities (Eres, Decety, Louis, & Molenberghs, 2015).

Affective empathy is typically referred to as the conscious experience of others’ emotional states, which requires a self-other distinction, and an understanding of the origin of the emotion. In other words, this component of empathy reflects one’s subjective experience of other beings’ emotions. Affective empathy differs from emotion contagion and mimicry, which are automatic responses and do not necessarily require the distinction between self and other. It is also different from sympathy and empathic concern since they don’t have to contain the sharing of emotions. Affective empathy has, on the other hand, been thought of as an umbrella term encompassing emotion contagion, mimicry, sympathy and empathic concern (Eres et al., 2015).

Cognitive empathy refers to the ability to understand others’ motivation (Decety, 2011). Some researchers refer to cognitive empathy as Theory of Mind (ToM) (Mazza et al., 2015), although others make a distinction between empathy and ToM. Kanske, Böckler, Trautwein and Singer (2015) investigated a novel functional magnetic resonance imaging (fMRI) paradigm called EmptaTom in order to reveal clearly separable neural networks for empathy and ToM. For the experience of empathy, there seemed to be a network
in the anterior insula, whereas for ToM, a network was found in the ventral temporoparietal
ejunction. EmptTom allows separation of the affective and cognitive routes to understanding
others (Kanske et al., 2015).

The understanding and experience of another person’s pain, as well as other
emotional states, is a characteristic of empathy. Many studies on empathy have been carried
out with specific focus on pain. The brain areas involved with the direct experience of pain
are also involved with empathy for the pain of others (Decety, Michalska, & Akitsuki, 2008)
which makes the study of pain important for the understanding of empathy.

Pain serves a function from an evolutionary perspective because it warns the
subject and, in turn, the surrounding beings. The behavioral expressions as well as empathy
for pain are necessary for us to be able to help and give care to the suffering individual (Craig,
2004). Facing a person that experiences pain can give rise to a variety of responses, ranging
from ignoring to helping (Goubert et al., 2005). Usually, the sharing of the feeling of pain is
an automatic response, although behavioral responses are distinguished by cognitive factors
such as perspective taking, and emotion regulation such as motivation (Eres & Molenberghs,
2013).

In this review, there will be a presentation of the similarities and differences
between the direct experience of pain and empathy for another person’s pain. The aim is to
explore what happens in the brain of a person who observes another person suffering from
pain in contrast to the direct experience of pain. First there will be a brief overview of the
phenomenon of empathy and its neural correlates. Then there will be an overview of the
physiology of pain and the different pathways and neural structures involved with painful
experience. This section will provide an understanding of the direct experience of pain, from
peripheral stimuli to the fundamental neural processes giving rise to a painful experience.
Thereafter, the essay will focus specifically on empathy for pain. Here prominent research in
this field will be presented, including the disparity of empathy for pain in different neural
deficits, genders and ages. Moreover, this section will also examine the factors which underlie
how empathy for pain can be altered and regulated.

**Empathy**

**Neural Correlates of Empathy**

A growing number of studies indicates that understanding and sharing of
emotions of others depends on a recruitment of the same neural structures both associated
with our own experience and when observing others experience the same thing (Rameson &
Lieberman, 2009). The simulation theory of empathy suggests that our understanding of
another being’s emotions and thought is gained when we use our own minds as a model
(Rameson & Lieberman, 2009) and the discovery of mirror neurons and shared networks have
been considered to support this notion (Gallese & Goldman, 1998). In the following, the
phenomenon of mirror neurons will be presented as well as an overview on its current debate.

**Mirror neurons.** In 1992, an interesting discovery was made that showed that
specific neurons in a monkey’s brain fire when the monkey reaches for objects, as well as
when it observes someone else perform the same action. This phenomenon was revealed by
recording specific cells with electrodes inserted into the brain of the monkey. The monkey
was then presented with a peanut and when it reached for this, the recorded cell fired. In
another experiment, the monkey observed the experimenter reach for a peanut instead, which
caused the very same cell in the monkey’s brain to fire. What makes these neurons special is
that there is no distinction between the monkey’s own performance of an action and the mere
observation of another performing the very same action (De Waal, 2009). This discovery has
been said to be as important to psychology as the discovery of DNA to biology, and the fact
that this was done in monkeys further shows that empathy is not unique to humans (De Waal,
2009). However, the existence of mirror neurons is not proven to be the same as empathy, and the role they play in empathy is not clear yet (Lamm & Majdandžić, 2015). There are differing opinions among scientists as to whether mirror neurons correlate with action understanding or if they are simply a part of the action. In the same way, the activity in shared networks involved with empathy for pain could either be thought of as a route to understanding the feelings of others or as a sign of it (Lamm & Majdandžić, 2015).

The hypothesis that mirror neurons reflect action understanding has been heavily questioned and Hickok (2009) puts forward arguments against this proposal. He states that “a motor representation cannot distinguish between the range of possible meanings associated with such an action” (Hickok, 2009, p. 1240). This means that an action consists of several elements and that the intentions and components of an action could be many. Therefore, because of this range of possible meanings and ways to achieve a goal, there has to be a clear distinction between the goal and the specific motor actions necessary to achieve it. The hypothesis that action understanding is a consequence of a similar activity in our own brain would then be false, either because mirror neurons do not code actions, or because motor representations are not the basis of action understanding (Hickok, 2009).

The brain areas that are associated with mirror neurons are collectively called the “mirror system” (Baron-Cohen, 2011). As mentioned earlier, these areas are active when an individual performs an action as well as when observing someone else performing the very same action. For ethical reasons, it has been somewhat difficult to establish which areas the human mirror system might contain, although it has been suggested that it involves the IFG, the inferior parietal lobule (IPL) and the inferior parietal sulcus (IPS) Although there is no direct evidence that mirror neurons reflect empathy (Lamm & Majdandžić, 2015), the mirror system is implicated in mimicry and emotion contagion. For example, when someone else
yawns and one involuntarily yawns too, these areas are activated. Actions such as these, which are called “mimetic” actions, occur automatically (Baron-Cohen, 2011).

**The empathy circuit.** The neuroscientific understanding of empathy has increased quickly, thanks to a growing number of studies (mostly carried out with fMRI because of its availability and precision) which have enabled us to associate different brain regions with components of empathy (Lamm, & Majdandžić, 2015). Frequently, the brain areas involved with empathy have been referred to as the empathy circuit (e.g. Baron-Cohen, 2011)

The medial prefrontal cortex (MPFC) is referred to as a centrality that processes social information. It is also involved with the ability to compare one’s own perspective with another’s. The dorsal part of this region (dMPFC) is associated with thinking about the thoughts and feelings of other people, as well as our own. The ventral part (vMPFC) is on the other hand involved with merely the thoughts of the self and one’s own mind, rather than someone else’s (Baron-Cohen, 2011). It has also been hypothesized by Damasio that this area has to do with the processing of emotional valence in actions. Damasio proposes a so called “somatic marker”, which is the emotional outcome of an action and the thing that makes us tend to repeat only the actions that we associate with positive emotions (Damasio, Everitt, & Bishop, 1996). Also, this theory is supported by findings demonstrating that the vMPFC is one of the regions involved with the control of mood-related behaviors (Lim, Janssen, Kocabicak, & Temel, 2015). The vMPFC is one of the regions that show abnormally low activation in people with low empathy (Baron-Cohen, 2011) and it also seems to be involved with cognitive empathy (Shamay-Tsoory, Aharon-Peretz, & Perry, 2009).

The orbitofrontal cortex (OFC) is a part of the vMPFC. When OFC is damaged, patients lose their social judgement which affects the social behavior. Further, OFC
impairments are often associated with empathy dysfunction and psychopathy (e.g., Baron-Cohen, 2011; Shamay-Tsoory et al., 2009).

Adjacent to the OFC is the frontal operculum (FO). The adjacent part of the FO is, together with the anterior insula, involved with the processing of other’s negative emotions and negative experiences such as pain. They are also associated with positive feelings of another, in that these two areas map the bodily feelings of others into the internal state of the observer (Jabbi, Swart, & Keysers, 2007). Also, the posterior insula has been suggested to support an early convergence of sensory and affective processing (Morrison, Löken, & Olausson, 2010).

Moving on to the area located inferior to the FO, called the inferior frontal gyrus (IFG), this area is important in the processing of emotional faces (Baron-Cohen, 2011). Moreover, the IFG is involved with affective empathy and if damaged, this capacity is heavily disturbed (Shamay-Tsoory et al., 2009).

The middle cingulate cortex (MCC) plays a role in empathy in that it is associated with bodily aspects of self-awareness (Baron-Cohen, 2011). Together with the anterior insula (AI) it is activated during the experience of pain as well as when observing others in pain (Baron-Cohen, 2011; Singer et al., 2004). Damage to these regions can disrupt the ability to recognize emotions such as happiness, disgust and pain (Baron-Cohen, 2011).

The temporoparietal junction (TPJ) seems to be important to ToM, in that it is associated with the judgement of other’s intentions and beliefs (Saxe & Kanwisher, 2003). It is also involved with the self-other distinction (Schulte-Rüther et al., 2008).

Superior temporal sulcus (STS) is associated to empathy because of animal studies revealing neurons in STS have been found to respond when the animal observes someone else’s gaze (Baron-Cohen, 2011). Further, this area seems to be involved with the
processing of biological motion and facial expressions of others. The STS might also play a role in emotional perspective taking. (Schulte-Rüther, Markowitsch, Shah, Fink & Piefke, 2008).

The last brain structure that has been concluded to be a part of the empathy circuit is the amygdala (Baron-Cohen, 2011). The amygdala is associated with emotional learning and regulation processing (Wager, Davidson, Hughes, Lindquist, & Ochsner, 2008). It is also involved with empathic regulation towards the emotional pain of others such as deliberate control of self-focused distress (Bruneau et al., 2015).

The abovementioned areas are the major structures implicated in empathy (Baron-Cohen, 2011) and moreover the most important regions to this thesis. In the following, it will be discussed how their activity may be represented in the observer of a person suffering from pain, as well as in the suffering individual. Keeping our current knowledge of empathy in mind, some differences between these activities and the consequences of how impairments to some of these areas may affect empathy will be presented.

**Pain**

**Theories of Pain**

Physical pain includes a number of events such as tissue damage, visceral unpleasantness, arousal, a change in the direction of attention, negative affect as well as a desire to withdraw from similar experiences. Most of these features are nonspecific when looked at individually, in that they do not occur merely as a reaction to pain. Therefore, nociceptive pain does not represent pain as such; rather, it represents the combination of several features (Zaki, Wager, Singer, Keysers, & Gazzola, 2016). This combination of events is referred to as nociceptive pain, which is the first hand-experience of physical pain (Zaki et al., 2016). The term derives from nociceptors; the kind of receptors that are activated when
non-neural tissue is damaged. In the skin, there are different nerve fiber endings, which possess different functions. These fibers are axons of cells and neurons that project to the dorsal root ganglia (DRG) or the trigeminal ganglia (TG) (Chuquilin, Alghalith, & Fernandez, 2016). The different types of fibers are categorized by means of their diameter and myelination. It is the small fibers with little or no myelination that are responsible for the sensation of pain, and that are called nociceptors (Chuquilin et al., 2016). C-fibers, which are unmyelinated and slowly conducting, are often polymodal and respond to noxious thermal mechanical stimuli (Julius & Basbaum, 2001). Also, many C-fibers respond to chemical noxious stimuli such as acid or capsaicin. Aδ-fibers are, on the other hand, slightly myelinated and therefore conduct faster than C-fibers (Weiss et al., 2008). They respond to intense mechanical stimuli, and can alternate in how they are affected by tissue damage or heat (Julius & Basbaum, 2001).

It has been assumed that Aδ-fibers mediate so called “first” pain, which is rapid, acute and sharp pain, whereas C-fibers are thought to mediate “second” pain, namely the delayed, more diffuse and dull pain (Julius & Basbaum, 2001). In relation to selective noxious stimulation of tiny parts of the skin, C-fiber stimulation was strongly associated with activity in the right frontal operculum and the anterior insula, whereas stimulation of Aδ-fibers was not. Based on current knowledge of these structures, it has been further suggested (Weiss et al., 2008) that C-fibers might be engaged in homeostatic and interoceptive functions in another way than Aδ-fibers, “producing a signal of greater emotional salience” (p. 1372). Information from the nociceptors travels to different parts of the brain via different pathways from the spinal cord (Apkarian, Bushnell, & Schweinhardt, 2013).

Historically, the study of pain has resulted in differing theories about its origins and characteristics. Specificity theory stated that pain is a specific modality, such as vision or hearing. According to this theory, pain receptors in the body tissue project to a specific center
in the brain, where it is processed (Melzack & Wall, 1996). However, it has been argued that clinical, physiological and psychological experiences do not support the idea of a direct transmission from stimulus and sensation to the brain (Melzack & Wall, 1967). For example, there is evidence from patients and cases in which the subject experiences severe pain even though the pain stimulus is mild, as well as when subjects do not experience pain at all despite powerful painful stimuli. Moreover, there have been difficulties in locating fibers that always respond to harmful stimuli (Melzack & Wall, 1967).

As a reaction to specificity theory, a number of alternative theories came to existence, which can be grouped under the term pattern theory. These ‘pattern theories’ suggested that there are no specific pain receptors; rather, the experience of pain arises from an intense stimulation of nonspecific receptors, which in turn creates a nerve impulse pattern (Melzack & Wall, 1996). However, most of the pattern theories failed to acknowledge the existence of highly specialized fibers and receptors (Melzack & Wall, 1967). The proposal of the so-called gate control theory of pain marked a significant change in thinking and theorizing about pain.

**Gate control theory of pain.**

The gate control theory of pain by Melzack and Wall (1967; 1996) contributed to the understanding of pain by its emphasis on central neural mechanisms. It forced the medical and biological sciences to consider the brain as an active system that modulates inputs (Melzack & Katz, 2004). The theory suggests a “gating mechanism” which mediated modulation of pain information and this proposal received great reception and research emerged to support or disprove it.

The human spinal cord includes gray matter that forms three pair of horns; the dorsal, lateral and ventral horns. Out of these three, it is the dorsal horns that have been shown to be important for the processing of pain in that they receive information from primary
afferent axons such as nociceptors that respond to for example tissue-damaging stimuli from the skin, muscle joints and viscera (Todd & Koerber, 2013). The gate control theory states that inhibitory interneurons in the dorsal horn are important to the control of incoming sensory information and are thereafter sent to the brain (Todd & Koerber, 2013). The foundation of the gate control theory rests upon the fact that impulses from peripheral stimulation are transmitted to the following three spinal cord systems: substantia gelatinosa fibers in the dorsal horn; dorsal column fibers that project to the brain; and the so called ‘T cells’ in the dorsal horn (Melzack & Wall, 1967). The substantia gelatinosa consists of small and densely packed cells that together form an extension of the spinal cord. In the dorsal horn, nerve impulses from peripheral fibers are thought to be modulated. Thus, the substantia gelatinosa functions as the gate control system. The modulation of the afferent patterns further activates T cells, which in turn gives rise to the activation of neural mechanisms which comprise an “action system”. In this system, the perception of the painful stimuli is processed, as well as the response to it. The gate control system in the substantia gelatinosa is affected by the so called “central control trigger” which contains of the afferent patterns in the dorsal column. The central control trigger causes the activation of selective brain processes, influencing how the nerve impulses will be modulated within the gate control system (Melzack & Wall, 1967).

The gate control theory suggests that the experience of pain is a consequence of an interaction between the three abovementioned systems (Melzack & Wall, 1967). Since the theory was proposed the role of the dorsal horn has been intensively studied; however, there is limited knowledge within this field. What is known is that the dorsal horn consists of four neuronal components; primary afferent axons, interneurons, projection neurons and descending axons. Altogether, these components make up for the response to and modulation of sensory and nociceptive information and the transmission of this information to various
parts of the brain and other spinal segments (Todd & Koerber, 2013). The next section will focus on pain and how the impulse projects from the onset of harmful stimuli to the brain, giving rise to the overall experience of pain.

**Pain Pathways**

The multidimensional experience of pain implies different pathways involving different structures in the brain. In order to clarify the broadness of pain, we need an understanding of these pathways and how they comprise several brain areas, resulting in the many components of the pain sensation.

The pathway most commonly associated with pain (Dostrovsky & Craig, 2013) is called the spinothalamic projection because pain related information is sent directly from the spinal column to the thalamus.

The information can also be sent from the thalamus to homeostatic control regions in the medulla and brain stem. Spinal input to the brain stem affects the spinal and forebrain activity, which in turn might influence pain experience (Dostrovsky & Craig, 2013). When the information is sent to the brain stem it is called spinobulbar projection. This pathway is involved with the integration of nociceptive activity with processes associated with homeostasis and behavior. However, direct projections to the hypothalamus and ventral forebrain are also possible.

In addition to the spinothalamic and spinobulbar projections, which are considered to be the two most prominent pathways, there are also indirect pathways that seem to be related to pain. These are the post-synaptic dorsal column (PSDC) system and the spinocervicothalamic (SCT) pathway. The PSDC and SCT pathways both originate from cells in the spinal dorsal horn and signals project from the brain stem to the forebrain (Dostrovsky & Craig, 2013).
The discovery of the abovementioned pathways expands our knowledge about the multidimensionality of pain because it shows that the experience of pain is due to several factors and projections and relates to different neural structures. However, it is important to keep in mind that this experience is due to the activity in many brain regions simultaneously. As Dostrovsky and Craig state, it is the “…constellation of activity across the entire brain that must constitute the basis for the conscious experience of pain.” (Dostrovsky & Craig, 2013, p. 196).

**Neural Correlates of Pain**

Information from nociceptors projects via different pathways to the brain, mostly through the thalamus, which is interconnected to different structures within the cerebral cortex (Dostrovsky & Craig, 2013). When talking about the neural correlates of pain one often refers to the involved brain structures as a “pain matrix” (Baron-Cohen, 2011; Singer et al., 2004). The pain matrix consists of the following areas: the primary somatosensory cortex (SI), the secondary somatosensory cortex (SII), insular regions, the anterior cingulate cortex (ACC), the movement-related areas such as the cerebellum and supplementary motor areas and the thalamus (Singer et al., 2004). The ACC and the MCC are associated with the affective-motivational aspects of pain and also with functions linked to emotional experiences (Lamm & Majdandžić, 2015).

Especially important to the study of pain is the thalamus. The lateral thalamus is associated with discriminative pain, whereas the medial thalamus is involved with the motivational aspects of pain. However, it is important to keep in mind that the sensation of pain does not occur within the thalamus, but its interconnection to the cerebral cortex gives rise to this particular experience (Dostrovsky & Craig, 2013).

As noted earlier, a growing number of studies suggest that a consistent cortical and subcortical network has been found to respond to pain in healthy subjects. Commonly, the
Empathy for Pain

Neural Correlates of Empathy for Pain

When one is experiencing empathy for another’s pain, this involves a complex process in which the sensory and emotional qualities of vicarious pain are extracted and then mapped onto neural substrates which may or may not be those that are activated in the direct experience of pain (Betti & Aglioti, 2016). However, some studies indicate that it is only the affective component of the pain matrix that is involved with empathy for pain (Singer et al., 2004) which suggests that it is only the emotional representation of pain that is shared between the observer and the sufferer (Avenanti, Paluello, Bufalari, & Aglioti, 2006).

One of the first studies with focus on the social neuroscientific study of empathy for pain was carried out by Singer et al. (2004). By using fMRI, the authors investigated which brain regions were active when participants experienced pain, as well as when observing another person suffering from pain. This provided evidence for pain-related responses and also confirmed that empathic experience does not involve activation of the entire pain matrix, but only the regions associated with the affective dimension of the experience of pain. The study was carried out with the help of 16 couples, based on the assumption that couples are likely to empathize with each other. The authors scanned the female partners with fMRI and exposed either them, or their partners, to pain using an electrode attached to the back of their right hands (Singer et al., 2004). A mirror was placed so that the female could see both her and her partner’s hand. Stimulation was either low (no
pain) or high (painful) and presenter to either the female or the male. When females were presented to pain (“self” condition), there was an increased activity in the following brain areas: contralateral SI/MI, bilateral SII with peak activation in contralateral posterior insula extending into SII, bilateral mid and anterior insula, ACC, right ventrolateral and mediodorsal thalamus, brainstem, and mid and right lateral cerebellum (Singer et al., 2004). These regions, which make up for the pain matrix have been associated with painful stimuli in several studies (Bruneau et al., 2015; Jacoby, Bruneau, Koster-Hale, & Saxe, 2016; Lamm, Decety, & Singer, 2011). When the male partners were presented with painful stimuli (“other” condition), the following brain regions showed activation in the female’s brains: ACC (more specifically, the anterior and posterior rostral zones), the AI bilaterally with an extension into inferior prefrontal cortex, cerebellum and the brainstem. These activations show that some of the areas in the pain matrix are activated also when observing another person suffering from pain. However, the absence of activity in the somatosensory cortex is one distinct factor that differentiates empathic pain from physical pain, in which there is activity in this region. Also, in the “other” condition, there were observed activations in the ventral and dorsal visual stream, including bilateral fusiform cortex, lateral occipital and right posterior superior temporal sulcus, the left inferior parietal cortex, and the left superior frontal cortex. (Singer et al., 2004) Results from this study showed that there was an overlapping neural activation in cingulate and insular cortices during the direct experience of pain as well as when empathizing with the pain of others. In other words, empathy recruits similar neural networks as the direct experience of the emotion one is showing empathy for (Singer et al., 2004). Because of these similarities between the neural activations for self-and-other-related experiences, it has been suggested that the ability to experience empathy is partially based upon the processing of our own emotions (Kanske et al., 2015).
**Shared networks.** As noted earlier, empathizing with another person’s feelings has been shown to activate the neural networks that are also related to the direct experience of the very same feeling (Betti & Aglioti, 2016). In order to study empathy on a neuroscientific level, researchers often study these shared neural networks in relation to pain. This is mostly done by either presenting participants with painful stimulation to their bodies, or by presenting them with pictures or cues that indicates that another person experiences pain. The most common way to measure the brain activity in such studies is by using fMRI. Thereafter, comparisons are made between the first-hand experience of pain and the observation of another person suffering from pain. These kinds of studies have repeatedly shown that shared neuronal networks exist (Singer & Klimecki, 2014).

When empathizing with another individual suffering from pain, we talk about empathic pain (Zaki et al., 2016). The overlap between nociceptive and empathic pain has been noticed and investigated for decades and research has shown that specific brain structures such as the anterior insula (AI) and parts of the cingulate cortex (CC) are typically activated both in the experience of nociceptive pain and empathic pain (e.g., Lamm et al., 2011; Singer et al., 2004). However, this activation of AI and CC might be represented in other psychological states as well, such as attention or arousal (Singer, Critchley, & Preuschoff, 2009). Hence, there is currently a debate among researchers on whether the similarities between nociceptive pain and empathic pain suggest shared pain-specific processes or if these findings are a consequence of incorrect reverse inference (Zaki et al., 2016). This would mean that neural activity is incorrectly associated with a certain cognitive process.

Even if pain is the most widely used and common way to study empathy, similar studies have also shown similar paradigms of a shared network in field of touch, disgust, taste and social rewards. A shared network has been observed in the somatosensory cortex in
relation to vicarious neutral touch, and in the medial orbitofrontal cortex in relation to vicarious pleasant touch. In the study of shared social rewards, a shared network has been found in the ventral striatum, and in the study of taste and disgust there is a shared network in parts of the AI (Singer & Klimecki, 2014).

**Somatosensory system.** In the experience of empathy for pain, both affective and sensorimotor pathways are involved. However, the question of what role the somatosensory cortex (SI) plays in this process remains unanswered (Betti & Aglioti, 2016). For example, experimental paradigms may affect the activation in the somatosensory cortex since it is involved with touch and some experiments show visual cues where models are being touched (Baron-Cohen, 2011; Lamm et al., 2011). Also, experiments in which participants are presented to abstract visual cues that indicate the pain of another, did not show significant activation of SI and SII (Singer et al., 2004). Although SI is mostly considered to be involved with somatic processing, it also seems to play an important role in complex cognitive functions such as social cognition. Activity in the somatosensory structures during observation of the emotional state of others could provide the observer with a somatic reflection of what that particular emotional state may feel like (Bufalari, Aprile, Avenanti, Di Russo, & Aglioti, 2007).

Bufalari et al. (2007) used somatosensory-evoked potentials (SEPs) together with EEG to investigate if observing a model suffering from pain or tactile stimuli modulates neural activity in the somatic system of the observer. SEPs are a noninvasive, non-painful way to assess somatosensory system functioning and were in this experiment obtained by electrical stimulation of the right median nerve at the participants’ wrists. Attendants were presented to video clips where models were experiencing pain or tactile stimuli. Activations in the primary somatosensory cortex (SI) correlated with the intensity but not the unpleasantness of the pain and touch. The results from this study suggest that neural activity
in SI is not only involved with the actual experience of pain and touch, but it also seems to be modulated by the observation of others’ bodily sensations (Bufalari et al., 2007).

**Factors Influencing Empathy for Pain**

There are several factors that can influence to what degree one feels empathy for another individual’s pain, such as the affective link or similarity between observer and sufferer (Loggia, Mogil, & Bushnell, 2008), the age (Bandstra, Chambers, McGrath, & Moore, 2011) and gender (Christov-Moore et al., 2014) of the observer and the context in which the empathy is experienced. Factors such as these will be explained and discussed in terms of behavioral and neural mechanisms in this following section.

**Age.** Already by the age of 5-6 years, it is very clear that children are able to recognize and identify pain in others, and refinements of this ability continue through to early adulthood (Deyo, Prkachin, & Mercer, 2004). However, little is known about how and when children develop or express empathy for another individual’s pain (Bandstra et al., 2011). The empathic response first emerges as a reaction of personal distress and is often accompanied with self-focused behavior such as self-soothing. As the child matures, the control of the own emotions typically becomes better and the focus on the needs of an individual in distress becomes greater (Bandstra et al., 2011). In a test where 120 children between the ages of 18 and 36 months were presented with simulations of an adult’s pain and sadness respectively, their empathy-related behaviors were investigated. The results in this study indicated that children tended to be more sensitive to others’ sadness, in which they became distressed and showed prosocial behavior. When presented with others’ pain, the children were more likely to continue playing. However, behaviors associated with empathic concern and personal distress emerged in both situations. It was speculated that the reason for a reduced reaction to the pain stimulus might be a consequence of the children not regarding the pain of others as
threatening to their selves. Further, this finding has been suggested to be due to the frequency of painful events that occur in childhood, thus leading the child to become inured to observing others in pain (Bandstra et al., 2011). Older children were more likely to react to the pain stimulus with empathic concern and less likely to react with personal distress than younger children. In the sadness condition, this age difference was however not present, suggesting that the developmental course of empathy for pain and empathy for sadness are different (Bandstra et al., 2011).

In one study investigating the development of empathy, fMRI was used to scan and compare children and adults (Decety & Michalska, 2010). Participants in the age of 7-40 years old were presented with animations depicting painful and non-painful conditions. Results from this study showed that children and adults have similar patterns of brain activity when observing other people in pain: in the ACC, somatosensory cortex, and periaqueductal gray (PAG) and the insula. Despite this, there are some important age differences in the neural activity associated with empathic pain. For example, the amygdala and the posterior insula are developed much earlier in childhood than other structures such as the dorsal and lateral vMPFC, which are slower to mature and later on become specialized for the evaluation of social stimuli (Decety & Michalska, 2010). Also, different parts of the prefrontal cortex (PFC) mature at different rates, indicating that the development of affective processing from childhood to adulthood is associated with reduced activity in the limbic affect processing systems, whereas there is an increased activity in other prefrontal systems (Decety & Michalska, 2010). Further, older adults seem to be more sensitive than younger people to the intentional harm of others (Chen, Chen, Decety, & Cheng, 2014). The empathic response in the mPFC and STS does not change with age, although, the activity in the AI and anterior mid-cingulate cortex in response to others’ pain has been shown to decline with age. This
finding indicates that the neural response associated with affective empathy lessens with age, whereas the response to perceived agency is preserved (Chen et al., 2014).

**Gender.** Sex differences in empathy-like behaviors have been reported in nonhuman animals such as primates and rodents and suggest that females possess greater levels of empathy in at least some species (Christov-Moore et al., 2014). It has been shown that there are human gender differences in empathy for pain, in that both the short-latency empathic response and the long-latency empathic response to a stimuli depicting someone suffering from pain differs (Han, Fan, & Mao, 2008). There also seems to be a gender difference in the activation of the MCC and the AI in relation to observing others in pain. When men observe someone they do not like or consider fair, they generally show less activity in these areas than when they like the suffering person (Singer et al., 2006).

Females have been shown to have higher emotional responsiveness and mirroring responses to the suffering of others, and they are also better at recognizing emotions (Christov-Moore et al., 2014). Further, it has been suggested that females tend to show more prosocial and altruistic behavior. In other words, females seem to be show higher affective empathy for other’s pain. In contrast, in terms of cognitive empathy, it has been suggested that males show more utilitarian behavior than females, accompanied by a greater recruitment of areas that are associated with cognitive control and cognition (Christov-Moore et al., 2014).

In a study where gender differences in the neural networks associated with empathy were investigated (Schulte-Rüther, Markowitsch, Shah, Fink, & Piefke, 2008), fMRI was used to scan subjects while they were presented with different emotion expressing faces. The participants were asked to either focus on their own emotional response to the presented picture, or to evaluate the emotional state that the observed face expressed. Females rated
their own response higher than males. The females’ brain activity in this task involved a
stronger activation in the right inferior frontal cortex and STS whereas the males showed a
stronger activity in the left TPJ. Since the TPJ is associated with the self-other distinction, this
suggests that males rely more on this distinction than females. In the task were the
participants were asked to evaluate the observed face’s emotional state, females showed an
increased activity of the right inferior frontal cortex in contrast to males. Taken together,
results from this study suggest that females recruit more brain areas containing mirror neurons
than males do and that these gender differences may indicate different strategies in how own
emotions are processed in response to others (Schulte-Rüther et al., 2008).

Empathy for non-human entities. The ability for humans to empathize with
other animals in a similar way as with their own offspring has been suggested to depend on an
instinct of nurturance (Prguda & Neumann, 2014). Using fMRI, Mathur, Cheon, Harada,
Scimeca and Chiao (2016) investigated whether the neural reactivity associated with empathy
for pain was different when directed to humans than to non-human entities. They measured
neural activity when subjects were presented with visual scenes depicting people, animals and
nature in either negative or neutral conditions. The same brain regions that increased in
activity while subjects were experiencing empathy for other people were active when they
observed animals and nature in harmful conditions (e.g. dorsal anterior cingulate cortex,
bilateral anterior insula). These findings suggest that the activity within these areas is not
specific to humans only, but also when empathizing with other animals and the nature
(Mathur et al., 2016). However, empathy for humans and other animals has shown to be
facilitated by the perceived phylogenetic similarity between the object and subject (Prguda &
Neumann, 2014). Stronger phasic skin conductance response (SCR) and subjective ratings of
empathic experience have been associated with human participants observing the suffering of
phylogenetically similar species than more different animals. The subjective ratings did not
differ much when subjects were presented to suffering humans, non-human primates and quadruped mammals. On the other hand, the arousal and subjective experience of empathic emotions were rated as much lower when observing birds suffering from pain (Prguda & Neumann, 2014). Also, SCR showed that participants were more emotionally aroused and directed more attention toward stimuli depicting suffering humans than to non-human primates. This response was further decreased when participants were presented to stimuli of suffering quadruped mammals, and even lower in the bird stimuli. This supports the idea that phylogenetic similarity plays an important role in empathy for the pain of others (Prguda & Neumann, 2014).

**Empathy among caregivers.** In medical practice, pain is most commonly defined by its pathological cause. In cases where a physical cause is not found, the patients’ pain is often thought to be imaginary (Ojala et al., 2015). In order to investigate “invisible” chronic pain, Ojala et al. (2015) studied the contact between patients and care givers. The patients report that their experience of pain is often underrated or denied. Further, many of these patients have problems trusting and believing in their helpers and they also have mental health problems together with the painful experience. Even though there is a current recommendation to treat chronic pain as a biopsychosocial experience, it is often thought to be a symptom of an underlying disease (Ojala et al., 2015). In other words, too little empathy among caregivers may have devastating effects on the health of patients. However, failure to help patients suffering from chronic pain may also have negative effect on the caregivers. Too much empathy can cause the helper to suffer more than usual with the patient, which can result in a desire to withdraw from this kind of work. Caregivers with too much empathy tend to continue with treatments even if they are not helping, or even worse, if they risk damaging the patient (Breivik, 2015).
Another factor that might have an effect on how caregivers react to a patient’s pain is their individual experience. Nursing students without clinical experience tend to rate mild pain as more painful and urgent than students with clinical experience (Chan & Hamamura, 2015). A possible explanation to this would be that students without this learning have not observed patients expressing their pain before and therefore overestimated mild pain. Also, students with clinical experience might have observed patients who reported their pain as higher than it actually was perceived, thus leading the student to rate mild pain as less urgent. Further, these students could be more used to seeing patients suffering from different levels of pain, and therefore grade mild pain as less urgent to treat in contrast to severe pain (Chan & Hamamura, 2015).

**Racial bias.** Research has shown that the brain response of an individual observing another one in pain can be different depending on the race of the observer and the suffering person. If the two are of the same ethnicity, there is a higher activity in the ACC and the bilateral insula, than if they are of different ethnicities (Cao, Contreras-Huerta, McFadyen, & Cunnington, 2015). In conditions where the observer and the sufferer are of different ethnicities, the ACC activity in the observer increases in line with the amount of contact between them. However, this increase of activation is not dependent on the closeness or the relationship between the two, rather, the amount of experience they have of each other in an every-day life context. This evidence supports the idea that racial bias changes in line with an increased experience and contact with new immigrants (Cao et al., 2015).

It has been suggested that two variants of a certain oxytocin receptor gene polymorphism are associated with racial bias in brain activities that are linked to implicit attitude and altruistic motivation (Luo et al., 2015). Racial bias of empathy is however not inevitable (Sheng & Han, 2012). In a study where Chinese adult subjects observed Asian and Caucasian faces reflecting neutral or painful expressions respectively, the racial bias was
manipulated. In order to identify the bias, participants were asked to make race judgments on the different faces presented, while detecting the brain activity with event-related potentials (ERP). The subjects’ ratings of the pain intensity in the pictures as well as their own reported self-unpleasantness was higher for pain than for neutral stimuli, while there was no significant difference between ratings of the effect of facial expression between Asian and Caucasian faces (Sheng & Han, 2012). However, when presented to same-race faces expressing pain, there was an increased neural response at 128-188 ms after the onset of stimuli. This effect did not occur when subjects observed other-race painful stimuli. In the following experiments, it was found that the racial bias was eliminated when participants were paying attention to the observed individual’s feeling of pain. Also, including the other-race individual in their own team for competitions had the same effect of an increased neural response (Sheng & Han, 2012).

Racial bias in empathy for the pain of others can cause pain treatment disparities. For example, it has been shown that African Americans receive lower quality pain treatment than European Americans (Drwecki, Moore, Ward, & Prkachin, 2011). A solution to this problem might be to induce the empathy in healthcare by interventions, which in turn would decrease the differences in provided pain treatment. This proposal rests upon the finding that perspective-taking can reduce pain treatment bias by upwards of 55% (Drwecki et al., 2011).

Important to keep in mind is that the results related to racial bias in empathy for the suffering of other might change over time and that it might also depend on the level and quality of contact between races (Cao et al., 2015).

Atypical Aspects of Empathy for Pain
As noted earlier, the ability to experience empathy is socially important (Bruneau et al., 2015). In this following section, some atypical forms of empathic abilities or impairments will be discussed.

**Synaesthesia for pain.** In synaesthesia for pain, one does not only empathize with the pain of another, but also experiences the observed or imagined pain as if it was one’s own. At face value, the neural mechanisms that seem to be involved with this kind of synaesthesia include so called “mirror systems”. This means that the same systems are active both when the synaesthete observes someone else experiencing pain as well as when the synaesthete directly experiences pain. Fitzgibbon, Giummarra, Georgiou-Karistianis, Enticott and Bradshaw (2010) propose that synaesthesia for pain might be the result of painful and/or traumatic experiences that causes disinhibition in the mirror system that underlies empathy for pain. (Fitzgibbon et al., 2010b) This phenomenon is common in individuals who have lost a limb and the synaesthetic pain experience is triggered specifically in response to other individuals’ pain (Fitzgibbon et al., 2010a).

One study investigated the motor cortical excitability in lower-limb amputees who experienced synaesthetic pain (Fitzgibbon et al., 2012). By using transcranial magnetic stimulation (TMS) administered to the motor cortex, it was found that changes in the motor cortical excitability did not appear to contribute to the synaesthetic pain experience. If the sensorimotor mirror system disinhibition is involved with synaesthetic pain, it may not be driven by motor cortical excitability. Rather, other mechanisms could underlie this phenomenon, such as the amount of attention directed towards the experience of pain. Paying attention to the somatic cause of the observed pain may trigger activity in the somatosensory cortex and therefore result in the observer’s painful sensation (Fitzgibbon et al., 2012). Finally, changes in cortical excitability in other brain regions should be investigated. Since the
dorsolateral PFC, ACC, insula and the parietal lobule are involved with pain processing, they could be of more use to look at in this study (Fitzgibbon et al., 2012).

However, the role of mirror neurons in synaesthesia for pain remains unclear and more research is needed to investigate whether both the affective and sensory areas of the pain matrix is activated when pain synaesthetes experiences empathic pain (Fitzgibbon et al., 2010b). Importantly, related to the ongoing debate on what role mirror neurons have in empathy (Lamm & Majdandžić, 2015), factors underlying the synaesthetic experience of pain, such as the affective link between observer and sufferer needs to be determined (Fitzgibbon et al., 2010b).

**Psychopathy.** It is well established that people with psychopathy lack the ability to feel affective arousal, affective empathy and caring for others’ well-being. As noted earlier, psychopathy is associated with impairments in the OFC (Baron-Cohen, 2011).

Since perspective taking has been shown to give rise to empathy and concern in healthy subjects, Decety, Chen, Harenski and Kiehl (2013) investigated to what extent perspective taking could affect the empathic ability in psychopaths. In their study, they used fMRI to scan subjects classified as high, intermediate and low psychopaths while they were presented with stimuli depicting body parts being injured and simultaneously instructed to adopt a perspective where they imagined their own and the others’ perspective. In the condition where they self-imagine condition, the subjects with high psychopathy showed activity in the anterior insula, anterior MCC, supplementary motor area, IFG, SI and the right amygdala, which reflects a typical response associated with empathy for pain. In the other-imagine condition, participants showed an atypical response in the AI and the amygdala with a connectivity with the OFC. This atypical connectivity points further to the empathy deficit in psychopathy (Decety et al., 2013).
According to Lishner, Hong, Jiang, Vitacco and Neumann (2015), the proposed link between psychopathy and impairments in affective empathy is emotional callousness. This was discovered in a study where psychopathy, narcissism and borderline personalities were tested for emotional contagion and empathic concern. There was little evidence of a consistent negative association between most measures of psychopathic, narcissistic and borderline traits and affective empathy change scores. However, there was an exception in callousness among psychopaths, which revealed consistent negative associations with affective empathy change scores. When presented to neutral stimuli, psychopaths’ callousness was associated with lower emotional contagion of sadness, anger and fear (Lishner et al., 2015).

**Huntington’s disease.** Individuals suffering from Huntington’s disease (HD) have been shown to have impairments in their ability to recognize emotions in others and they also show deficits in empathy (Baez et al., 2015). In an experiment, manifest HD patients, first-degree asymptomatic relatives and healthy control subjects completed three different tests; two of emotion recognition, one of empathy for pain. In the first task, participants were presented with morphed faces illustrating six basic emotions (happiness, surprise, disgust, sadness, fear and anger) and instructed to identify the emotion as soon as it was recognized. The second test, called the Emotion Evaluation Test (EET), participants were presented with short videotaped vignettes were actors illustrated a basic emotion. This presentation was followed by a forced-choice task in which the participants were to choose the viewed emotion (Baez et al., 2015). In the Empathy for Pain Task (EPT), participants were presented with 24 animated situations, either depicting intentional or accidental harm to another being, or neutral situations. The subjects were asked to press a button as soon as they understand the situation and were then instructed to answer questions about the presented situation and its context. Accuracy, reaction time and ratings were measured during the experiment. The
results from this study showed that both HD patients and their first-degree asymptomatic relatives had an impaired ability to recognize negative emotions in faces. Also, HD patients’ ability to understand the intentionality of others’ actions was compromised. These results suggest that impairments and difficulties in emotion recognition might be a potential biomarker of HD onset and progression (Baez et al., 2015).

Asperger’s syndrome. It has also been shown that people with Asperger syndrome (AS) may have a reduced empathic response to the pain of others (Minio-Paluello, Baron-Cohen, Avenanti, Walsh, & Aglioti, 2009). Subjects were presented with video clips that showed model hands being penetrated with a needle in a specific muscle. Simultaneously, the response of the same hand muscles was recorded in the subjects with motor-evoked potentials (MEP). The MEP did not show any reduction of the amplitude in AS participants, whereas this reduction was observed in healthy control subjects (Minio-Paluello et al., 2009). Also, TMS revealed that there was no neurophysiological modulation of the AS participants’ corticospinal system when presented with the video clips, in contrast to controls. Further, AS participants represented the pain of others in relation to their self-oriented arousal when observing the videos. The lack of embodiment of other’s pain suggests that people with AS have empathic difficulties (Minio-Paluello et al., 2009).

However, much research on AS patient’s empathic abilities has been said to focus on cognitive empathy or self-report questionnaires, and not on affective empathy (Dziobek et al., 2008). This limitation in the study of empathy among AS individuals is suggested to derive from a lack of appropriate instruments that could dissociate cognitive empathy from affective empathy. In a study using a so called Multifaceted Empathy Test (MET) that measures both components of empathy, greater ecological validity could be assessed than with self-report questionnaires because the test included photorealistic stimuli (Dziobek et al., 2008). In this study, AS patients and control subjects were presented with a
series of photographs, mostly depicting emotionally charged situations. The cognitive empathy was assessed when the participant was asked to infer the mental states of the observed individual in the photograph, whereas the affective empathy was assessed by the subjects’ ratings of their emotional reactions to the photographs. Results showed that AS patients had difficulties in cognitive, but not in affective aspects of empathy. This suggests that the amount of concern for the suffering of others is not different in AS patients than control subjects (Dziobek et al., 2008).

**Post-traumatic stress disorder.** Research has shown that individuals suffering from post-traumatic stress disorder (PTSD) have impairments in affective empathy, but not in cognitive empathy (Mazza et al., 2015). This result was found in a study in which PTSD patients and healthy control subjects performed a modified version of the MET and were simultaneously scanned with fMRI. Participants were instructed to answer three questions about the presented photographs depicting negative, positive or neutral emotions. First, they were asked to infer the valence of the mental state of the depicted individuals. Thereafter, implicit affective empathy was measured when participants were asked to rate the level of arousal experienced when presented to a picture. The explicit affective empathy was assessed when participants rated the empathic concern they felt for the depicted individuals (Mazza et al., 2015). During the measurement of cognitive empathy, there was an increased activation in the right medial frontal gyrus and the left inferior frontal gyrus in PTSD patients, but not in controls. In the implicit affective empathy, PTSD patients showed a greater activity in the left palladium and the right insula, whereas control subjects showed an increased activity in the right inferior frontal gyrus. The explicit affective empathy showed a reduced activity in the left insula and the left inferior frontal gyrus in the PTSD patients. These results indicate that there is a dissociation between emotional and affective empathy in PTSD patients (Mazza et al., 2015).
Regulation of Empathy for Pain

Repeated exposure to others’ pain can have devastating effects on the observing individual, such as burnout, personal distress or compassion fatigue (Decety, Yang, & Cheng, 2010). Therefore, the ability to regulate empathy for pain is necessary, particularly among health care professionals who often encounter suffering individuals. As mentioned earlier, too much empathy among caregivers may have negative effects on their wellbeing as well as the treatment of the patients (Breivik, 2015). Research has shown that physicians rate the intensity and unpleasantness of pain in others as lower than control subjects, and that the neural response is different in the sense that physicians down-regulate the sensory processing when witnessing others in pain (Decety et al., 2010). This regulation has been suggested to have many beneficial outcomes because it allows physicians to focus on the treatment and assistance for their patients instead of counterproductive feelings of alarm and fear (Decety et al., 2010).

Empathy for pain has also been shown to be regulated by transcranial direct current stimulation (tDCS) to the dorsolateral prefrontal cortex (DLPFC) (Rêgo et al., 2015; Wang, Wang, Hu, & Li, 2014). Both left and right DLPFC seem to be involved with self-regulation and general affective modulation, and the right DLPFC has been associated with the evaluation of valence and arousal of other’s pain (Rêgo et al., 2015). The understanding that tDCS can modulate empathy for pain leads to the suggestion that this method could be used as a potential tool for modulating diseases that are accompanied with deficits in empathy (Wang et al., 2014).

There is equivocal evidence on the role of the amygdala in regulation of pain empathy. This might be because some experiments are focused on the emotional pain of others, while others investigate the physical pain of others (Bruneau et al., 2015). A recent
study has shown that the amygdala is involved with the deliberate regulation of empathy towards the emotional pain of others, but not to their physical pain (Bruneau et al., 2015). Moreover, regulation of empathy for emotional pain activates regions in the LPFC and deactivates the amygdala, whereas regulation of empathy for physical pain activates largely distinct regions such as AI, and had no effect on amygdala (Bruneau et al., 2015).

The neural underpinnings of pain experience have been shown to be influenced by top-down attention, in the sense that the experience of pain becomes less remarkable when attention is drawn to something else than the noxious stimuli (Gu & Han, 2007). Gu and Han investigated whether the neural substrates of empathy for pain are also modulated by similar top-down mechanisms. Participants were scanned with fMRI and simultaneously presented to pictures or cartoons of hands that were exposed to either painful or neutral stimulation. In one condition, the subjects were asked to evaluate the intensity of pain perceived by the model, while in the other condition, they were to count the number of hands on the display. In contrast to the neutral condition with counting, the rating of pain intensity in painful pictures or cartoons induced increased activity in ACC/paracingulate and the right middle frontal gyrus (Gu & Han, 2007). There was also a difference in how the stimuli were presented: for pictures in the pain-related stimuli, there was an increased activation in the inferior frontal cortex bilaterally and the right insula/putamen. When presented with cartoons, there was an increased activation in the left parietal cortex, the postcentral gyrus, and the occipitotemporal cortex. Also, the activity in the ACC was stronger for the pictures than for the cartoons. None of the aforementioned brain regions were active when participants were asked to count the number of hands presented to them. The results of this study show that empathy for pain seems to be modulated by top-down attention as well as the contextual presentation of stimuli (Gu & Han, 2007).
Empathy Affects Pain Perception

We have now seen that many factors can affect and modulate the empathic experience for another individual’s pain. From the sufferer’s perspective, empathy directed towards oneself may affect the pain experience (Hurter, Paloyelis, Williams, & Fotopoulou, 2014).

The pain experience has been shown to be influenced by the social context as well as by empathy from a partner (Hurter et al., 2014). The higher the empathy from subjects’ partners was the higher the intensity of pain was rated. However, pain tolerance and facial expression was not influenced by empathy from another. These results indicate that the belief that a partner is feeling empathy for one’s pain leads the subject to experience the pain intensity as higher, even though behavioral response and communication between partners did not affect the pain sensation to the same degree. Hurter et al. (2014) proposes that empathy from a partner may cause the subject to focus on their pain experience because the empathic response from the other signals a painful value (Hurter et al., 2014).

The degree to which an observer experiences empathy for another person’s pain depends on the affective link between the two (Sessa & Meconi, 2015). Individuals that have high empathy for another person in pain tend to rate their own pain experience as more intense when presented to similar harmful stimuli as the observed person. If the empathy towards the other is lower, then the observer’s pain experience will be rated as lower too (Loggia et al., 2008). By manipulating the empathy towards the other, the experience of pain can be modulated. Since this finding was compared to neutral stimuli as well, this seems to imply that empathy itself alters the perception of pain, and not necessarily the observation of pain behaviors (Loggia et al., 2008).

Further, studies have shown that subjects rate their pain as higher when
observing painful scenes (such as models suffering from pain, pictures of wounds) than when observing neutral scenes. This might be the result of the degree of empathy that the subject experiences, but other explanations are also possible. First, the mere observation of someone in pain is likely to induce an overall negative mood, which in itself has been shown to increase the intensity of pain perception (Rainville, Bao, & Chrétien, 2005). Second, the response can be autonomic as a result of classical conditioning, in that the image of a wound has been associated with the experience of pain throughout our lives (Rainville et al., 2005). The third factor that can give rise to the empathic pain response is that imitation can be elicited by observation of another being suffering from pain. This so-called social modelling could be one explanation for differences in pain ratings in some of the studies in this field (Loggia et al., 2008).

**Conclusions**

Empathy is for most of us a well-known construct, yet it is hard to define. Consisting of several subcomponents and factors, a growing body of research, often carried out with fMRI, begins to bring clarity to the concept of empathy. Compelling evidence indicates a shared neural network for the empathic experience of others’ emotions and the direct experience of the very same emotion.

Much research on empathy has focused on pain and the shared networks associated with individuals empathizing with the pain of others. Specifically, activity in brain structures such as the AI and parts of the CC are typically associated both with nociceptive and empathic pain. Importantly, these structures might also be associated with attention or arousal as well.

In one of the first studies on empathy for pain (Singer et al., 2004), it was found that only the brain areas in the pain matrix associated with the affective dimension were active
in individuals observing others in pain. Results from several studies indicate that the ACC, AI, PFC, cerebellum and brainstem are activated in both the physical and the empathic pain experience. However, an absence of activity in the somatosensory cortex in empathic pain could be one factor that differentiates empathy for pain and physical pain. Recent research has questioned the role of the somatosensory cortex in empathic pain, since this area is associated with touch. In some studies on the subject, activation in this area has been shown, although one possible explanation to this might be that the experimental paradigms influence the individual since the observed individual experiences the sense of touch.

This thesis has further discussed the different factors that might give rise to different empathic experiences and abilities. Evidence show that empathy is refined with age and also that brain regions such as the amygdala, insula and the PFC mature at different rates, which indicates that the development of affective processing is associated with a reduced activity in the limbic areas and an induced activity in other prefrontal systems. There are also gender differences in the ability to experience empathy for pain. For example, females have a higher emotional responsivity and mirroring responses, and they also show more prosocial behavior than men. On the other hand, men seem to show more utilitarian behavior and recruit areas associated with cognition to a greater extent than females. To what degree humans emphasize with others is dependent on the phylogenetic similarity and relationship between observer and sufferer. If the two are of different races, there is a higher activity in the ACC and in the bilateral insula of the observer, when seeing the other being exposed to painful stimuli.

While some individuals possess an unusually high empathic ability, others seem to lack this capacity. For example, psychopaths have impairments in their affective empathy while individuals with Asperger’s syndrome have difficulties in cognitive, but not in affective
empathy. The fact that empathic abilities and impairments can differentiate in such a degree between people supports the notion that empathy is a multidimensional construct.

Whether the overlap between nociceptive and empathic pain is due to shared neural networks or just, perhaps, the result of an incorrect reverse inference, is a question still unanswered. Also, some studies suggest that the perception of others’ pain may reflect the processing of threats, rather than being an automatic pro-social response (Ibáñez et al., 2011). This means that empathy for pain might in fact be a signal of danger, due to the possible threat that we recognize in others’ expressions.

In order to investigate the consistency of previous findings suggesting that the direct experience of pain as well as empathy for pain is underpinned by the same neural substrates, meta-analyses of several previous studies have been carried out (Lamm, et al., 2011). The findings confirmed a shared network in the bilateral anterior insular cortex and in the medial/anterior cingulate cortex. This network is referred to as a core network underlying empathy for pain, and was activated together with other brain regions; depending on the different types of experiments they analyzed (Lamm et al., 2011). For example, participants viewed pictures of various body parts in painful situations activated brain areas in the observer that are associated with action understanding, such as the inferior parietal/ventral premotor cortices. When the participant on the other hand was presented to abstract visual information about the suffering of another, areas associated with inferring and representing mental states of self and other (such as the precuneus, ventral medial prefrontal cortex, superior temporal cortex and temporo-parietal junction) were instead more active (Lamm et al., 2011). Furthermore, it was found that somatosensory areas were only activated in the picture-based experiments. This meta-analytic investigation led to the conclusion that social neuroscience paradigms provide reliable and accurate insights into the field of empathy (Lamm et al., 2011).
Many of the studies reported in this review have utilized fMRI. It is commonly acknowledged that because of the vagueness and imprecision in the hemodynamic response and the fact that the neural activity is only indirectly measured results in a limitation in the use of fMRI (Lamm & Majdandžić, 2015). Also, fMRI data is almost always analyzed on group level after each individual’s data has been smoothed which may lead to misinterpretations about activations that might in fact not be present at individual levels (Fitzgibbon et al., 2010b). At a general level, these limitations should always be borne in mind in interpretation of research findings, and this applies to the current review. For example, in a study in which it was investigated to what degree cingulate areas involved with the processing of self- and other-pain shared the same neural basis, this problem was emphasized (Morrison & Downing, 2007). In this study, participants were scanned with fMRI as they experienced either physical pain or empathic pain. It was found that the group-averaged data showed overlapping activity in the cingulate and clear activation peaks for physical and empathic pain. Importantly, not all individuals showed this overlap of activity, which indicated the problem with analyzing group data and not individual data (Morrison & Downing).

Another problem in using fMRI is its coarse spatial resolution. Each voxel covers thousands of neurons, which means that possible differences in firing and interaction patterns are not detectable with fMRI. Other measuring techniques, such as EEG and MEP-TMS also have this kind of problem, since these scan many neurons at a time (Lamm & Majdandžić, 2015). The abovementioned limitations imply a difficulty in deciding what role shared activations play in empathy. More fine-grained resolution in combination with a multivariate imaging analysis method that detects information rather than activation would be a possible solution to this problem (Lamm & Majdandžić, 2015).

The study of empathy for pain has improved our knowledge in the field significantly. Since it has been observed that there are neurological and biological differences
in empathy in humans, this might also help us to widen our understanding of behavioral and psychological differences. However, the research still needs to be expanded. The importance of this field rests upon potential treatments to empathic dysfunctions and others in need of an empathic response such as patients suffering from “invisible” chronic pain. One question that needs to be answered is what role the somatosensory system has in the experience of empathy for the pain of another. Could potential activity in this area be due to experimental paradigms, or does this activity reflect something else? Further, individual differences need to be evaluated and compared to group differences. Also, the role of mirror neurons in empathy needs further investigation, such as other techniques to measure empathy and its many facets.

While pain is an interesting method for studying empathy, more research should be carried out on other aspects of empathy. For example, there has been little focus on the positive emotions within the construct of empathy. Future studies will hopefully contribute to the field with potential explanations to when, how and why we experience empathy for others’ pain as well as why this ability differentiates among individuals and contexts. Also, the cognitive neuroscience of empathy for pain needs to be complemented with the work from other academic disciplines such as psychological and evolitional research and philosophical theories. This is necessary because neuroscience cannot explain the entire phenomenon of empathy for pain; other factors such as the emotional and experiential components need to be investigated from different perspectives.
References


