Aus der Klinik für Neurologie
der Heinrich-Heine-Universität Düsseldorf

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Gender differences in empathy - evidence from self- reports, behavioral data and neural correlates

Dissertation

zur Erlangung des Grades eines Doktors der Medizin
der Medizinischen Fakultät der Heinrich-Heine-Universität Düsseldorf

vorgelegt von

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2019

Als Inauguraldissertation gedruckt mit Genehmigung der Medizinischen Fakultät der Heinrich-Heine Universität Düsseldorf

gez.:

Dekan: Univ.-Prof. Dr. med. N. Klöcker

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Für Ian Steinhäuser

“Empathy isn´t just listening, it´s asking the questions whose answers need to be listened to. Empathy requires inquiry as much as imagination. Empathy requires knowing you know nothing. Empathy means acknowledging a horizon of context that extends perpetually beyond what you can see (.)

Jamison, L. (2014): The Empathy Exams. Essays, 1. Edition. London, p. 5

Parts of this dissertation have been published.

Publications in peer-reviewed scientific journals:

1. Prochnow D, **Steinhäuser L**, Brunheim S, Seitz RJ. (2014). Different mechanisms underlying emotional state reasoning in young and old adults: evidence from behavioral and neuroimaging data. *Journal of Comparative Neurology and Psychology, 2(1): 1-8*

2. Prochnow D, Brunheim S, **Steinhäuser L**, Seitz RJ. (2014). Reasoning about the implications of facial expressions: a behavioral and fMRI study on low and high social impact. *Brain and Cognition, 90: 165-173*

I. Summary

Empathy can be defined as the ability to correctly attribute a certain emotion to a facial expression and hence infer the other person's feelings and intentions. It is a fundamental capability for meaningful everyday human interaction. Empathy is a complex concept and the aim of this study was to investigate the question of gender-differences in empathic behavior by using self-report questionnaires, behavioral data and investigating the corresponding neural correlates.

We mapped the brain activation patterns of 26 healthy, right handed volunteers (12 women /14 men) by using functional magnetic imaging while the participants were performing an empathic reasoning paradigm. They first viewed a facial expression showing a certain emotion (happiness, anger, fear and sadness) and consequently had to choose a sentence out of a forced choice menu that described what could have happened to the person. Before and after the trial they had to complete self-report-questionnaires (TAS-20, SPF) and prove their facial affect recognition skills (BFRT, MITE, DCERT).

Our results show that women rated themselves more empathic than men. But contrary to the general view we could not detect a female superiority for empathic reasoning, but demonstrated that men are equally well equipped with empathic skills. Women and men showed similar brain activation patterns with a similar behavioral performance on the ERP and there was no hint of a clear pattern concerning the gender related use of the hemispheres while empathic reasoning. Also, regarding the recognition of emotions of low and high social impact, there was no activation pattern which assigned the recognition of certain emotions to women or men.

The final paragraph of this study deals with the interpretation of the results and their possible implications.

II. Zusammenfassung

Empathie beschreibt die Fähigkeit in einem bestimmten Gesichtsausdruck eine Emotion zu erkennen und in Folge dessen die Gefühle und Intentionen eines Mitmenschen richtig nachzuvollziehen. Sie stellt eine fundamentale Fähigkeit im täglichen zwischenmenschlichen Umgang dar. Empathie ist ein komplexes Konzept und das Ziel dieser Arbeit war es, mit Hilfe von Selbstreport-Fragebögen, Verhaltensdaten und durch die Untersuchung der korrespondierenden Hirnregionen, die Frage nach geschlechtsspezifischen Unterschieden bezüglich empathischen Verhaltens zu erforschen.

Mit Hilfe von funktioneller Magnetresonanztomografie wurden die Hirnaktivierungsmuster von 26 freiwilligen und gesunden Rechtshändern abgebildet (12 Frauen/14 Männer) während diese ein Experiment zu empathischem Einfühlungsvermögen absolvierten. Zuerst wurde den Absolventen ein Gesichtsausdruck mit einer bestimmten Emotion präsentiert (Freude, Wut, Angst und Trauer) und anschließend musste aus einem festgelegten Auswahlmenü ein passender Satz gewählt werden. Der Satz sollte am zutreffendsten beschreiben, was der Person gerade passiert sein könnte. Vor und nach dem Experiment bearbeiteten die Probanden Selbstreport-Fragebögen (TAS-20, SPF) und ihre Fähigkeit zur Emotionserkennung in Gesichtern (BFRT, MITE, DCERT) wurde getestet.

Unsere Ergebnisse zeigten, dass Frauen ihre Empathiefähigkeit als besser einschätzen. Entgegen der generell vorherrschenden Meinung wurde aufgezeigt, dass Frauen kein größeres Empathievermögen als Männer besitzen, sondern, dass Männer mit mindestens genauso guten empathischen Fähigkeiten wie Frauen ausgestattet sind. Die beiden Geschlechter zeigten ähnliche Hirnaktivierungsmuster und erzielten gleiche Ergebnisse während der Absolvierung des Experiments zu empathischem Verhalten und es konnte diesbezüglich auch keine geschlechtsspezifische Lateralisierung der Hemisphären detektiert werden. Auch die Erkennung von Emotionen mit niedriger oder hoher sozialer Relevanz zeigte keine geschlechtsspezifische Tendenz.

Der letzte Paragraph der Arbeit behandelt die Ergebnisse der Studie sowie deren mögliche Auswirkungen.

III. Index of abbreviations

ACC	anterior cingulate cortex
AI	anterior Insula
(A)KDEF	(averaged) Karolinska directed emotional faces
BDI	Beck´s depression index
BFRT	Benton facial recognition test
BOLD	blood oxygen level dependend
CT	Computertomograph
DCERT	difficulty controlled emotion recognition test
DMFC	dorsomedial frontal cortex
DLFC	dorsolateral frontal cortex
EA	empathic accuracy
ERP	empathic reasoning paradigm
fMRI	functional magnetic resonance imaging
FT	fetal testosterone
H1	Hydrogen
hMNS	human mirror neuron system
HQ	handedness quotient
Hz	Hertz
IFG	inferior frontal gyrus
IPL	inferior parietal lobule
IRI	interpersonal reactivity index
LH	left hemisphere
M	Mean
MITE	mind in the eye test

MN	mirror neuron
MPFC	medial prefrontal cortex
Ms	Milliseconds
n. sign.	not significant
RH	right hemisphere
SD	standard deviation
SPL	superior parietal lobule
STS	superior temporal sulcus
TOM	theory of mind
TE	time echo
TP	temporal poles
TPJ	temporo-parietal junction
TR	time of repetition
VMFC	ventromedial frontal cortex

IV. Index

1 Introduction

Simply put, *Empathy* describes the capacity to share and comprehend another person´s emotion. As a social species, human beings are equipped with the ability to "put themselves in someone else´s shoes", i.e. resonate with the emotional state of their counterpart in order for interpersonal relationships to function (e.g. Singer & Klimecki, 2014). If a person shows empathic behavior it suggests that the person shares the same emotion as the one observed. Baron-Cohen (2004) stresses the necessity of this "affective state" by explaining, that "Empathy stands for the drive to identify the mental state of others in order to predict their behavior and respond with an appropriate emotion" So one can state that it builds an important basis in everyday social life and provides prosocial behavior (Singer and Lamm, 2009). For this purpose, "the main emotional communicator is the face and it is also the most researched one" (de Gelder, 2005). It is an everyday social task and essential to communication and human interaction to read and decode facial expressions correctly, so one can react with an adequate behavior (Jakobs, 1997). Misinterpreting an angry or aggressive face, for example, could be, dramatically speaking, fatal. Especially in Western culture, it is still a common opinion, that women are the more empathic gender (Manstead, 2000). The persisting stereotype states that women are said to be more interested in caring for others and their well-being. Men, in contrast, seem to be more pragmatic and solution-orientated, they have a tendency to follow rules and norms, which is referred to as "justice orientation" (Giligan, 1982). This different behavior can be explained by social gender roles (Eagly, 1978) as well as with an biological, scientific approach.

The intention of this study was to dig deeper into these concepts and, despite the already existing research, maybe shed a new light on this interesting topic and support current and future research.

2 Theoretical Background

2.1 Empathy- prerequisites and related concepts

2.1.1 Empathy

The term Empathy derives from Greek “empatheia” (em=in; pathos=feeling) .The English term empathy originates from the German word “Einfühlung” (to feel into) which originally has been used to describe emotions connected with nature or art. Later on, it was used as a more general item to qualify each other as “minded creatures” (Stueber, 2008). It has to be noted, that the concept of empathy has a multidimensional aspect, meaning that there are many factors that influence and shape its outcome, as well as there are several terms accompanying the concept of empathy that are not to be equated. *Mimicry* is defined as “the tendency to automatically synchronize affective expressions, vocalizations, postures, and movements with those of another person” (Hatfield, 1994, p.151). *Emotional contagion* describes the takeover of a certain observed emotion regardless of one´s own actual emotional state and can already be observed in infants (e.g. baby starts crying when it hears another baby crying). Therefore it is also called “primitive emotion” (Hatfield, 2009) and denoted as the plainest form of empathy. Mimicry or emotional contagion are said to often precede empathy, but are not sufficient to undergo an entire empathic experience (Singer and Lamm, 2009), because empathy entails the feature to distinct between the fact that another person is experiencing a certain emotion and not oneself. If this self- other- boundary is nullified the affective concept cannot be called empathy (Singer and Klimecki, 2014). *Sympathy,* another concept often linked with empathy, is defined as a “feeling for someone, generally coupled with the wish to see them better off or happier”, as well as *compassion, “*an emotional and motivational state characterized by feelings of loving-kindness and a genuine wish for the well-being of others” and *Empathic concern*: “an emotional and motivational state characterized by the desire to help and promote others’ welfare” (Bernhardt and Singer, 2012, p.3). These terms do not - like empathy - necessarily implicate the sharing of the same emotion. They rather describe feelings *for* another person (e.g. pity), whereas empathy means feeling *with* the other person (Singer and Lamm, 2009). For instance, if the person observed is sad, empathic behavior would implicate to share this sadness, whereas compassion or sympathy would rather lead to a caring attitude aiming to make the counterpart feel better (Bernhardt and Singer, 2012). Another interesting question is whether “empathic reactions” are always equal or if there is a way to modulate their outcome. Engen and Singer (2013) claim, that there are different factors that influence our empathic response. The characteristics of the emphasizing person, meaning for example age, gender or mood can have a severe modulating influence. The attitude towards the object of empathy (enemy, friend) plays an important role, too. Furthermore the contextual appraisal (e.g. beliefs about other´s emotional state) and the features of the other´s emotional state (intensity, valence) can severely affect the empathic experience (Engen and Singer, 2013). The examples given make it clear that empathy is a flexible concept, which can be influenced by several factors and vary from person to person.

It becomes apparent that empathy, one of the core concepts in social human interaction, is a complex and difficult system and object of neuropsychological research presented in this thesis. An important aspect of empathic processing is that most of the time, the empathic response evolves automatically and subconsciously, i.e. the emotion is shared instantaneously (so-called bottom-up information processing). But it is important to mention, that the empathic response can be controlled - meaning strengthened or attenuated - by so-called top-down information processing, too. Especially some areas in the prefrontal and cingulate cortex seem to modulate the intensity of our empathic response if necessary (Decety and Lamm, 2006). This "meta-cognitive feedback loop" is essential for a full empathic experience, taking into account, that empathy is no all-or none phenomenon and can be influenced by various factors as already mentioned before (Singer and Lamm, 2009). Another interesting and important aspect is the question of different neural networks which support the different concepts of empathy. As one can imagine, an important prerequisite for empathic behavior is the ability to recognize faces. "A face is the most distinctive and widely used key to a person's identity, and the loss of ability to recognize faces experienced by some neurological (prosopagnostic) patients has a profound effect on their lives" (Bruce and Young, 1986, p.305).

2.1.2 Face Perception and Emotion Recognition

Haxby et al. (2000) divide the neural correlates for face perception in a core system and an extended system, whereas the extended system can be co-recruited optionally. There are three crucial areas representing the core system for the visual analysis of the face: The inferior occipital gyrus, the lateral fusiform gyrus and the superior temporal sulcus (STS) (Haxby et al., 2000). The first exists for the early perception of the facial features and forwards the information to the other two areas. The fusiform gyrus processes the static features of the face, meaning identity in the first place. Interestingly, this area seems to be activated more by faces than by any other stimuli and therefore has been called *"the fusiform face area"*(Adolphs, 2002). In contrary, the STS recognizes the changeable aspects of the face, like expression, eye gaze or lip movement (Haxby et al., 2000, Perrett et al., 1982). According to Haxby (2000), the representation of the identity must be independent of the representation of the changeable features of the face because if that would not be the case, a change in expression could lead to a misinterpretation of identity. The extended system for further processing of the different facial features that are to be decoded consists of the anterior temporal region for identity, name and biographical information, the intraparietal sulcus for spatially directed attention and the auditory cortex for speech perception. Furthermore, the Amygdala, the Insula and the limbic system are crucial for emotion recognition (Haxby et al., 2000). It becomes clear, that there is a complex neuro-anatomical system that is involved in face perception.

One important concept to be discussed when it comes to face perception and associated emotion recognition is the "Appraisal Theory". Human beings are constantly confronted with a mass of emotions that are to be decoded and understood. To save cognitive resources and avoid sensual overload, "Appraisal Theory" postulates that the observer permanently uses a "filter" to extract only relevant emotions and stimuli and reacts according to the subjective relevance of the observed emotion (Ellsworth, 2003) . Of course, there are many factors that influence the extent and effort of interpreting the counterparts' emotions. For example, it will be much easier to decode the facial emotions of a well-known person than of a stranger.

The question whether certain emotions can be recognized easier or faster than others in an emotional reasoning paradigm like the one used in this study outlines an interesting issue to be investigated. Apparently, there are emotions that have a greater "social valence" or significance to the observer, i.e. they have an immediate impact on the observer´s well-being and are therefore detected faster and more accurately (Ellsworth, 2003, Rohr et al., 2012). Anger and happiness are called "emotions of high social impact" whereas fear and sadness are referred to as emotions of "low social impact" applying to the possible reactions evoked by the emotion (Prochnow et al., 2014b). Emotions of high social impact like anger can have an immediate effect on the observer (e.g. preparing for a fight or escape) and are - applying "Appraisal Theory" - more relevant to the observer than the emotions sadness or fear, that do not affect the observer in terms of e.g. threat but rather the person experiencing the emotion itself (Ruys and Stapel, 2008).

Furthermore, a relevant issue about face perception/processing is the duration in which an emotional facial expression can be recognized. It is known, that the perception of faces works automatically and rapidly and "the perceptive process under conditions of awareness" (Prochnow et al., 2013, p.271) to correctly read a facial expression takes approximately 30-50 milliseconds (ms) (e.g. Bar et al., 2006, Eger et al., 2003). The best way to proof this question is using "Affective Primacy Paradigms". "Affective priming investigates whether the evaluation of a first stimulus, the prime, that is to be ignored, affects the processing of subsequent stimuli." (Murphy and Zajonc, 1993)

2.1.3 Human Mirror Neuron System (hMNS)

The discovery of a class of visuomotor neurons, called Mirror Neurons (MN) in 1992 marked a new step in neuropsychological research. Conducting an experiment with macaque monkeys, Rizzolatti and coworkers discovered a group of motor action neurons located in premotor area F5 that discharged while the monkey was performing a certain motor act (movement with the presence of a goal), a fact that is not necessarily surprising. The new finding was that these neurons also discharged while the monkey observed an experimenter performing the same motor act (Gallese et al., 1996; Rizzolatti, 1996). A new mechanism was discovered, that provided - through mirroring - a direct understanding of the actions and emotions of others without higher order cognitive mediation (Rizzolatti et al., 2009).

The MNs are separated in two main categories: strictly congruent MNs and broadly congruent MNs. The strictly congruent MNs (about one third of all MNs) are only activated if the observed action exactly resembles the conducted movement. The later (two thirds of all MNs) fire if the movement is similar, goal or logically related (Gallese et al., 1996, Rizzolatti and Craighero, 2004). Besides area F5, the inferior parietal lobule (IPL) also was found to contain MNs, these two areas belonging to the parieto-frontal circuit that connects frontal and parietal areas for sensomotorical integration and therefore coordinates action movement (Cattaneo and Rizzolatti, 2009, Iacoboni and Dapretto, 2006). Of course the question arose, if there was a similar system in the human brain. Up to date, there is no direct evidence that proofs the existence of MNs in the human brain, but many experiments have been conducted that support their existence indirectly (Grafton et al., 1996, Keysers and Gazzola, 2010, Rizzolatti et al., 1996). In the human brain the MNS is embedded in the motor system (Ferrari and Rizzolatti, 2014) and corresponds well with the anatomical location of monkey MN areas. There are two main regions: The already mentioned parieto-frontal circuit - consisting of the rostral part of the IPL, the posterior part of the inferior frontal gyrus (IFG) and the lower part of the precentral gyrus. It plays an important role in understanding goals and intentions of others, as well as imitation learning (Iacoboni et al., 2005). There is another group of MNs located in the limbic area (anterior Insula, frontal cortex) and these are the basis for emotion recognition (Gallese et al., 2004). Furthermore, a small group of MNs based in Broca´s area was revealed and being claimed to participate in language development (Rizzolatti and Arbib, 1998).

The mechanism of the hMNS serves a neuropsychological approach for a variety of essential social interactions and does not have a unique purpose (Iacoboni and Dapretto, 2006). By transforming visual information into a motor act that is internally generated, it helps the observer understand the behavior of the observed action (Gallese et al., 1996, Kohler et al., 2002, Rizzolatti et al., 1996). Action understanding is certainly one of the most important features but the hMNS provides even more functions. Generating an internal "motor copy" of an observed action the possibility of imitation learning is given to the observer (Iacoboni et al., 1999, Rizzolatti and Craighero, 2004). Intention to comprehend why the person observed is doing what he or she is doing (e.g. Why is the girl picking the apple?) is based on the function of the hMNS, too (Gallese and Goldman, 1998). The fact, that the hMNS builds the basis of empathy by helping the individual to understand the intention behind the observed action (Iacoboni et al., 2005, Rizzolatti and Craighero, 2004) is especially important for our experiment. Wicker et al. (2003) conducted an fMRI study in which participants were firstly confronted with disgusting odorants and afterwards saw video clips of people with a disgusted facial expression. In both cases activation in the anterior Insula and the anterior cingulate cortex was recorded (Wicker et al., 2003). This provides convincing evidence that the hMNS plays a fundamental role in understanding the behavior of others and therefore in empathy as well. In addition "higher forms" of empathy, such as theory of mind (ToM) or mentalizing are based on the mirroring mechanism, but here it is not only the hMNS but also other brain areas (e.g. the STS) that support these empathic processes. Finally, there is research about how the hMNS is involved in the development of language (Rizzolatti and Arbib, 1998, Rizzolatti and Craighero, 2004). Put in clinical context, it is said, that it is highly plausible that dysfunctions of the hMNS could lead to deficits in social behavior (Iacoboni and Dapretto, 2006). In children with potentially socially isolating disorders like autism the skills in which the hMNS seems to be involved, meaning action or intention understanding, as well as empathy are underdeveloped or not existent (Cattaneo et al., 2007, Williams et al., 2001).

2.1.4 Theory of Mind

Another important concept closely related to empathy is the ability of reasoning about mental states, beliefs, desires or intentions of our fellow beings in order to explain and predict their behavior. There are three main terms that basically describe the same phenomenon, but were introduced by different authors: Theory of mind (ToM) (Premack, 1978), Mentalizing (Frith et al., 1991) and intentional stance (Dennett, 1987). Mentalizing does not equal empathy (Singer and Lamm, 2009) - the differences will be explained in the following passage - still, it is believed to be an important part of the empathic process and hence this concept is also often referred to as *"cognitive empathy"*(Blair, 2005, Shamay-Tsoory et al., 2009). The ToM-System is said to be responsible for the already mentioned "top-down information processing" that helps to modulate the empathic response (Groen et al., 2013). The concept of *"cognitive empathy"* (including ToM and perspective taking, which will be explained in detail later on) stands in contrast to *"emotional empathy"*, which is referred to as "the capacity to experience affective reactions to the observed experiences of others or share a "fellow feeling" (Shamay-Tsoory, 2011, p.18), meaning for example the systems like *emotional contagion* that have been already mentioned above, but with the discrimination, that emotional empathy allows a discrimination between one´s own and another person´s feeling. There is further evidence that supports the existence of these two systems that are necessary to enable a complete empathic experience. In a phylogenetical approach, De Waal (2008) stated that *emotional contagion* is the phylogenetical oldest system and cognitive empathy, that for example also includes perspective taking, does not fully develop until childhood or even adolescence. Each system is attributed with its own neurochemical transmitter. For cognitive empathy *Dopamin* is the responsible transmitter and the emotional empathy system is represented through *Oxytocin* (Shamay-Tsoory, 2011). The subdivision of empathy in these two systems has been stated by several researchers (Shamay-Tsoory et al., 2009) and gains further corroboration through the different neural systems they refer to, which will be explicitly explained in the following chapters. It is assumed, that when an empathic answer is needed, both systems work simultaneously and even interact (Van Overwalle and Baetens, 2009). Mentalizing is thought to represent one of the higher emotional functions and first signs of its practise become visible at the age of 18 months. Fully developed mentalizing abilities can be observed in children aged four to six years (Frith and Frith, 2003). According to Vogeley and colleagues (2001) "[Mentalizing] is an essential social skill as it plays a crucial role in interindividual communication" (Vogeley et al., 2001, p.170). Interestingly, ToM is not monodimensional, but can be - like empathy - subdivided in an affective and a cognitive component, too. Affective ToM does not equal emotional empathy, because it represents an emotional form of mentalizing. It enables the observer to infer with another person's emotions, whereas the cognitive form of ToM is crucial for inferring the beliefs and intentions of the observed person (Shamay-Tsoory, 2011). It is to mention, that mentalizing becomes especially important if one´s own emotional state and the emotion of the observed person do not match. Apparently, the concept of ToM is based on an associated neural network, which has been proven in several studies using different neuroimaging techniques (Fletcher et al., 1995, Goel et al., 1995, Vogeley et al., 2001). The anatomical regions regularly involved in mentalizing are the medial prefrontal cortex (MPFC), especially the anterior paracingulate cortex, the STS, the temporo-parietal junction (TPJ) and the anterior temporal poles (TP) (Frith, 2001, Frith and Frith, 2006).

The important role of internal stance becomes even more obvious when one is confronted with its failure. Patients who suffer from neurological diseases like autism (Lombardo et al., 2011) or advanced multiple sclerosis (Banati et al., 2010), display clear impairment when they are challenged with the task to interfere with their own or other people´s emotions. The term "Mindblindedness" is used to describe this deficit.

2.1.5 Perspective Taking

Perspective taking constitutes another empathy-related phenomenon. Mead (1934) and Piaget (1932) both claimed that perspective taking plays one of the most important roles in social human interaction

(Davis et al., 1996) and represents “the stepping stone in human empathy” (Jackson et al., 2006, p.752). “Perspective Taking involves actively considering a particular situation - or the world more generally - from another person’s point of view” (Goldstein et al., 2014, p.942). What demarcates this concept from empathy is that the latter describes the possibility to experience the same emotion as the one observed. When observing another person in pain, for example, perspective taking can generate two kinds of reactions: a feeling of compassion and sympathy for the suffering individual or a feeling of distress and discomfort because of the situation (Batson et al., 1991). Another interesting aspect about perspective taking presents the assumption that its “performance” improves with adolescence. Van der Graaff and colleagues (2014) described three main effects: Firstly, according to Piaget (1932/1965), adolescents reach “formal operations”, Piaget’s final stage of cognitive capacity, i.e. that they are able to observe a conversation from an “outside view” and take other than the own opinion into account. This represents a fundamental step towards perspective taking. Furthermore, Hoffmann (2000) claims that with adolescence, the awareness of the fact that an actual emotional situation can be influenced by various factors that might even not be present at the moment, increases. Thirdly, it is said that the neural circuits supporting perspective taking are not fully developed until adolescence (Crone and Dahl, 2012). Perspective taking plays an important role in developing a full blown empathic experience and this is why it is numbered among the concept of cognitive empathy.

Since it becomes obvious that the concepts related to empathy are numerous and not easily comprehensible, Prochnow (2014) developed a scheme of the concepts of empathy, explaining how they are related and associated and shedding some light on that complex topic (Figure 1). The concepts are exemplified in a pyramid, in which “emotional contagion” builds the basis, or most basic form of empathy. It´s neural correlate would be the anterior Insula (AI). Higher-ranked is the concept of “emotional empathy”, which has been described above and is correlated with MN- associated areas like the IFG. The next stage of this concept is the concept of “cognitive empathy” or “affective ToM” which can be equally used and are neuroanatomical-wise represented by the anterior cingulate cortex (ACC) and the dorsomedial frontal cortex (DMFC). The tip of the “empathy pyramid” is formed by the “cognitive ToM”-concept and associated with the superior temporal sulcus (STS), the paracingulate cortex, the temporo-parietal junction (TPJ) and the temporal poles (TP), also already mentioned above. The medial prefrontal cortex (MPFC) represents both concepts on the top end of the pyramid (cognitive empathy and affective/cognitive ToM). This figure illustrates, that the higher order forms of empathy come into effect if the basic forms are recruited beforehand and if they are necessary for a specific task.

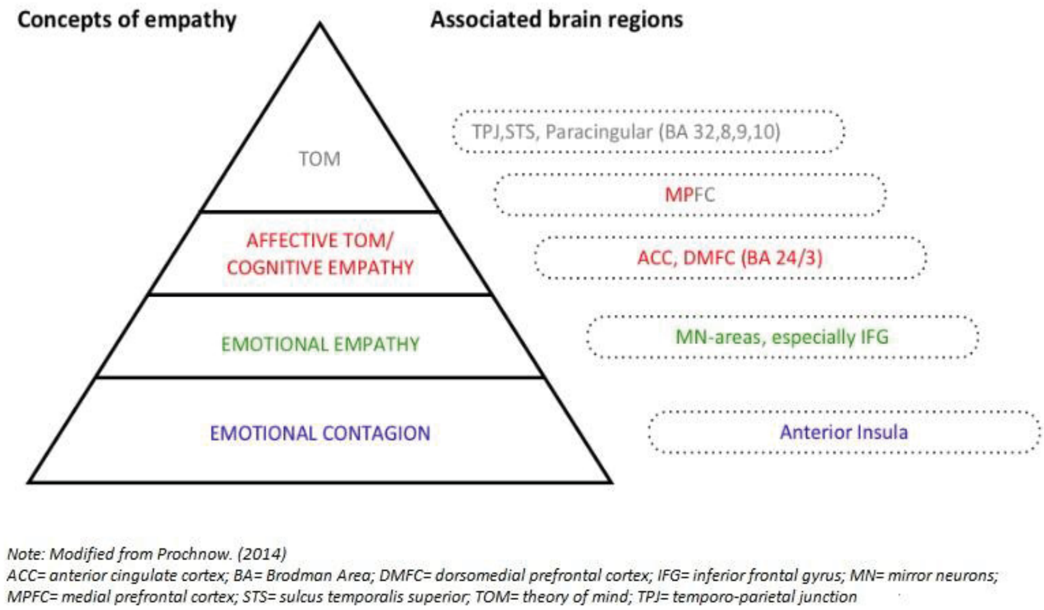


Figure 1: Concepts of empathy. Different levels of empathy shown in the pyramid from base to top. The associated brain regions are shown on the right side of the pyramid. The brain regions and associated areas are presented in matching colors.

2.2 Neural correlates of empathy

With empathy being a complex and essential concept in everyday human life, it is important to illustrate and explain the neural correlates and networks that enable and form the basis of empathic behavior. These neural networks have been investigated a lot with the help of neuroimaging techniques like fMRI using, among others, the so- called "empathy for pain paradigms" (Apkarian et al., 2005, Bushnell et al., 1999, Peyron et al., 2000). The brain regions which were activated while undergoing these paradigms, were activated both when the participant was experiencing pain him- or herself and when the participant was observing another person (e.g. a beloved one) being exposed to a painful stimulus. These results led to the "Shared network hypothesis" "which states that empathic experiences are subserved by activation of the same neural networks which are activated in the first-person experience of an affective state" (Engen and Singer, 2013, p.23) . As explained in the preceding chapter, there are several concepts (i.e. ToM) that support an empathic experience and come into action when necessary. The same with the supporting neural networks: There are additional networks that can be co-recruited depending on the individual situation.

In general, it can be stated, that the right hemisphere seems to be more involved in empathy than the left hemisphere (Etcoff, 1984) and that there is a strong right parietal involvement (Ruby and Decety, 2003).The neuroanatomical networks supporting empathy can be divided according to the two forms of empathy that have already been introduced beforehand. According to Shamay-Tsoory (2011), there is one “system” supporting the emotional or affective component of empathy comprising the IFG, the IPL, the ACC and the AI. These brain regions are illustrated in Figure 2. They are said to represent “low-level empathic responses” (Carr et al., 2003, Lamm et al., 2007, Prochnow et al., 2013, Schulte-Ruther et al., 2007, Seitz et al., 2008). Representatives for the neural circuits supporting the cognitive form of empathy are parts of the prefrontal cortex: the MPFC, the dorsolateral frontal cortex (DLFC), the dorsomedial frontal cortex (DMFC) and the ventromedial frontal cortex (VMFC) (Frith and Frith, 2003, Shamay-Tsoory et al., 2009, Vogeley et al., 2001), the TPJ (Saxe and Kanwisher, 2003) and the STS. These areas are shown in Figure 3. They are counted to the system of “higher-order-empathic responses”. There is active interaction between the two systems, but the division is reasonable as they differ behaviorally, developmentally, regarding neurochemical processes and, importantly, neuroanatomically (Shamay-Tsoory, 2011).

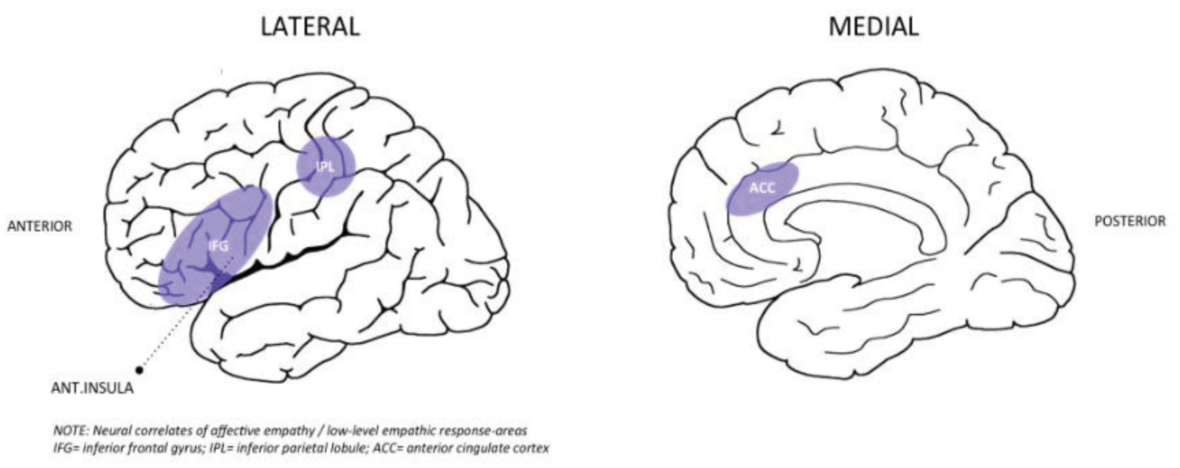


Figure 2: Schematic drawing of the neural correlates of affective empathy/ low-level empathic response areas. The lateral and the medial part of the brain are illustrated. Presenting the location of the ACC, the anterior Insula, the IFG and IPL in the human brain.

The IFG (Brodmann´s Area (BA) 44/45), a supramodal motor area, is called "the core structure of emotional empathy" and mainly responsible for emotional contagion and emotion recognition (Liakakis et al., 2011, Shamay-Tsoory et al., 2009). Harbouring the hMNS, it is said to be responsible for identifying goals and intentions of actions by "their resemblance to stored representations for these actions" (Rizzolatti et al., 2009, p.27). The IFG is also said to be involved in the modulation of language comprehension because of its vicinity to Broca´s area. The IPL (BA 39/40) represents the hMNS as well and helps simulate for example facial expressions. The ACC area also seems to have a central role in attributing intentions and goals to other people and is activated if the observed events are highly relevant for one´s own actions or reactions (Kampe et al., 2003).The AI builds the connection between frontal motor areas and the limbic system (Carr et al., 2003). It controls the current state of the emotions within the organism through multimodal connections with the amygdale, the hippocampus, the cingulate gyrus and the orbitofrontal cortex (Critchley et al., 2002). Furthermore, the Insula is mostly associated with negative emotions like pain and distress (Derbyshire et al., 1997), hunger and thirst (Tataranni et al., 1999) as well as anger and disgust (Phillips et al., 1997).The brain area related to the higher-level-empathy system, the MPFC "subserves the attribution of more enduring traits and qualities about the self and other people" (Shamay-Tsoory, 2011, p.21). The MPFC can be divided into dorsomedial and ventromedial regions (Mitchell et al., 2005). The dorsomedial part is said to participate in the affective aspect of ToM (Lindenberg et al., 2012, Shamay-Tsoory and Aharon-Peretz, 2007). The ventromedial area of the prefrontal cortex is part of the system that supports cognitive empathy (Shamay-Tsoory et al., 2009). The dorsolateral part is said to be part of decision-making ability (Veltman et al., 2003), as well as the discrimination of emotional expressions and subsequent decisions (Prochnow et al., 2013, Prochnow et al., 2014a). This area is closely connected to the ACC and IFG (Cieslik et al., 2013), both highly relevant regions regarding empathic reasoning. The TPJ is responsible for pre-processing and said to be a prerequisite for mentalizing (Schulte-Ruther et al., 2007). In addition, it is important for the discrimination between self and other, which is a crucial precondition for ToM (Decety and Sommerville, 2003) and is one of the main regions taking part in the inference of other people´s goals and beliefs (Saxe and Kanwisher, 2003).The TPJ holds one of the central roles in the neural system supporting ToM. Finally, the STS as well seems to be involved in the determination of other people´s mental states through "perceptual processing of socially relevant cues (e.g. biological, motion and facial expressions)" (Frith and Frith, 2003, p.463). It becomes clear that the brain areas mentioned above each play their individual part in generating an empathic response to adequate stimuli.

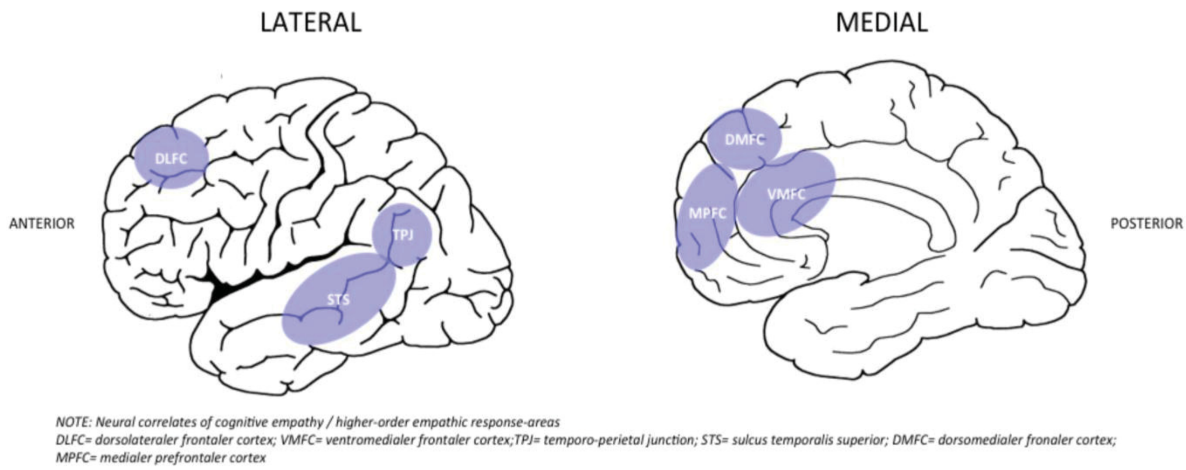


Figure 3: Schematic drawing of the neural correlates of cognitive empathy/ higher-order empathic response areas. The lateral and the medial part of the brain are illustrated. Presenting the location of DMFC, DLFC, MPFC, STS, TPJ and VMFC in the human brain.

2.3 Gender differences in empathy

Neuropsychological research has recently addressed the question whether empathy is a mainly female domain. There are several findings that seem to support this hypothesis. Females tend to rate themselves more empathic than men in self-report questionnaires (e.g. Interpersonal Reactivity Index, IRI) (Derntl et al., 2010, Groen et al., 2013, Schulte-Ruther et al., 2008). Apparently, females experience emotions in a more complex and fierce manner and report about negative emotions more often than males (Fischer et al., 2004, Tobin et al., 2000) . In addition, women have been shown to display a stronger susceptibility towards threatening or frightening events (Kring and Gordon, 1998). Female facial expressivity is more distinct than male mimic (Kring and Gordon, 1998). Sonny-Borgstrom and colleagues (2008) claim that this difference in expressivity might have an influence on emotional contagion and eventually empathic behavior. Women amplify the imitation of facial expressions; men, on the contrary tend to appear to suppress an imitative response to displayed facial expressions (Sonnby-Borgstrom et al., 2008). Furthermore, there is research that claims that women show superior performance in emotion recognition tasks and also when it comes to emotion expression (Hall and Matsumoto, 2004). Especially with reference to behavioral data or self-report questionnaires, Groen and colleagues (2013) state that “numerous studies confirmed that females compared to males have an advantage in social-cognitive and affective functions that are related to experiencing and expressing empathy" (Groen et al., 2013, p.142). Considering this information, it is comprehensible that disorders like autism - characterized by a lack of empathy are more commonly found in men than in women (Chakrabarti, 2006). Gender differences have furthermore been observed when it comes to the recognition of certain emotions in faces. Women tend to easier recognize fearful and sad facial expressions (Mandal and Palchoudhury, 1985, Nowicki and Hartigan, 1988), whereas men are superior in identifying expressions of anger (Mandal and Palchoudhury, 1985). However, there has been growing evidence that the "gender and empathy question" might not simply be answered with a female dominance in this matter as it has been assumed so far. Women and men seem to follow different approaches regarding an empathic answer. Evidence points towards a more affective or emotional process in women whereas men handle empathy rather in a cognitive (i.e. mentalizing) manner (Baron-Cohen, 2004). It is assumed, that women and men do hardly differ when it comes to the experience of the emotional component of empathy when, for example emotional pictures are viewed. The main distinctions appear within the cognitive empathy experience, when a more complex empathic behavior is required (Groen et al., 2013). This becomes even more apparent looking at the supporting neural networks that are differently recruited by women and men. Another interesting aspect that seems to influence "empathic skills" is the fact that, as already mentioned, the ability to empathize relies on the development of certain brain structures and circuits. These circuits are influenced by fetal Testosterone (fT), which is said to be inversely correlated with social abilities like eye-contact in infancy or peer relationship. Male foetuses are exposed to higher levels of testosterone than female ones, which might be another explanation for female superiority in this field (Chapman et al., 2006). It has to be stated that there are more and more studies showing gender equality in behavioral data (empathic questionnaires) which challenges the female "empathic dominance" hypothesis even more. Hyde (2005) highlights "that the differences should not be exaggerated because it can serve as a self-fulfilling prophesy by maintaining gender stereotypes. Nevertheless, studying the exact nature of the differences can provide knowledge of the areas where the stereotypical thinking occurs."(Hyde, 2005, p.582)

2.4 Neural correlates of empathy-related gender differences

Essentially both sexes rely on the same neural correlates for empathy and share parts of it for empathizing. Still, while undergoing an empathic paradigm, women recruit more empathy-related brain areas than men who rather activate preferentially cognitive-related cortical regions (Derntl et al., 2010). The gender differences in the activation of neural networks while processing positive or negative emotions also affect the various recruitment of frontal brain regions, as well as subcortical regions like the Amygdala (Kemp et al., 2004, Lee et al., 2002). Especially the latter presents an overall stronger activation in females while undergoing an emotional task (Derntl et al., 2010). Schulte-Rüther et al. (2008) highlighted that the activation of different neural networks affected the mentalizing- process as well. Both, females and males recruited networks associated with hMNS, but the activation in these areas was stronger in women (especially right IFG and right STS). The areas containing the hMNS are said to be responsible for *emotional contagion*, among others, a concept that women seem to rely on more than men do when it comes to empathic behavior. The male participants, in contrast, showed stronger activation of the TPJ, an area related to the cognitive processes of ToM (Schulte-Ruther et al., 2008). Another interesting fact regarding this topic illustrates the gender-depended lateralization activating certain empathy-related brain areas. Lateralization of brain functions describes the phenomenon that certain functions or processes (e.g. emotional or cognitive) are dominantly more represented in one hemisphere of the brain than the other. Basically, men show greater lateralization of brain function than women (McGlone, 1978). The lateralization also affects subcortical regions like the amygdala (Cahill et al., 2001, Killgore and Yurgelun-Todd, 2001). These processes of emphasizing in one brain hemisphere are assumed to occur because of differential gonadal hormone levels; especially estrogens seem to modulate this process (McEwen et al., 1998, Williams, 1998). It is likely that these gender-related strategies of processing emotion are one of the main reasons for the observed gender differences in empathy.

2.5 Functional magnetic resonance imaging (fMRI)

In this study we used functional magnetic resonance imaging (fMRI) to identify the brain areas being activated while undergoing an empathic reasoning paradigm. The fMRI is a research tool to detect changes of brain activity related to so-called neural activation tasks. Signal changes in the brain can be depicted with higher sensitivity than for example with the computed tomograph (CT) (Kauffmann G. W. , 2006, p.116). There are four physical phenomena that need to be explained to understand how a MRI works. Atoms with an uneven nucleon number (e.g. hydrogen (H1) are suitable for the use for the MRI because spinning around their own axis the nucleons create a magnetic dipole moment. Because of its high amount in the human body hydrogen fulfils this requirement. Secondly, the "chaos-principle" indicates that H1-ions in the human body are not in order. Confronted with a strong magnetic field the protons will align themselves along the main axis, namely in an energy-poorer, parallel, or in an energized, anti-parallel form. A further phenomenon is "the resonance" of the protons which is created through high-frequency impulses (radio waves). The impulses lead to an "activation" of the protons (convicting them from an energy-poor state into an anti-parallel state), as well as a "synchronisation" of the protons. The scaffolding of the MRI-picture is formed through a responding high-frequency-signal which occurs when the energized protons convert back into an energy-poorer, parallel state. The energized protons themselves create radio waves that can be detected. The last component of creating an MRI-picture are the T1-relaxation (spin-lattice-relaxation) and the T2-relaxation (spin-spin-relaxation). The endurance of these relaxation processes varies depending on the tissue (e.g. strong differences between fat and water). Thus, different areas can be differentiated depending on the strength of the signal. Depending on which part of the body has to be evaluated the examiner chooses a T1-weighted image (e.g. cerebral cortex, identifying fatty tissue) or a T2-weighted picture (edema, inflammation). In the MRI images there are different signal intensities depending on three main factors: Firstly, the parameter of the tissue (r, representing the number of protons in a certain volume= proton density), secondly, the sequence type (T1-weighted or T2-weighted) and thirdly the choice of parameter (time of repetition (TR), time to echo (TE) and the flip-angle). The TR describes the span of time between two energizing impulses sent from the magnet, the TE is the span of time between the impulse and the recognition of the re-sent signal from the patient and the flip-angle comes to 90° in a simple and commonly used spin-echo-sequence. A sequence defines the temporally defined interaction of a high-frequency impulse and the spatial mapping (Kauffmann G. W. , 2006, p. 117-125).

Another important matter to be explained is how the spatial mapping works. This happens during the high-frequency impulse, an additional wind ensures that defined magnetic field intensity only appears in a circumscribed, determined area while the neighbouring areas show different magnetic field intensity and will not be energized (Kauffmann G. W. , 2006, p. 122). The hardware of the MRI consists of the magnet; there are gradient- and shim-winds, as well as sending- and receiving-winds. Furthermore, a computer for data analysis and calculation of the images is needed. (Kauffmann G. W. , 2006, p. 121). Contraindications for the use of the MRI are any ferromagnetic metals such as iron, nickel or cobalt because they could lead to interactions with the magnetic field and cause severe injuries through burning or movement. Although there has not been any evidence for a teratogenic impact of MRI-scanning, pregnant women in their first trimester should not attend an examination. Claustrophobia could be a problem preventing the patient to lay still for a certain span of time in the fMRI scanner.

The concept of the fMRI is based on the fact that oxygen- poor haemoglobin reacts differently than oxygen-rich haemoglobin in the magnetic field. Being diamagnetic, oxygen-rich blood generates a stronger signal in T2 weighted sequences of the fMRI than the deoxygenated blood. Due to the fact that activated brain cells consume oxygen which is transported by blood in the brain, the flow increases in currently oxygenated brain areas. Also known as the blood oxygen dependend contrast effect (BOLD-Effect), an activation of certain brain cells increases the amount of oxygenated blood, which leads to a weaker signal in the supplying blood capillaries and adjacent brain tissue which can be measured by the fMRI. The fMRI depicts “where” certain brain areas are activated, but it can also answer questions about “what” the activity reflects and “why” the activity is occurring. This happens by separating brain regions by the time course of their BOLD changes in event-related-design or mixed-design studies (Donaldson, 2004).

2.6 Purpose of the study

The motivation for the current study was to further investigate the brain areas and neural circuits underlying the concept of empathy. Empathy is a multimodal concept that can be influenced and modulated by many factors internally and externally. Its adequate performance is essential in everyday human life for interpersonal relationships, understanding the emotions, intentions, beliefs or goals of others and may even have a protective function. The main interest of this dissertation is the question of gender differences in empathy. One goal is to find out whether the typical stereotype of a female superiority in this field, like for example stated by Simon Baron-Cohen in his book “The essential difference” (Baron-Cohen, 2004) still applies or if there are limitations to this commonly spread opinion. To the best of our knowledge, we are the first to use a difficulty-adjusted emotion recognition paradigm (DCERT), which is, regarding representing “real-life” facial affect recognition, superior to the established paradigms like the Ekman 60 Faces Test (Ekman, 1976). Our empathic reasoning paradigm extends the research by testing higher-order empathic skills and simultaneously scanning the corresponding brain regions. Our research group already published a paper regarding the topic if there are detectable differences in empathy comparing old and young participants, so that the gender question was not far to seek (Prochnow D. , 2014). We also already investigated reasoning about emotions of higher and lower social impact more closely (Prochnow et al., 2014b), so that it is interesting to combine these to questions and investigate them in this dissertation. To our knowledge, this aspect has not been investigated by any other research group so far. Furthermore, it might direct attention to subsequent research regarding diseases that are characterized by a lack of empathy, for example autism spectrum diseases or progressed Multiple Sclerosis.

2.7 Hypotheses

For this behavioural and fMRI study the following hypotheses were generated

1) *Compared to men, women consider themselves more empathic in self-report questionnaires* (Derntl et al., 2010, Rueckert and Naybar, 2008, Schulte-Ruther et al., 2008)

2) *Compared to men, women perform better in tasks requiring empathy like the Benton Facial Recognition Test, Mind in the Eye Test and facial affect recognition, show a clear advantage in the experience and expression of empathy and superior facial expression processing as well as emotion recognition*.(Groen et al., 2013, Hall and Matsumoto, 2004, McClure, 2000)

3) *Compared to men, women perform more accurately on and react faster to facial expressions related to a low degree of social impact (e.g. fear)*, *whereas men are superior inferring affective states of high social impact (e.g. anger)* (Mandal and Palchoudhury, 1985, Nowicki and Hartigan, 1988)

4) *Emotion processing involves lateralization of brain functions to the right hemisphere.* (Decety and Jackson, 2004, Hall and Matsumoto, 2004, Killgore and Yurgelun-Todd, 2001)

5) *Men and women share important nodes of the empathy network such as the anterior Insula, the Amygdala and the IFG* (Derntl et al., 2010, Schulte-Ruther et al., 2008)

6) *Men and women recruit different neural networks supporting different components of empathy, i.e. women rely on brain areas representing emotional empathy (e.g. IFG), whereas men draw on rather cognitive-related TOM-areas (e.g. MPFC)* (Derntl et al., 2010, Hofer et al., 2006, Koch et al., 2007, Schulte-Ruther et al., 2008)

3 Material and Methods

3.1 Subjects

3.1.1 Sample

From July 2012 to October 2012, 26 healthy volunteers (12 women/14 men) between the age of 22 and 61 years were recruited for the study. The women´s mean age was 41.2 (standard deviation (SD): 13.9), and the men´s mean age was 35.8 (SD: 10.0).The participants showed 13.9 (SD: 3.0) respectively 13.9 (SD: 3.1) years of education. Recruitment was mainly conducted through flyer advertisement, email contribution and word- or mouth advertising. Additionally the attendees gained a compensation of 20€ with the completion of the trial.

All participants were provided detailed information about the process of the trial so they could supply their informed written consent. Experiments were approved by the local Ethics Committee (attribution number 3805; February 27th 2012) and according to the Declaration of Helsinki.

3.1.2 Inclusion and exclusion criteria

The volunteers had to be at least 18 years old and their vision had to be normal or corrected to normal. Right-handedness was a prerequisite for participation, which was tested by the Edinburgh handedness inventory (cut of: handedness quotient (HQ) ≥ 67) (Oldfield, 1971). Further inclusion criteria were German mother tongue and no contradictions for the scanning procedure in the fMRI (such as claustrophobia, metals, cardiac pacemakers or pregnancy). Mental or psychological disorders, as well as momentarily straining emotional situations prohibited a participation in the study due to the fact that the empathizing skills could be constrained.

Certain results in the pre-testing phase had to be met in order to participate in the study. The volunteers were tested for signs of depression using the Beck´s depression inventory (BDI) (cut of: ≤ 9) (Hautzinger, 1995) . In addition, the Benton facial recognition test (BFRT) (cut of: ≥ 41) (Benton, 1994) had to be successfully completed.

3.1.3 Standardized questionnaires and tests

Before they underwent the actual empathic reasoning paradigm in the fMRI, the participants had to complete the Edinburgh handedness inventory (Oldfield, 1971), an easy and widely used assessment of handedness. Another component was the BDI (Hautzinger, 1995) to analyze the participant´s current mood. This questionnaire is proven to be reliable (Cronbach´s $\alpha \geq 0.84$) and valid. The BFRT (Benton, 1994) was the last pre-testing task that had to be completed to confirm normal facial recognition abilities. Reliability and validity has been repeatedly tested and verified.

During the post-fMRI-scanning phase the volunteers completed the Toronto alexithymia scale-20 (TAS-20) (Bagby et al., 1994b) to check their general emotional competence. This self-report-questionnaire is experimentally verified to be reliable (Cronbach´s $\alpha = 0.67$-0.84) and valid. The Saarbrückener Persönlichkeitsfragebogen (SPF) - the German version of the interpersonal reactivity index (IRI) (Davis, 1980) is a self-report questionnaire investigating the subject´s self reported empathy, the ability of perspective taking, fantasy and personal distress. This test also has been repeatedly proven reliable (Cronbach´s $\alpha = 0.78$) and proves to be valid. Eventually the mind in the eye-test (MITE) (Baron-Cohen et al., 2001) had to be conducted measuring emotional state reasoning. This test is also proven to be reliable and valid.

3.1.4 Self-programmed tests and software

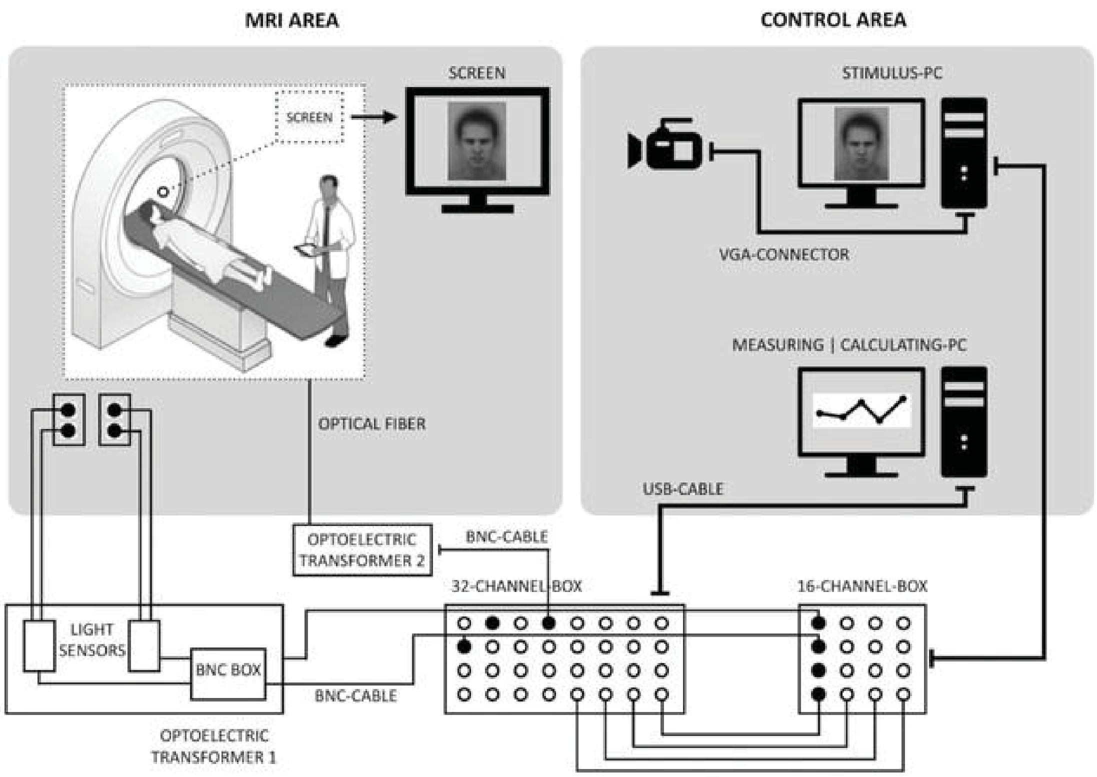
The self-programmed fMRI-compatible empathic reasoning paradigm (ERP) constituted the most important component of the study since it combined empathic reasoning and brain scanning, hence highlighting the brain circuits that were involved in empathic behavior. Lasting approximately 45 minutes, this was the most time-consuming part of the trial. For a short summary, the participants were shown different male and female emotional faces and had to decide what could have happened to the person choosing one out of four stated respond sentences via respond grip (Table 1). Thereby an emphasizing behavior was required while observing the emotions presented during the trial.

The difficulty controlled emotion recognition test (DCERT) is a self-programmed computer-trial, where the subjects were required to designate the emotion presented in six different male and female face expressions. The test screened for difficulties in discriminating between the different basic emotions happiness, sadness, disgust, fear, anger and surprise and served to confirm the results in the ERP. It was built similar to the Ekmann-60–faces-test. The test comprised 48 black and white facial expressions retrieved from the Karolinska Directed Emotional Faces (KDEF, Lundqvist, 1998a). Resting on difficulty indices calculated on the basis on previous data using the Ekman-60-Faces Test in 61 healthy controls (Prochnow et al., 2011), easily recognizable expressions like happiness were presented shorter than more difficult expressions such as fear (Prochnow et al., 2014b). After a certain emotional face expression was being shown, the participant had to choose the corresponding emotion from a predefined choice menu, each emotion being linked to a certain key on the keyboard of the computer. The emotion named in the choice menu was marked in different colors matching the corresponding key on the keyboard. The DCERT had been tested for its usability with approximately 10 volunteers before it was deployed in this study.

3.1.5 fMRI-setup

The fMRI-setup is presented in a schematic overview in Figure 4. The control-area was situated next door to the MRI-room and a window guaranteed permanent observation of the examination. To perform the ERP the participant had to lie down on the stretcher of the fMRI and hold one “respond grip” in each hand. Then a head device with a mirror attached was adjusted to the participant´s head so the projection of the paradigm could be recognized through the mirror properly. The face images were projected onto a semi-transparent screen in the dimmed fMRI area with a LCD-Beamer, type MT-1050 (NEC Co., Tokyo), resolution 800X600 pixel and a picture repetition time of 60 Hz. The LCD-beamer was positioned in the control-area and the instructors adjusted the focus of the pictures up to the point of ideal sight for the participant. The participant had to confirm his or her decision by pressing one of the four corresponding buttons on the respond grip. This action led to discontinuity of the photoelectric barrier, which was build from four fiberglass cables that were connected to a light sensor, type FX-311 (Panasonic Electric Works SUNX Co. Ltd., Osaka). An electric signal was triggered by interaction of the light sensor and a BNC-modem, acting as an optoelectric converter and positioned outside of the MRI. The electric signal was transported via BNC to a 32-canal-USB-box (MH GmbH, Erftstadt) as well as an 16-canal-box and forwarded to the stimulation-computer (System: Windows XP Professional SP3; Intel Pentium Dual-Core E5500 2; 8GHZ CPU; 2GB DDR2-SDRAM; 150GB SATA-harddrive; ATI Radeon HD3450 Display card), which was positioned in the control-area. Here the stimuli of the ERP were presented via MRI-trigger and projected on the semi-transparent screen. The presentation program *Presentation 14.9* (Neurobehavioral Systems Inc., Albany CA) accounted for the assessment and recording of the pressed response button and evaluated the correctness of the given answer. Furthermore, the program itself generated a certain electric signal depending on the presented stimulus type, which was sent via six different channels to the 32-canal-USB-box. The 32-canal-USB-box registered the signals coming from the respond grips, the MRI and the stimulation computer and forwarded this information via USB-cable to the recording computer. (system: Windows XP Professional SP3; Intel Core 2 Duo E6300 1,86GHZ CPU; 1GB DDR3-SDRAM; 75GB SATA-harddrive; Intel Q965 Express (IGP) Display card), which was also located in the control-area. The recording computer provided a measure tool which recorded all incoming signals with the program *EdWin* (MH GmbH, Erftstadt) and showed them graphically on a screen with a program called *RTEWin* (MH GmbH, Erftstadt). The data in edt-format was being culled for each single channel and fMRI signal based on *Matlab 2011b* (The MathWorks Inc., Natick MA).

Scanning was performed on a 3 T Siemens Trio TIM MRI scanner (Erlangen, Germany) utilizing an EPI-GE sequence (TR = 2000 ms, TE = 30 ms, flip-angle = 90°, FOV = 192 x 192 x 112 mm^3, acquisition matrix = 128 x 128 pixels). In each run, 1200 volumes were acquired. A 3D-T1-weighted MP-RAGE (magnetization prepared gradient echo) sequence (TR = 2300 ms, TE = 2.98 ms, flip angle = 90°) with high resolution consisting of 192 sagital slices (in-plane resolution = 1 mm x 1 mm, slice thickness = 1 mm, interslice gap = 0 mm) was also acquired in each subject. After data processing, the whole brain was covered by 28 transversal slices oriented parallel to the bi-commissural plane (in-plane resolution = 1.5 mm x 1.5 mm, slice thickness = 4.0 mm, interslice gap = 0 mm, FOV = 256 x 256 x 192 mm^3, acquisition matrix = 256 x 256 pixels).



Schematic presentation of the fMRI setup. Left the MRI area with the scanner and the patient as well as the screen presenting the emotional pictures. Right the separated control area including the beamer, stimulus-PC and measuring/calculating-PC. Areas were connected through two optoelectric transformers which were connected to the light sensors on the one hand and a BNC-box/cable on the other hand. Information was operated through a 32/16-channel box.

Figure 4: Schematic presentation of the fMRI-setup

3.2 Procedure

The trial consisted of three main parts the subjects had to undergo and lasted in total approximately 1.5 hours. For the pre-fMRI-testing as well as the post-fMRI-testing phase we used a standardized set of certain questionnaires and tests every subject had to complete in order to rule out any contradiction for participation (pre- testing) and for testing different aspects of emotion processing (post-scanning) (Prochnow et al., 2014b). Additionally, the post-scanning phase was enlarged by the self-programmed DCERT to test difficulty-adjusted emotion recognition.

3.2.1 Pre-scanning

The "pre-MRI-testing" contained a short medical history, the accomplishment of the Edinburgh handedness inventory (Oldfield, 1971), the BDI (Hautzinger, 1995) and the BFRT (Benton, 1994). These tests served as exclusion criteria for the following fMRI- testing when the predetermined cut-of-scores were not achieved.

The participants were asked for their handedness, metal (e.g. prosthesis), cardiac pacemakers, and pregnancy and if they were momentarily confronted with emotionally draining situations. It had to be checked if there was a need for glasses or contact lenses due to the fact that the fMRI- capable glasses only provided correction of full vision to an extend of +/- 3.0 dioptres. The Edinburgh inventory was used to assess handedness with the HQ calculated with the following formula: total right- total left/ total right + total left (Oldfield, 1971). We used the BDI which is one of the most widely used instruments for measuring the severity of depression (Hautzinger, 1995). The passing of this test was an important condition for non-biased judgment of emotion, which is one of the main factors in this study. Furthermore the BFRT which is a widely distributed tool to assess face recognition abilities (Benton, 1994) had to be completed.

In addition the participants received the instruction for the task in the fMRI-scanner and the process was explained in detail.

3.2.2 Empathic Reasoning Paradigm (ERP)

Before starting the MRI, the instructions for the testing sequence as well as the handling of the "respond grips" were explained in detail. The participants were allocated two "respond grips", one for the left and one for the right hand. These tools were equipped with two answering buttons per grip. The buttons could be pressed with the corresponding thumb or index finger depending on the correctness of the selected answer. To achieve the right decision one had to abide the following instructions: The attendee was shown a black and white male or female face with a neutral expression which morphed into a certain facial expression (happiness, sadness, anger or fear). Pictures were taken from the averaged Karolinska directed emotional faces (AKDEF, Lundqvist, 1998b). The task was to imagine meeting this person in an everyday situation and to decide "what could have happened to this person" (Prochnow et al., 2014b). Face presentation was preceded by a fixation cross to gain the participants attention and followed by a menu of choice with 4 corresponding sentences giving possible scenarios that could have been held responsible for the shown emotion (e.g „Er/Sie hat geheiratet" for happiness or „Er/Sie hat einen Horrorfilm gesehen" for fear). Each sentence corresponding to a certain button on the respond grip, the participant had to choose the right sentence pressing the referring button. If more than one sentence seemed to be appropriate, the volunteer had to decide for the one that seemed more likely. The span of time for the answer was limited so that the sequence of the trial continued after seconds of time regardless of the fact if the subject answered or not. Additionally to the facial expressions we installed a control picture showing a scrambled face ensued after a jittered time interval by 4 random sentences (e.g. "die Sonne scheint").When detecting this picture, the participant was asked to choose the sentence "Diesen Knopf drücken". "The control condition allowed for controlling reading, motor and memory related activity" (Prochnow et al., 2014b, p.167)

As mentioned before there were two faces, one male and one female face, which presented four different emotions (happiness, sadness, anger and fear). The degree of emotional expression was varying between emotions in relation to difficulty based on difficulty indices calculated from previous data using Ekman and Friesen´s pictures of facial affect (Johnson et al., 1976) in 61 healthy volunteers (Prochnow et al., 2011). "For example, happiness as the only positive and easily recognizable emotion was presented at a degree of only 50% of the maximal expression, while fear as the most difficult expression was shown at 100%" (Prochnow et al., 2014b, p.166). Furthermore a scrambled "control"-picture was shown, which was generated by fragmenting the original image into areas that were 10 X 10 pixel in size and then put back in randomized order. Through this process the original information of the image was garbled.192 images were shown in total. This complied with 24 pictures per emotion per male or female face. Additionally, there were 48 control pictures shown in randomized order. One trial is defined as the span of time between the presenting of a face and the choice of the corresponding sentence via button press. The maximum duration of one trial was 12600 ms, varying depending on the jitter as well as the reaction of the participant (needed time for button press). The pictures were presented in randomized order for 1400 ms. Beforehand a "fixations-cross" was shown for 200 ms followed by a 400 ms lasting black screen. After that a jitter with the chosen repetition time (TR) of 2000 ms was followed by the menu of choice appearing on the screen. The menu of choice contained one target sentence and 3 distraction sentences whereas the position of the sentences changed and was presented in randomized order. Also, the sentences were almost identical in length.

There were 3 target sentences for each of the four corresponding emotions in total (Table 1). The respond sentences lasted for 7 seconds (sec) on the screen in which the participant was asked to press the corresponding button on the handle grip. If the button was not pressed, a new trial began. If the button was pressed, the screen turned black for another 1600 ms and the trial was completed. The beginning of a new trial had to be triggered by the fMRI. The exact procedure is illustrated in Figure 5.

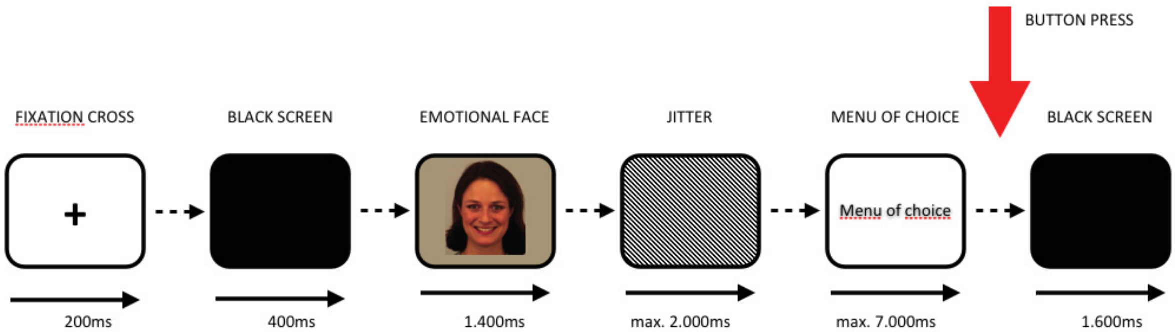


Figure 5: Procedure of the empathy reasoning paradigm during fMRI

Before starting the actual test each participant had to undergo a training session. This had to be performed to get used to the environment and noise of the scanner as well as to the handling of the respond grips, and to get a feeling for the given respond time. 12 facial expressions were presented. One had to press the buttons as instructed and in case the training was completed successfully (gaining 100%) the actual testing was started. If the training was not accomplished satisfactorily (meaning no facial expression and less than two control pictures were correctly chosen), the training could be repeated for a second try. If the test was again completed unsuccessfully, the whole session had to be cancelled.

“Due to the adaptive nature of the experimental trial, scanning duration varied between the participants. Average scanning duration was 35 minutes. FMRI scanning was followed by anatomical scanning of approximately 12 minutes” (Prochnow et al., 2014b, p.167)

facial expression	choice of response sentences
scrambled	"Diese Taste drücken"
happy	"Er/Sie hat geheiratet"
	"Er/Sie hat jemanden gesehen, den Er/Sie mag"
	"Er/Sie hat eine Jobzusage bekommen"
sad	"Er/Sie war auf einer Beerdigung"
	"Er/Sie wurde verlassen"
	"Er/Sie ist durch eine Prüfung gefallen"
angry	"Er/Sie wurde bespuckt"
	"Er/Sie hat einen Strafzettel bekommen"
	"Sein/Ihr Auto wurde zerkratzt"
fearful	"Er/Sie wurde von jemanden bedroht"
	"Er/Sie wurde verfolgt"
	"Er/Sie hat einen Horrorfilm gesehen"

Table 1: Respond sentences for the four different emotions

3.2.3 Post-scanning

Two self reports for screening general emotional competence and self-reported empathy were used. The TAS-20 (Bagby et al., 1994a) and the SPF (the German version of the IRI) (Davis, 1980). Cut-of-scores lay at ≤ 52 for the TAS-20. The SPF was divided in different sub-categories: perspective-taking ≥ 13, fantasy ≥ 10 and empathy ≥ 12. After completing their self-reported questionnaires, the DCERT, which is explained in detail in chapter 3.2.2., had to be performed.

The final paradigm was the MITE (Baron-Cohen et al., 1997), measuring adult mentalizing-abilities and emotional state reasoning. Here the participant had to recognize emotions only from pairs of eyes. As a result the sum of the items was counted.

3.3 Statistical data analysis

3.3.1 Behavioral data analysis

As an initial step the behavioral data were tested for normal distribution using the Kolmogorov-Smirnov test. The analysis of behavioral data was performed with the SPSS software (PASW, Predictive Analysis Software, version 20). In order to analyze data regarding the stated hypotheses one overall single factor analysis of variance (ANOVA) was used to reduce α-accumulation and for comparison of means .The correlations were tested using Spearman coefficients. (see also Prochnow et al., 2014b)

3.3.2 FMRI data analysis

Imaging data from the fMRI was processed using the Brainvoyager QX software package (Brain Innovation, Maastricht, Netherlands). The 2-D slice time-course image data were co-registered with the volumetric 3-D Gradient Echo data sets from the same session in each participant. The functional images were spatially normalized and in between the scans realigned to correct head movement. To enhance image structures, data were pre-processed by using Gaussian spatial smoothing (FWHM= 6mm). Furthermore, temporal filtering as well as removal of linear trends was applied to the data in terms of pre-processing. A random effects group analysis based on a deconvolution general linear model (GLM) was used to capture BOLD changes in a rapid-event related design. To contrast conditions, the following regressors were determined: *baseline* (scrambled facial expressions) and *face* (face expressions with high and low self-relevance), whereas the highly relevant expressions are labeled as *"self- relevant"* and include happy and angry faces and the low- relevance expressions as *"other- relevant",* representing sad and fearful facial expressions. Further regressors were *decision*, and *control* (for motor and reading related activity). The regressor *decision* was also subdivided in self-relevant decision and other-relevant decision. It is to note, that for mapping the brain activation patterns related to the event *decision*, all answers, meaning right and false decisions were taken into account. A threshold of $p < 0.005$ (uncorrected) was applied to all data. The threshold was combined with a cluster-size threshold of 10 voxels for partial correction of multiple comparison (Goebel et al., 2006).

The coordinates of the activated brain areas are presented in Talaraich space (Talaraich and Tournoux, 1988)

4 Results

4.1 Behavioral data

The subjects were all right-handed, women scoring a mean (m) of 94.5 (SD=8.2) and men 83.0 (SD=11.0) on Oldfield´s handedness inventory. For the BDI, women (m=3.3, SD=3.8) showed higher results than men (m=1.9, SD=2.5) (p=0.033). This had no further effect on the trial, since inclusion criteria was to score ≤ 9, which was by far not reached. Both sexes showed sufficient facial recognition abilities with women reaching a mean of 47.7 (SD=2.6) and men 48.2 (SD=2.5), no significant difference at hand. After the fMRI-trial both sexes scored equally on the TAS-20 (women: m=38.4, SD=6.7; men: m=39.7, SD=9.5; n.sign.). The total result of the SPF did not reveal any significance (women: m=44.8, SD=7.2; men: m=43.5, SD=4.2), but for the subcategory of *Empathy* women rated themselves significantly higher (women: m=15.9; SD=2.5; men: m=14.1; SD=1.7; p=0.042). The other subcategories *Fantasy* (women: m=15.2; SD=2.3; men: m=13.8; SD: 2.1) and *Perspective Taking* (women: m=15.9; SD=2.8; men: m=15.6; SD=2.0) showed no significances. A summary is given in Figure 6.

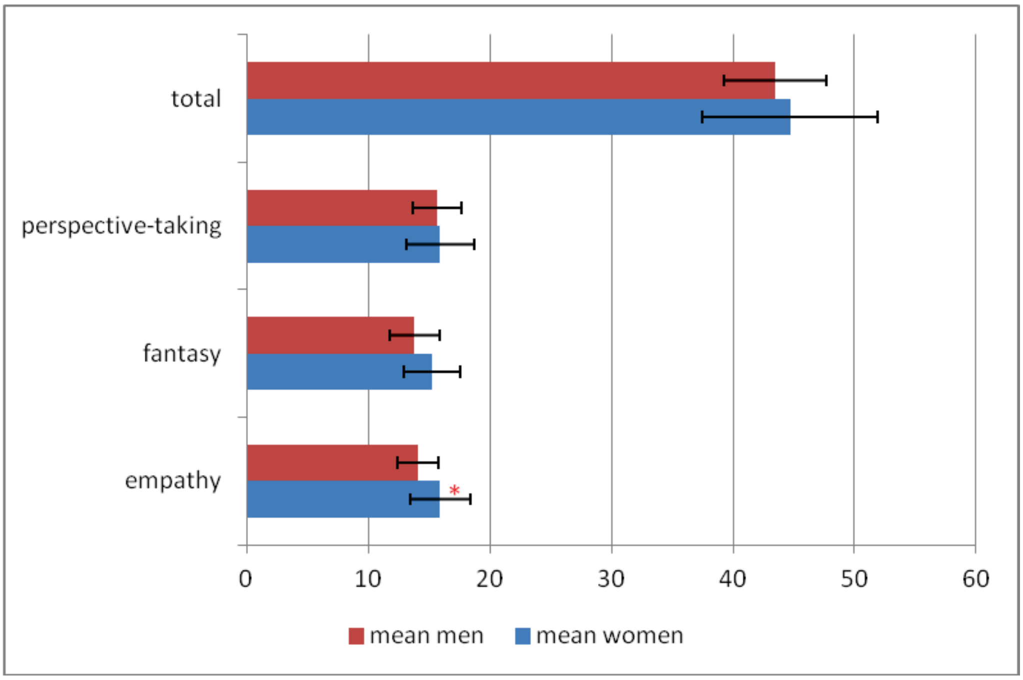


Figure 6: SPF. Mean values of women (blue) and men (red). The total score as well as the subcategories (perspective taking, fantasy and empathy) are shown. The red star highlights a significant difference between the genders in the subcategory empathy. The black bars show the standard deviation of each emotion.

Detecting emotions from isolated pairs of eyes in the MITE did not show any differences between women (m=82.3, SD=9.4) and men (m=79.1, SD=10.8). The DCERT, which required the recognition of 6 basic emotions in faces, was completed satisfactorily. *Happiness* (women: m=100.0, SD=0; men: m=99.1, SD=3.5), *Anger* (women: m=97.9, SD=7.2; men: m=97.3, SD=7.3), *Sadness* (women: m=94.6, SD=6.7; men: m=91.9, SD: 23.5), *Disgust* (women: m=93.7,SD:8.6; men: m=95.6, SD:10.2), *Surprise* (women: m=93.6, SD=8.6; men: m=95.6; SD:10.2) and *Fear* (women: m=63.3, SD=28.9; men: M=60.5, SD=34.7). In total women scored a mean of 90.0 (SD=5.2) and men a mean of 89.1 (SD=9.4). The results are illustrated in Figure 7.

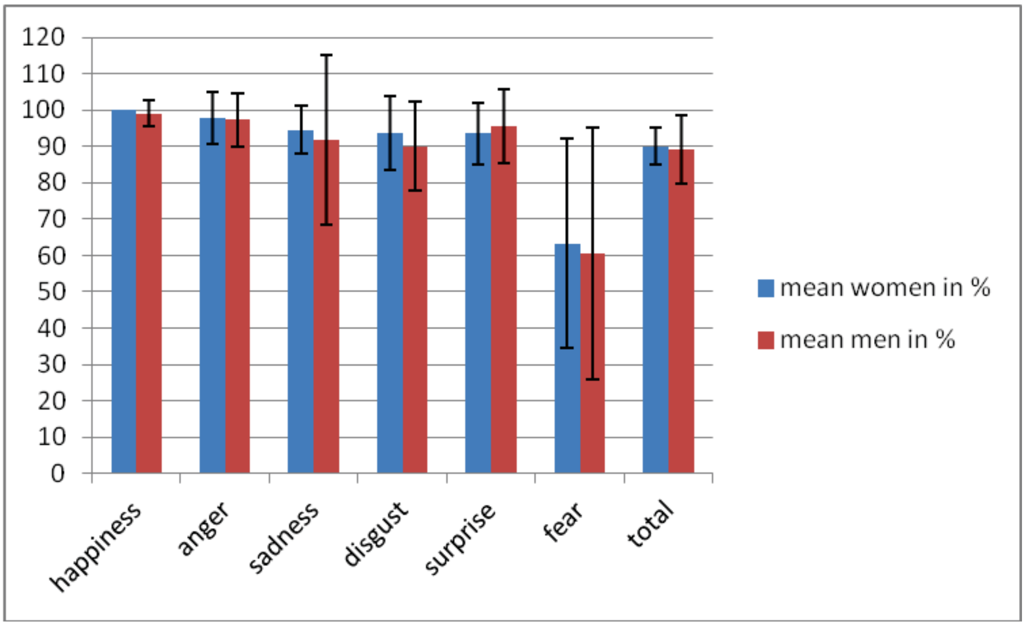


Figure 7: DCERT. Mean scores of women (blue) and men (red) in percent (%) for the total results as well as the subcategories (happiness, anger, sadness, disgust, surprise and fear). Black bars represent the standard deviation.

The results of the "main task", the Empathic Reasoning Paradigm (ERP), were divided into the two main groups of *accuracy* and *reaction time* and each result for the corresponding emotion (happiness, anger, sadness and fear). For accuracy, no significant differences comparing men and women came to light. Starting with the women´s results for *accuracy* in total (m=72.8, SD=12.3), for anger (m=59.6, SD=24.5), happiness (m=97.0, SD=3.1), sadness (m=83.7, SD=11.3), and fear (m=50.8, SD=27.2). Men´s results for the total score (m=75.9, SD=19.8), for anger (m=71.1, SD=25.0), happiness (m=93.3, SD=8.9), sadness (m=78.0, SD=20.0), and fear (m=60.8, SD=33.6).The control condition for accuracy did not show and significances, too. Women (m=98.5, SD=2.4) and men (m=96.2, SD=5.0). For the numbers, see Figure 8 and Table 2.

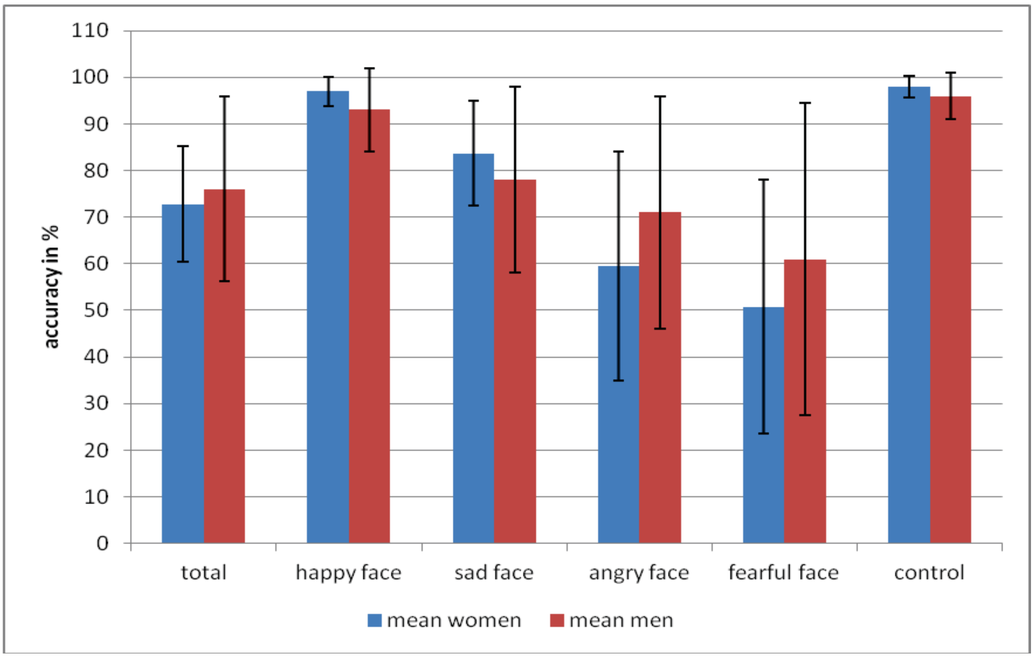


Figure 8: ERP-accuracy in percent (%). Mean score reached by women (blue) and men (red) in the categories (total score, happy face, sad face, angry face, fearful face and control condition). Black bars show the standard deviation.

Women			**Men**				
	N	**mean**/(SD)/*range*		**N**	**mean**/(SD)/*range*	**p**	**Cohen´s d**
Total	12	**72.83** (12.34) *51.00-95.00*	**total**	13	**75.85** (19.78) *40.00-98.00*	0.655	0.2
happy face	12	**97.00** (03.13) *91.00-100.00*	**happy face**	13	**93.31** (08.86) *70.00-100.00*	0.186	0.6
Sad Face	12	***83.67*** *(11.30)* *58.00-95.00*	**sad face**	13	**78.00** (19.97) *39.00-100.00*	0.397	0.4
angry face	12	**59.58** (24.47) *10.00-93.00*	**angry face**	13	**71.08** (24.96) *18.00-97.00*	0.258	0.5
fearful face	12	**50.83** (27.17) *04.00-93.00*	**fearful face**	13	**60.77** (33.58) *10.00-100.00*	0.427	0.3
Control	12	**98.50** (02.43) *93.00-100.00*	**control**	13	**96.23** (04.97) *81.00-100.00*	0.166	0.6

Table 2: ERP-accuracy, comparing women and men. n = number of participants; p = probability (t-value/significance); SD = standard deviation.

Also, there were no significant differences regarding *reaction time* in the ERP. Again, starting with the women´s results in total (m=2819.8, SD=419.5), for anger (m=5012.4, SD=1159.8), happiness (m=2457.2, SD=334.3), sadness (m=2337.9, SD=494.2) and fear (m=1471.6, SD=770.2). Men´s total (m=2937.5, SD=430.1), results for anger (m=5204.9, SD=2047.6), happiness (m=2538.36, SD=482.1), sadness (m=2256.2, SD=510.1) and fear (m=1749.3, SD=871.2). Here, the control condition also did not show any salience (women: m=1526.1, SD=152.3; men: m=1708.3, SD=398.5). The numbers are given in Figure 9 and Table 3.

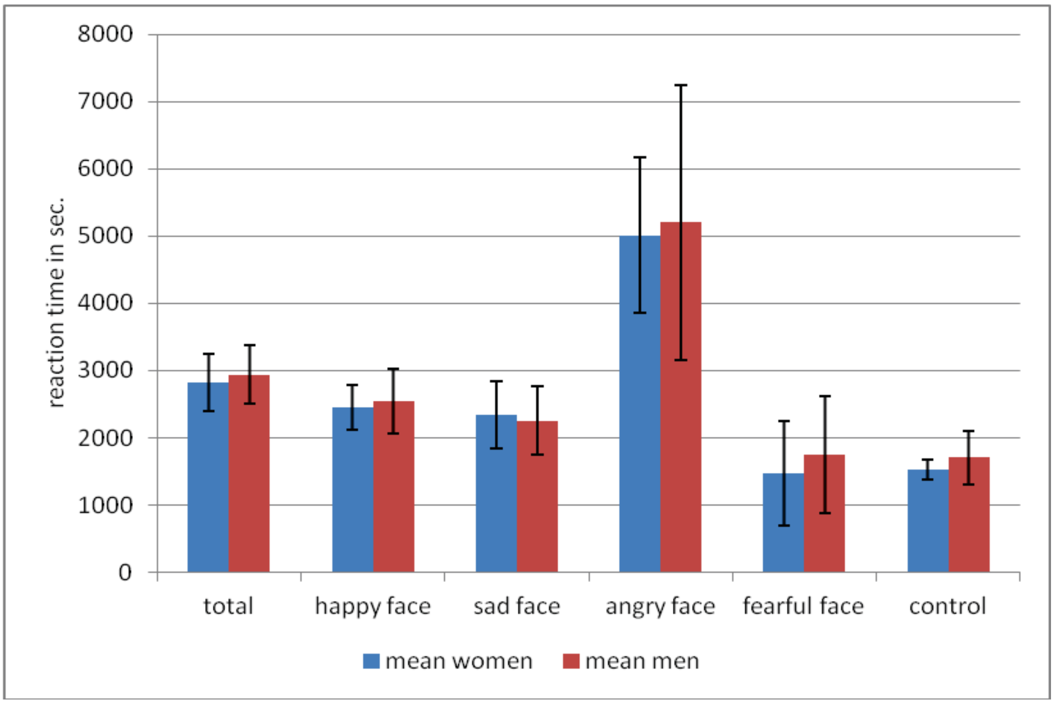


Figure 9: ERP-reaction time in seconds (sec.) of women (blue) and men (red). Black bars show the standard deviation.

women			**Men**				
	N	**mean**/(SD)/*range*		**N**	**mean**//SD)/*range*	**p**	**Cohen´s d**
total	12	**2819.75** (419.55) *3514.00-6853.00*	**total**	14	**2937.50** (430.13) *2373.00-3814.00*	0.488	0.3
happy face	12	**2457.17** (334.31) *1847.00-2827.00*	**happy face**	14	**2538.36** (482.14) *1510.00-3299.00*	0.628	0.2

	N	**mean**/(SD)/*range*		N	**mean**//SD)/*range*	p	Cohen´s d
sad face	12	**2337.92** (494.21) *1333.00-2762.00*	**sad face**	14	**2256.21** (510.05) *1291.00-3135.00*	0.683	0.2
angry face	12	**5012.42**(1159.76) *3514.00-6853.00*	**angry face**	14	**5204.86**(2047.64) *2568.00-9436.00*	0.776	0.1
fearful face	12	**1471.58** (770.20) *132.00-2672.00*	**fearful face**	14	**1749.29** (871.18) *474.00-3148.00*	0.401	0.3
control	12	**1526.08** (152.29) *1220.00-1715.00*	**control**	14	**1708.29** (398.51) *1289.0-2620.00*	0.149	0.6

Table 3: ERP-reaction time comparing women and men. n = number of participants; p = probability (t-value/significance); SD = standard deviation.

4.2 Whole brain fMRI data

In the first step we examined the brain activation patterns for women and men separately. A distinction was made between the so-called *"Main-effects"* (including "*Facial expression*" and *"Decision"*) and the *"Specific effects"* (here we tested the conditions *"self and other-relevant face"* and *"self and other-relevant decision"*). Note that, as already illustrated beforehand, self-relevant emotions included happiness and anger, whereas other-relevant emotions described sadness and fear.

For women, the main effects resulted in a higher blood flow especially in the parietal gyrus (e.g. BA 7, BA 40) and some activation was found in the frontal brain areas (e.g. BA 8, BA 45). The fusiform face area (FFA) was also highlighted during the main task. Furthermore, activation of precentral (e.g. BA 6), postcentral (e.g. BA 3) and temporal regions (BA 21) could be detected. Specific effects mainly activated areas in the frontal gyrus (e.g. BA 8, BA 9, BA 45, BA 47) and some activation was found in the limbic (BA 32) and the precentral (BA 4, BA 6) areas. In terms of hemispheric dominance, a strong lateralization to the left could be observed, but regarding the main effects the hemispheres were activated alike. All involved areas are summarized in Table 4.

main effects	hemisphere/ region	Label	BA	x	y	z	t	voxel
facial expression	R	FFA		47	-68	-3	3.896	308
	R	temporal	21	44	-2	30	3.476	154
Decision	R	postcentral	3	59	-14	24	3.766	426
	R	precentral	6	59	1	30	3.446	30
	R	IPL	40	41	-41	54	3.678	2204
	R	SPL	7	38	-53	63	3.507	78
	R	SPL	7	35	-59	51	3.541	69
	R	Claustrum		26	16	15	3.182	17
	L	MFG/DMFC	8	-7	22	48	3.881	420
	L	Declive		-7	-71	-22	3.598	175
	L	IFG	45	-34	25	3	3.868	842
	L	precentral	6	-34	-11	66	3.614	126
	L	IPL	40	-46	-44	51	3.716	455
	L	IFG	45	-58	19	3	3.404	41
	L	precentral	6	-61	-2	39	3.674	376
	L	postcentral	3	-58	-17	30	3.279	13
specific effects								
self-relevant face	R	temporal	21	69	-38	-3	3.557	10
	L	precentral	6	-16	1	51	3.438	13
other-relevant face	R	precentral	6	47	-5	30	3.883	187
	R	precentral	6	41	-5	42	3.238	26
	L	limbic/ACC	32	-19	43	6	3.210	11
self-relevant decision	L	MFG	8	-7	22	48	3.330	279
	L	Thalamus		-10	-5	3	3.463	22
	L	IFG	45	-34	25	3	3.568	162
	L	MFG	9	-43	13	33	3.626	1185
	L	IFG	45	-46	22	12	3.557	222
	L	IFG	45	-58	19	3	3.678	131
other-relevant decision	L	MFG/DMFC	8	-7	28	48	3.609	526
	L	IFG	47	-31	22	-3	3.558	416
	L	precentral	4	-52	-5	15	3.608	14

Table 4: Whole brain activation in women. P ≤ 0.005, 10 voxels; L = left; R = right; BA = Brodmann Area and coordinates (x,y,z,); ACC = anterior cingulated cortex; ; FFA = fusiform face area; DMFC = dorsomedial frontal cortex; IFG = inferior frontal gyrus; IPL = inferior parietal lobule; MFG = middle frontal gyrus

For men the main effects aroused predominantly occipital areas (e.g. BA 18, BA 19), as well as precentral regions (e.g. BA 4, BA6). Additionally, the precuneus and the declive of the cerebellum were activated, besides smaller areas in frontal and parietal locations.The specific effect condition activated frontal brain areas (e.g. BA 8, BA 45) and limbic regions (e.g. BA 32). In addition, some activation in the precentral (e.g. BA 6) and postcentral (e.g. BA 2) regions, the occipital (e.g. BA 19) area and parietal regions (e.g. BA 40) could be found. The activation of both hemispheres was balanced, with the left hemisphere showing more activation areas. For detailed figures consult Table 5.

main effects	**hemisphere/ region**	**Label**	**BA**	**x**	**y**	**z**	**t**	**voxel**
facial expression	R	Declive		44	-53	-22	3.441	68
	R	Occipital	19	44	-74	-6	3.308	12
	L	Occipital	19	-46	-74	-6	3.848	372
Decision	R	Precuneus	19	35	-71	33	3.825	160
	R	Precentral	6	32	-14	57	3.269	25
	R	Declive		23	-65	-22	3.589	57
	R	Pallidum		20	-5	-6	3.854	13
	R	Declive		11	-56	-12	3.452	45
	L	SFG	8	-1	16	51	4.175	1160
	R	Occipital	19	5	-77	33	3.401	33
	R	Occipital	18	2	-77	-6	3.752	1119
	L	Occipital	17	-1	-83	12	3.500	41
	L	MFG	6	-4	-8	54	3.371	43
	L	Occipital	17	-10	-89	-3	3.581	111
	L	Precuneus	7	-16	-80	45	3.248	161
	L	Declive		-22	-59	-12	3.343	16
	L	Declive		-31	-65	-15	3.513	22
	L	Insula	13	-34	19	6	3.390	216
	L	Precentral	4	-34	-23	48	3.726	202
	L	Precentral	6	-43	-14	66	3.835	906
	L	IFG	45	-46	19	9	3.337	13
	L	MFG	6	-55	7	42	3.542	188
	L	IPL	40	-59	-32	51	3.622	365
specific effects								
self-relevant face	R	STG	22	59	-47	15	3.331	10
	R	MFG	8	41	25	42	3.803	25
	R	Declive		35	-62	-12	3.267	18
	R	Declive		11	-62	-12	4.121	162
	R	Culmen		5	-53	-6	3.677	31

main effects	hemisphere/ region	Label	BA	x	y	z	t	voxel
self-relevant face	R	limbic/ACC	25	2	19	0	3.395	16
	L	Precuneus	7	-22	-50	48	3.511	22
	L	postcentral	2	-31	-20	33	3.787	194
	L	Fusiform	37	-34	-47	-12	3.519	25
	L	postcentral	3	-40	-20	51	3.477	45
other-relevant face	R	Precentral	6	44	1	36	3.393	14
	R	Culmen		41	-53	-22	3.670	163
	R	Occipital	18	38	-83	-9	3.580	58
	R	IPL	40	32	-50	39	3.335	29
	L	postcentral	3	-28	-32	48	3.563	44
	L	IPL	40	-31	-47	54	3.529	36
	L	Occipital	19	-46	-74	6	3.659	332
self-relevant decision	R	IFG	45	35	25	-3	3.323	58
	R	limbic/ACC	32	11	10	42	3.330	16
	R	limbic/ACC	32	11	25	33	3.200	11
	L	SFG	8	-1	16	51	4.487	2.513
	L	Occipital	18	-7	-86	-9	3.726	449
	L	Precuneus		-13	-80	45	3.280	34
	L	Caudatus		-13	4	9	3.434	18
	L	Precuneus		-19	-74	51	3.221	11
	L	IPL	40	-37	-56	42	4.123	1063
	L	IFG	47	-34	25	0	4.330	2995
	L	Frontal	10	-43	40	-3	3.307	19
	L	MFG	46	-52	25	24	3.592	301
	L	Precentral	6	-61	-2	39	3.820	462
other-relevant decision	R	Pallidum		20	-5	-6	3.501	12
	L	Occipital	18	-4	-71	3	3.449	71
	L	MFG	32	-7	13	45	3.709	152
	L	SPL	7	-40	-59	51	3.379	53
	L	IFG	45	-43	19	9	3.183	14

Table 5: Whole brain activation in men. P ≤ 0.005; 10 voxels, L = left; R = right; BA = Brodmann Area and coordinates (x,y,z); ACC = anterior cingulate cortex; IFG = inferior frontal gyrus; IPL = inferior parietal lobule; MFG = middle frontal gyrus; SFG = superior frontal gyrus; SPL = superior parietal lobule; STG = superior temporal gyrus

Furthermore, we compared the BOLD changes between women and men. The main condition *"face"* activated more brain areas in women, especially frontal areas, e.g. BA 10, BA 39 or BA 11. In men one single activation in the SPL could be observed (BA 7). *"Decision"* activated enhanced blood flow for women frontal (e.g. BA 8) and parietal (e.g. BA 41), for men frontal (e.g. BA 8) and postcentral (e.g. BA 3). Much different activation was shown for the specific effects. For women *"self-relevant face"* activated the Putamen, whereas in men predominantly occipital brain areas (e.g. BA 17, BA 18), as well as pre- and postcentral areas were activated. *"Other-relevant face"* activated BA 6 in women and frontal and parietal areas in men. The condition *"self-relevant decision"* enhanced the blood flow in female occipital (e.g. BA18) and limbic areas, in men, mostly frontal regions (BA9, for example) were registered. Finally, for *"other relevant decision"* women and men showed activation in the same frontal areas (e.g. BA 8, BA 9). For detailed results, see Table 6.

main effects	**hemisphere/ region**	**Label**	**BA**	**X**	**y**	**z**	**t**	**voxel**
facial expression (women vs. men)	R	MFG, temporal	39	44	-62	27	3.186	139
	R	MFG, temporal	39	47	-71	24	2.896	13
	R	MFG, temporal	39	38	-68	21	3.656	203
	R	MFG	10	41	49	-3	3.644	75
	R	MFG	10	35	58	9	3.560	57
	R	Putamen		23	-2	0	3.848	230
	L	IFG	7	-13	25	-13	3.875	71
	L	Limbic	31	-19	-47	21	3.188	322
	L	SFG	10	-22	58	0	3.159	52
	L	Putamen		-28	4	-9	3.566	36
	L	MFG	11	-31	52	-12	3.315	121
	L	MFG	10	-40	52	-3	3.684	158
	L	MFG	6	-49	13	51	3.799	174
	L	Temporal		-49	-17	0	3.102	20
	L	IPL	40	-61	-38	36	3.232	93
facial expression (men vs. women)	L	SPL	7	-28	-47	57	3.910	450
Decision (women vs. men)	L	Thalamus		-16	-8	12	3.689	29
	L	MFG	8	-49	19	42	3.479	33
	L	Temporal	41	-55	-23	9	3.858	63
Decision (men vs. women)	R	MFG	8	29	19	36	3.755	144

main effects	hemisphere/ region	Label	BA	X	y	z	t	voxel
decision (men vs. women)	R	MFG	9	23	34	24	3.897	177
	L	Postentral	3	-28	-32	57	3.388	15
	L	Postcentral	3	-34	-20	45	4.043	143
specific effects								
self-relevant face (women vs. men)	R	Putamen		26	-2	-3	3.418	51
self-relevant face (men vs. women)	R	STG	39	59	-56	28	3.983	58
	R	Postcentral	2	48	-35	63	3.353	16
	R	Limbic	28	17	-20	-18	3.584	11
	R	Putamen		14	13	-3	3.651	2.513
	R	Occipital	18	5	-95	-15	3.733	449
	L	Caudatus		-1	19	3	3.347	34
	L	Occipital	18	-7	-62	3	3.525	18
	L	Occipital	17	-10	-86	6	4.146	11
	L	Occipital	19	-16	-62	3	3.300	1063
	L	Precentral	6	-28	-14	66	3.812	2995
	L	Occipital	19	-28	-80	6	3.314	19
	L	MFG	9	-31	28	30	3.339	204
other-relevant face (women vs. men)	R	Precentral	6	38	-8	36	3.880	23
	R	Putamen		23	1	3	5.095	273
	L	MFG	6	-40	7	60	3.567	39
other-relevant face (men vs. women)	R	MFG	9	35	28	36	3.688	31
	L	SPL	7	-25	-47	57	4.257	481
self-relevant decision (women vs. men)	R	Occipital	18	32	-80	-3	3.504	34
	R	Occipital	17	17	-83	0	3.507	230
	L	Hypothalamus		-7	-5	-6	3.665	37
	L	Limbic	34	-22	-11	-15	3.291	21
	L	STG	22	-55	-2	0	3.603	10
self-relevant decision (men vs. women)	R	MFG	9	29	19	33	3.612	42
	R	SFG	10	23	46	27	3.293	15
	L	Precentral	4	-31	-29	48	3.725	83
other-relevant decision (women vs. men)	L	Cerebellum/ Culmen		-13	-32	-18	4.137	54
	L	MFG	8	-49	19	39	3.756	67

specific effects	hemisphere/ region	Label	BA	X	y	z	t	voxel
other-relevant decision (men vs. women)	R	MFG	9	62	22	30	3.327	34
	R	MFG	8	26	19	33	3.422	39
	R	Precuneus	20	-50	33	3.511	32	
	L	Occipital	19	-34	-62	9	3.649	98

Table 6: **Whole brain activation in women vs. men. P ≤ 0.005; 10 voxels, L = Left, R = Right; BA = Brodmann Area; SPL = Superior Parietal Lobule; SPF = Superior Frontal Gyrus; STG = superior temporal gyrus; ant. DMFC = Anterior Part of Dorsomedial Frontal Cortex; MFG = middle frontal gyrus**

4.3 Regional data

Based on the results from the whole brain analysis we defined 13 regions of interest (ROIs) that were strongly activated and highly representative for empathic reasoning. The ROIs that were most significant were the IFG (BA 45) and another part of the IFG (BA 47), the Insula (BA 13), the MFG (BA 6), another region of the MFG (BA 8) and the IPL (BA 40) in the left and the right hemisphere.

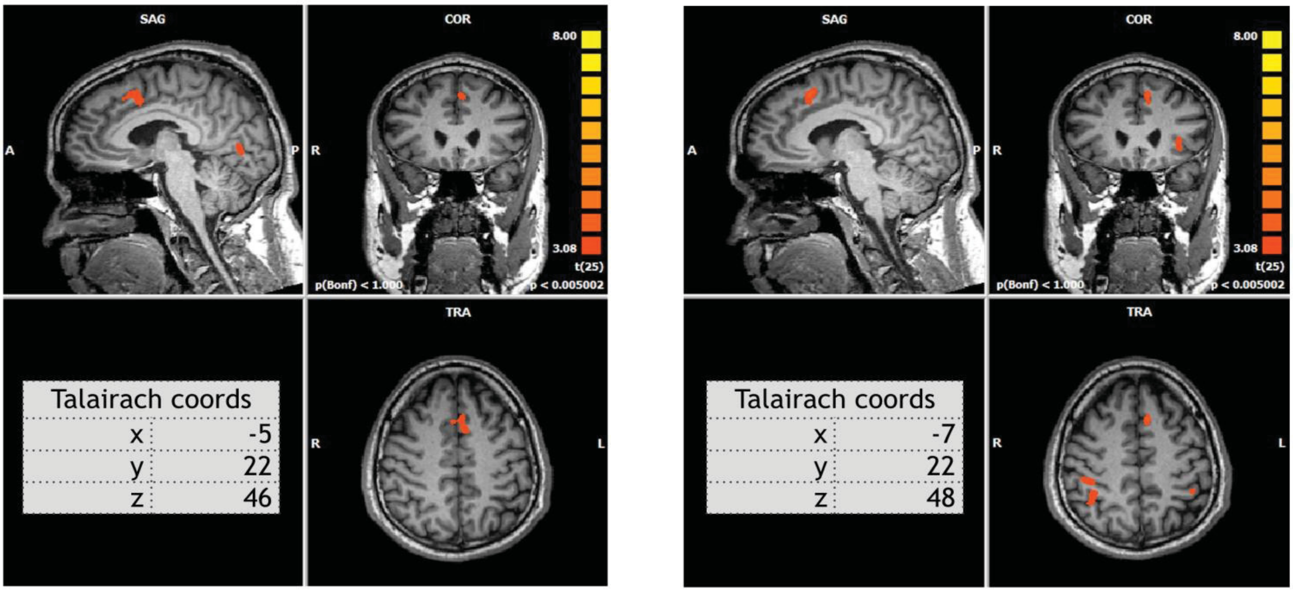


Figure 10: **Left figure: Localization of the activated left medial frontal gyrus (MFG, orange) as found during the condition "decision" in men. Right figure: Localization of the activated left medial frontal gyrus (MFG, orange) in women under the condition "decision". The significant voxels were color coded for each area. Sagittal plane (SAG, upper corner left), coronar plane (COR, upper corner right) and transversal plane (TRA, lower corner right). Corresponded Talairach coordinates are shown in milimeter (mm, lower corner left). Directions are given: A= anterior; P=posterior; R=right; L=left; probability (p) < 0.005**

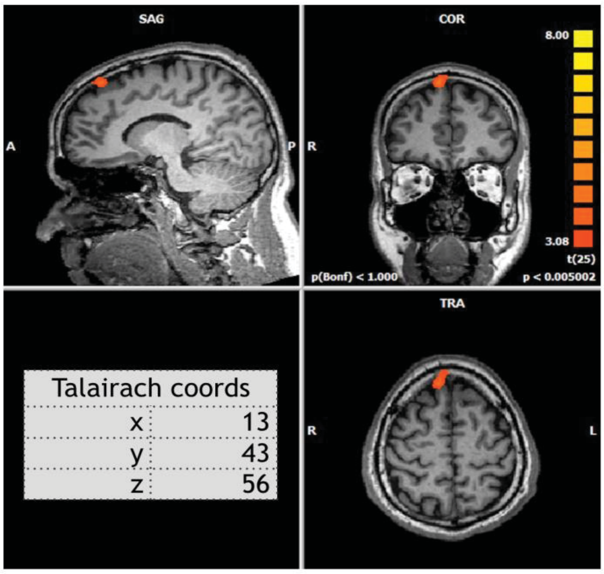


Figure 11: Localization of the activated right dorsomedial frontal cortex (DMFC, orange) as found during the condition “decision” in women vs. men. The significant voxels were color coded for each area. Sagittal plane (SAG, upper corner left), coronar plane (COR, upper corner right) and transversal plane (TRA, lower corner right). Corresponded Talairach coordinates are shown in milimeter (mm, lower corner left). Directions are given: A= anterior; P =posterior; R =right; L =left; probability (p) < 0.005

4.4 Correlation between behavioral and fMRI data

Using Spearman´s rho correlations no significant correlation of the behavioral data were found (Table 7). The correlation between the behavioral and the fMRI data was tested for the ERP, the DCERT and reaction time (RT) (Table 7). Here, significances were found solely for the male participants. The better the male participants succeeded in the DCERT (meaning emotion recognition) under the condition “other- relevant face” the greater was the activation of the MFG (BA 6). Better empathic reasoning (ERP) under the condition of “other-relevant decision” correlated with a strong activation of the MFG (BA 6). Also, the better the empathic reasoning (ERP) under the condition of “other-relevant face”, the higher the activation of the MFG (BA 8). Furthermore some correlations regarding the reaction time could be detected (Table 8). The faster the male participants under the condition of “other-relevant decision” reacted, the more activation was found in the MFG (BA 8). Also, the faster the reaction under the condition of “self-relevant decision” the more the IPL (BA 40) became activated.

	men		women	
	r	P	r	p
ERP/DCERT	0.431	0.142	0.270	0.396
SPF/ERP	0.168	0.601	0.297	0.297
SPF/DCERT	0.053	0.864	0.355	0.257
ERP/MITE	0.396	0.180	0.418	0.177

Table 7: Correlations of the behavioral data under various conditions for men and women. No significant differences detected. r = Spearman´s rho; p = probability (t-value/significance); DCERT- difficulty controlled emotion recognition test; ERP = empathic reasoning paradigm; MITE = mind in the eye tes; SPF = Saarbrückener Persönlichkeitsfragebogen

women			**Men**		
Condition	**r**	**p**	**condition**	**r**	**p**
	-	-	DCERT/MFG(BA6) other- rel. face	0.536	0.048
	-	-	ERP/MFG(BA6) other-rel. decision	0.602	0.029
	-	-	ERP/MFG(BA8 links) other-rel. face	0.573	0.041
	-	-	RT/MFG(BA8) other-rel. decision	0.635	0.015
	-	-	RT/IPL(BA40 rechts) Self-rel. decision	0.552	0.041

Table 8: Correlations of the behavioral data vs. fMRI-data for women and men. r = Spearman´s rho; p = probability (t-value/significance); DCERT = difficulty controlled emotion recognition test; MFG = middle frontal gyrus; ERP = empathic reasoning paradigm; IPL = inferior parietal lobule

5 Discussion

The discussion will be structured according to main results, methological aspects, limitations of the study and future perspectives.

5.1 Compared to men, women consider themselves more empathic in self-report questionnaires.

In accordance with our hypothesis the female participants scored significantly higher on the subcategory *empathy* in the SPF than the males. Women are said to show greater emotional and empathic abilities and rate themselves that way in corresponding questionnaires (Baron-Cohen and Wheelwright, 2004, Eisenberg and Miller, 1987, Rueckert and Naybar, 2008). "While women assume that it is expected to be more empathic as a female and thus are more likely to describe themselves according to this gender stereotype, men refrain from describing themselves as more emotional since this is not part of the ''typical'' male stereotype" (Derntl et al., 2010, p.79) "Due to the fact, that the assumption of women being more empathic mostly relies on these self- report questionnaires, the credibility of this thesis can be doubted and the question arises if the outcome of the questionnaires might just serve certain stereotypes. "Stereotypes are socially shared cognitive representations (e.g., knowledge, expectations) regarding social groups" (Niedlich et al., 2015, p.1439) and gender stereotypes or gender roles in particular are defined as "socially and culturally defined prescriptions and beliefs about the behavior and emotions of men and women" (Anselmi, 1998, p.195) Heilmann (2012) stated that agency and all concomitant character traits (e.g. independence, self-confidence) are rather masculine , whereas the traditional female stereotype has been described as "nice, but incompetent" (Niedlich et al., 2015, p.1439), attributing less agency to women, but rather "warm" character traits like compassion, empathy, communion or dependency (Tyler, 1965). Interestingly, the prejudices about women are not only shared by men, but women also underestimate female agency-competence and rather expect women to be more the nursing, clerical or service type (Goldberg, 1968). With these widely acknowledged gender stereotypes at hand, it makes sense, that women evaluate themselves more empathic than men, probably mostly on a preconscious, implicit level (Kiefer and Sekaquaptewa, 2007). This happens even if women do explicitly not approve of gender stereotyping. A further example of the strong influence of stereotypes becomes apparent in a study Krendl and colleagues (2008) conducted: Female participants had to complete a mathematical exam. In the control condition, they recruited brain areas associated with mathematics (e.g. angular gyrus), whereas, when reminded of stereotypes regarding women´s underperformance in this subject, they recruited brain areas related to emotional and social processing (ventral anterior cingulated cortex). So the participants acted according to their expected stereotype and recruited respective brain areas (Derntl et al., 2010). This phenomenon is known as the "stereotype threat" (Steele, 1995). It is to mention, that these stereotypes surely emerge from the traditional view of gender roles - "Home-makers vs. resource providers" (Mayor, 2015, p.3) - and these again influence the self-evaluating behavior of women and men. It becomes clear, that the stereotypes seem to have a great influence on the behavior regarding the self-reporting questionnaires on empathy.

5.2 Compared to men, women perform better in tasks requiring empathy like the Benton Facial Recognition Test, Mind in the Eye Test and facial affect recognition, show a clear advantage in the experience and expression of empathy and superior facial expression processing as well as emotion recognition.

The hypothesis is not entirely confirmed by the results of this study and women did not score higher than men. Rather, the BFRT measuring face recognition skills independent of emotion recognition showed a male superiority in the results (men: 48.2 and women: 47.7). It is to mention that this test is no tool for emotion recognition but face recognition. Also, in the ERP - the main task of the experiment requiring higher order empathic skills - men scored slightly higher than women. Thus it becomes clear that the proposed hypothesis is not supported by the results of the study. Several reasons explaining this phenomenon should be taken into consideration.

Reading facial expressions and nonverbal cues is essential for the development of close and intimate inter-human relationships (e.g. Nowicki, 1992). These skills are an important prerequisite for empathy which is constantly used in everyday human life and social interaction. Interestingly, psychiatric disorders that are defined by a lack of empathy like for example autism spectrum disease are more frequently diagnosed in men than in women (Chakrabarti and Baron-Cohen, 2006, Schulte-Ruther et al., 2008), which hints at the possibility of reduced empathic abilities in men in general.

Moreover, there are a number of studies that claim a female superiority in the sensitivity to social signals (e.g. Baron-Cohen and Wheelwright, 2004, Hoffmann, 2000, McClure, 2000). For example, McClure (2000) claims that women outperform men in reading facial expressions to label the observed person´s current emotion. In general it seems that women have better abilities to read these nonverbal or external cues (Hall and Matsumoto, 2004) and therefore perform better in identifying facial affect (Guntekin and Basar, 2007, Thayer and Johnsen, 2000). Some explanation for this female superiority, like traditional gender roles and stereotypes are only partly supported by our data as women outperformed men in the MITE and the DCERT, but not in the other two tests. In accordance with observations, there is growing research claiming that there is no relevant gender-difference in facial emotion recognition or at least doubts about the specificity and size of the female advantage in facial emotion recognition (Dimitrovsky et al., 1998, Grimshaw et al., 2004, Rahman et al., 2004). The suggestion is that the gender-difference rather affects the associated neural correlates (Derntl et al., 2010, Kemp et al., 2004, Lee et al., 2002). This allegation will be discussed later on, especially in hypothesis 6. So, there seems to be a female superiority in recognizing emotions from faces but "due to conflicting results it is still not clear if this is true for all emotions in all situations and all expressers" (McClure, 2000)

Besides facial affect recognition (tested with the BFRT and the MITE) and emotion recognition (tested with the DCERT) on the one hand, this study examined the gender-differences regarding the skills of empathic accuracy (EA) using the ERP on the other hand. EA describes the ability of an individual to "accurately infer what another person is thinking or feeling" (Ickes, 2000) and is describes as being an "important skill that affects people´s social adjustment in all phases of their life" (Goleman, 1995)

Therefore, it has to be discussed, why the given results do not show a clear female advantage in performing on these EA-tasks. Firstly, Nitschke and colleagues (2015) found that women´s empathic abilities decline under a stressful environmental setting, whereas male performance on empathic accuracy (EA) improves. In an experimental setting, participants had to undergo a baseline EA-test and 3 weeks later another test after exposure to the "Trier social stress test" with the results mentioned above. Since our empathic reasoning paradigm featured three stressors, limited amount of time for the button press (time pressure) and the possibility to fail during the test phase, as well as the factor of competition/rivalry (the final score in percent), there are several factors that create a stressful setting for completing the task. More importantly, the task had to be completed while lying in the MRI which creates a tight and uncomfortable as well as noisy environment. Another explanation for the results could be the already mentioned fact of the given "competition" or reward in terms of an as high as possible final score and therefore the motivation to outdo the other participants. After the test phase, the participants knew that they could reach a final score as high as 100%. This might have motivated the male subjects to put more effort in the given paradigm and hence produce a better outcome. Kristi Klein and Sarah Hodges (2001) created a setting in which empathic accuracy was rewarded with payments which resulted in a performance improvement of both sexes extinguishing any difference between the male and female performance. So the gender differences in EA rather seem to originate from different motivation than from a lack of male ability (Ickes, 2000). Likewise, this assumption is strongly corroborated by a quantitative meta-analysis by Ickes, Gesn and Graham (2000). They support the thesis of the "motivational interpretation" by Eisenberg and Lennon (1983) who argue that a female advantage in empathic accuracy can only be observed in tasks, where the participants are aware of the fact that their empathic skills are evaluated or "empathy-related gender-role expectations are made salient".

For a summary it can be stated, that there are several factors like for example stress or motivation, as well as traditional stereotypes that influence the participants` outcome on the different empathy- tasks. The hypothesis declaring a female advantage in this field of emotion recognition cannot be fully supported; it becomes rather obvious that men´s abilities regarding this field are underestimated.

5.3 Compared to men, women perform more accurately on and react faster to facial expressions related to a low degree of social impact (e.g. fear), whereas men are superior inferring affective states of high social impact (e.g. anger).

The accuracy and latency of recognizing emotions from especially an unknown person depends on the pertinence and the possible consequences for the observer´s wellbeing (Rohr et al., 2012). Emotions of high social impact (happiness and anger), that might need a fast reaction in order to protect oneself eventuate in faster and more accurate empathic reasoning than sadness and fear, which are considered to be emotions of low social impact (Prochnow et al., 2014b).The question to be discussed is, whether there is a gender-difference in recognizing emotions of high and low social impact. For the main part, this was tested with the DCERT and the ERP. Firstly, the overall-performance in the DCERT was superior to the performance in the ERP and always above the level of chance (25%). The reason for this might be the more challenging assignment in the ERP that combined explicit facial affect recognition with implicit emotion attribution (Prochnow et al., 2014b). Furthermore, this is aggravated by the fact that the participants did not only have to judge "static" facial expressions, but the faces morphed into a certain expression. The DCERT on the one hand was completely dominated by women, presenting superior performance in all relevant categories (total, happiness, anger, fear and sadness) and confirming the already discussed fact, that women outperform men in reading facial expressions (Baron-Cohen and Wheelwright, 2004, McClure, 2000). It has to be mentioned, however, that the difference in the performance for happy and angry faces was vanishingly low (w: 100% vs. m: 99.1% for happiness and w: 97.9% vs. m: 97.3% for anger). A more distinct advance could be observed for the emotions sadness (w: 94.6% vs. m: 91.9%) and fear (w: 63.3% vs. m: 60.5%). So although there is an overall female dominance in this test, there is a perceptible tendency, showing that men perform better on the emotions of high social impact than the one´s of low social impact. It has to be mentioned, that the results did not show any significant differences, the differences were of the descriptive type. In addition, fear was the emotion that was recognized least by both sexes in both paradigms (DCERT and ERP) highlighting again its low social impact.

Interestingly, the ERP on the other hand showed different results. To start, "anger" resulted in the longest reaction time for women and men, which seems to be counterintuitive since a rapid reaction would be mandatory for defense or fleeing. These results might indicate the relevance of the right assignment since wrong judgment could have fatal consequences. "Fear", on the other hand, was indeed the most falsely assigned emotion, but needed the shortest reaction time, probably because a wrong assignment would not lead to any consequences for the observer. For all the other emotions no stark differences could be detected.

The total performance was dominated by the male participants (m: 75.8% vs. w: 72.8%). Furthermore men performed better on detecting angry faces (m: 71.1% vs. w: 59.6%) and fearful faces (m: 60.1% vs. w: 50.1%). No significances came to light, but for the angry faces a Cohen´s d of 0.5, pointing out a medium strong tendency towards the male performance, could be detected. Consequently, a female superiority was shown for happy facial expressions (w: 97.0% vs. m: 93.3%) and sad facial expressions (w: 83.7% vs. m: 78.0%). Here, a Cohen´s d of 0.6 for happiness came to light, showing a medium strong tendency towards the female performance. Obviously, the hypothesis cannot be confirmed for the ERP. One reason for this could be the already mentioned higher requirements compared to the DCERT including not only the mere labeling of the emotion but also the inferring of the reason for the presented emotion. Taking an evolutionary point of view into account, where women used to be the care-givers and house-keepers and men were in charge for protection and food-supply, the outcome of the ERP does make sense. For one thing, it would be of advantage for women to recognize emotions generally well, but especially happy facial expressions, so they know that everything is in order with the family and sad facial expressions as an indicator for a thirsty baby or a troubled offspring. For men, for the other thing, correctly detecting angry facial expressions was essential in order to protect their family and housing from external threat (Forni-Santos and Osorio, 2015, Kret and De Gelder, 2012). But also the knowledge of your competitor being fearful could be an advantage in former times, but also today, for instance when competing for a certain job position or in an argument. Being aware of the counterpart being intimidated makes one more confident and therefore more convincing. Another interesting point about the results is given by the standard deviation for accuracy in the ERP regarding the emotions anger and especially fear for women and men alike. There seem to be big individual differences in the performances on empathic reasoning for these emotions. There are some studies that claim that women are better in decoding negative facial expressions than men including anger, which women decoded at lower emotional saturation levels (Miura, 1993, Montagne et al., 2005). Contrary to this, Forni-Santos and colleagues conducted a systematic review on the influence of gender on the recognition of facial expressions of the six basic emotions (happiness, sadness, disgust, anger, surprise, and fear). They claimed that no definite conclusions concerning the observer´s gender of the recognition of a certain emotion could be drawn mostly because of different approaches of the different studies and small sample sizes. Concerning accuracy, they found an overall female superiority for recognizing all 6 emotions "as a set", but there was almost no gender-difference for the recognition of happiness. It is to assume that here the ceiling effect comes to be effective. The recognition of the other emotions showed more inconsistency including anger and sadness (Forni-Santos and Osorio, 2015). These findings are in large parts supported by the results of this study. To sum it up, our results show no clear gender-related pattern regarding an advantage of the recognition of certain emotions. In fact, it seems that the superiority of the recognition of certain emotions rather depends on the paradigm and the motivation taking different theories (e.g. evolutionary based ones) into account.

5.4 Emotion processing involves lateralization of brain functions to the right hemisphere.

Hypothesis 4 is based on current literature arguing for gender-specific differences in lateralization of empathic reasoning processing (e.g. Killgore and Yurgelun-Todd, 2001, Kret and De Gelder, 2012, Rueckert and Naybar, 2008). Lateralization describes the phenomenon that certain brain functions (like for example language) are more dominantly represented in one hemisphere than in the other. The statement by Kret and colleagues (2012) and also corroborated by several other authors claiming that "some studies suggest that hemispheric cerebral activation differences in emotion processing are sex dependent" will be evaluated in the following section and it will be demonstrated if there are any hints of this proposition in our research.

There are several studies discussing this topic with deviant results. For example, lateralization differences in women and men were shown for facial perception (Women lateralize to the left and men to the right) (Njemanze, 2004, Njemanze, 2007). Furthermore, in a lesion study by Tanel and colleagues (2005) patients with VMPC- damage and their emotion processing was investigated. Men showed decreased emotion processing abilities when the lesions were located in the right VMPC whereas for women the opposite applied. On the other hand, Agcaoglu and colleagues (2015) found no gender differences in lateralization; neither did Nielsen and colleagues (2013). The inconsistency of the results is corroborated by a meta-analysis by Wager et al. (2003) pointing out that there is no overall right hemispheric lateralization for emotion processing and that the lateralization of emotion processing is more complicated and region specific than assumed. There is research claiming that both hemispheres are involved in emotion processing but that there are certain areas that are specialized in specific emotions and that here a gender-specific effect can be observed (Wager et al., 2003). For example, Cahill and colleagues showed a clear gender- related lateralization for the Amygdala for emotion processing (Cahill et al., 2001, Killgore and Yurgelun-Todd, 2001) and similar findings apply to the Hippocampus (Frings et al., 2006). Since neither of these regions were used in terms of a region of interest by our participants, we cannot discuss this statement with our data.

Interestingly, this study revealed a dominance of the LH during the empathic reasoning paradigm for men and women alike, as well as under the condition of men vs. women. Both activated the LH all over the paradigm more often than the RH . This does not support the findings described above stating a RH-dominance for empathy processing. These results undermine the statement by Wager et al. (2003) that apparently there is no clear right and left hemispheric dominance for emotion processing or facial recognition and that the gender-effect in lateralization is hard to define, too. Examining the conditions separately, women and men drew on both hemispheres alike. Only regarding the "specific effects" an interesting observation was made. Women only used the LH, whereas men also used the RH for the empathic processing. This does not go in line with the findings of Bourne and colleagues (2005). They proposed that women's activation patterns during facial recognition tasks are more bilaterally spread and therefore have better access to different neuronal brain networks in each hemisphere due to more efficient interhemispheric communication (Bourne, 2005). In the same study, a stronger right-hemispheric lateralization for men was shown and it was concluded that generally, men are more strongly lateralized than females (see also Inglis and Lawson, 1981, McGlone, 1978). Under this condition, however, men seem to be more bilaterally spread. Our results hint at the fact that women and men both seem to draw on both hemispheres alike. One reason for the predominant use of the LH in our paradigm might be the fact that the task was perceived as a more cognitive one by the participants may it be implicit or explicit. As explained above, the LH is mainly used for cognitive processes so maybe the participants (especially men) had to draw on cognitive resources for a correct decoding of the emotional facial expressions. As already discussed in preceding hypotheses it might be because of evolutionary reasons that certain emotions are easier recognized by females or the other way around (e.g. Forni-Santos and Osorio, 2015, Kret and De Gelder, 2012) and that the emotions that are harder to decode for men (e.g. sadness) need the involvement of additive cognitive resources. The bilateral activation, thus the recruiting of more cognitive areas in the male brains could hint at the fact that the task was more demanding for men in general. Furthermore, since the menu of choice consisted of four written sentences, the use of the language-dominant hemisphere does make sense in this context and may explain the deviating results to our study from 2013 claiming a dominant use of the RH when it comes to decoding emotional expressions. In this study "only" the observing of the morphing facial expressions and a button press was needed. There was no forced choice menu including the mentioned four written sentences. (Prochnow et al., 2013)

There was no stark gender-difference to be observed in our study when it comes to lateralization while empathic reasoning which hinted at the fact that both genders used similar resources or strategies (especially regarding lateralization) for empathic reasoning and this coincided with some recent meta-analyses (e.g. Wager et al., 2003).

5.5 Men and women share important nodes of the empathy network such as the anterior Insula, the Amygdala and the IFG (BA 44/45).

In the study some brain activations overlapped between men and women but in processing the main condition “facial expression” women and men did not rely on the same brain regions. Thus, they seemed to have different approaches to recognizing emotional faces, whereas under the main condition “decision” both sexes activated the IFG and the IPL, which harbour the hMNS and represent emotion recognition and emotional contagion (Shamay-Tsoory et al., 2009). Also, the premotor cortex was activated which is said to be involved in planning movement and understanding the action of others (Churchland et al., 2006, di Pellegrino et al., 1992). The activation of the premotor cortex related to the required button press- the motor action that was not excluded in our data analysis and therefore might have an influence on the activated brain areas. Another common field activated under the condition of “decision” is the MFG/DMFC which represents the affective aspect of theory of mind (Shamay-Tsoory et al., 2009) and might be an indicator for the personal relevance of the choice. It is important to mention that the brain areas for empathic reasoning generally activated by women and men are mostly the same, but it seemed to be dependent on the condition when they were being used and this differed between sexes. As already discussed earlier, most of these areas are representatives of the empathy network and used for affect reading as for example proved by Prochnow and colleagues (2013). Processing the emotional stimulus “self-relevant face” does not reveal any similar activation under the stimulus “other-relevant face” the precentral area shows enhanced blood flow in both sexes. For the specific effects (“self-relevant-decision” and “other-relevant-decision”) women and men activate the IFG and the MFG, thus one area representing the emotional and the other the cognitive aspect of empathy. There was much more activation to be observed under the condition of “self-relevant decision” for men: IFG, IPL, limbic areas, MFG and others. The functions have been explained above and apparently the recruitment is needed here for the male participants. This could be for the already mentioned motivational purposes, since self-relevant decision might have an impact for the observer eventually. This is corroborated by the fact that less activation patterns were found under the condition of "other-relevant decision" for men, whereas women recruited approximately the same amount of brain areas for both conditions.

There are many studies investigating the neural networks supporting empathy, empathic processing and related concepts (e.g. Bernhardt and Singer, 2012, Engen and Singer, 2013, Kampe et al., 2003, Shamay-Tsoory, 2011) Interestingly, studies that handle the topic of gender and empathy-related networks mainly demonstrate gender-differences in the recruitment of brain areas related to empathy (e.g. Derntl et al., 2010, Kemp et al., 2004, Rueckert and Naybar, 2008, Schulte-Ruther et al., 2008). Therefore the conclusion, that there are gender- specific, different strategies for empathic reasoning is not far to seek and that different conditions seem to be differently assessed. Women and men had recourse to the same regions that represent different kinds of empathy, but they mostly used them under different conditions. Furthermore, the empathic performance or outcome did not seem to be affected by the differing strategies, since, as mentioned above, there was no evidence for clear superiority for women or men in empathic reasoning.

5.6 Men and women recruit different neural networks supporting different components of empathy, i.e. women rely on brain areas representing emotional empathy (e.g. IFG), whereas men draw on rather cognitive-related ToM areas (e.g. MPFC).

We expected that women undergoing an empathy-related task used brain areas that represent emotional empathy (e.g. IFG), whereas men rather rely on areas representing cognitive-related empathy (e.g. MPFC). (Derntl et al., 2010, Koch et al., 2007, Schulte-Ruther et al., 2008)

Schulte-Ruther and colleagues (2008) claim that the female outperformance regarding empathy is based on their recruitment of the hMNS areas and that men rather rely on the TOM-related areas, thus approaching their own emotions and the respond to other´s emotions in a more cognitive way. As already pointed out in the proceeding hypotheses, we couldn´t detect a clear advantage regarding empathic behavior in women. Furthermore, our results do not reveal a clear separation of the use of areas of emotional empathy in women and areas of cognitive empathy in men. It seems like women and men – depending on the paradigm- use the areas alike, which will be analyzed in greater detail in the following hypothesis using our study´s results.

During the processing of the emotional stimulus “facial expression” which represented one of the main conditions, men mainly used the occipital brain area representing the visual pathway and women relied on temporal brain areas as well as the fusiform face area (FFA) which is used for recognizing faces. No further empathic processing seemed to be required here, since no further brain areas regarding empathic processing were activated. The main effect “Decision” recruited empathy related areas in women and men alike, but both used emotional empathy areas (IPL, IFG) as well as cognitive related areas (DMFC, MFG). The DMFC especially is used for early recognition of emotional gestures or expressions (Prochnow et al., 2013); our results showed that this area was used by women and men alike. Lee and colleagues (2005) found that men constantly recruit the Insula during emotion recognition, which can be supported by our data. However, it has to be mentioned that in our paradigm they recruited the left Insula. In contrast, Lee and all (2005) claim, that especially the right Insula is recruited. But as already discussed before, the lateralization processes in our study did not match with the findings of other researchers. While processing the emotional stimulus “self-relevant face” on the one hand some empathy related areas (MFG,ACC) were activated by men, women on the other hand did not recruit any empathy related areas at all, whereas the operation of the stimulus “other relevant face” on the contrary reveals the opposite, meaning only women recruiting empathy related areas (ACC, limbic areas). It seems like for the recognition of the emotions happiness and anger men needed to rely on emotional as well as cognitive related empathy areas, whereas women did not need this cognitive support. The opposite applies for the emotions of sadness and fear. There are several studies claiming that women and men use different brain areas when processing happy and sad emotions (Canli et al., 2002, Lee et al., 2005), which can be confirmed by our data. For the specific effects (“self-relevant decision” and “other-relevant decision”) women and men recruit emotional and cognitive empathic brain areas alike, only for the condition “self-relevant decision” men recruit clearly more areas than women. In general it was observed that brain areas related to emotional empathy came to assistance much more frequently than brain areas related to cognitive empathy while performing the ERP. Maybe the need for a fast decision (limited time in the paradigm) was one reason for “only” recruiting emotional empathy areas and that there was no time for the use of areas related to higher order empathy (TOM-related areas). Another aspect could be the assumption that there was scarcely the need to bring in TOM-related areas, maybe because of the repetitive character of the paradigm and that only special conditions (see above) required this recruitment. All in all we cannot prove a distinct pattern regarding a clear distribution of the recruitment of certain brain areas as e.g. claimed by Derntl and colleagues (Derntl et al., 2010)

6 Limitations

The sample size of our study was relatively small, which is not an uncommon phenomenon in fMRI studies taking into account, that the inclusion and exclusion criteria were very stringent. Thus, our study can only be considered as explorative. Also, the drop-out rate was comparatively high due to e.g. artefacts during the scanning process (see also Prochnow et al., 2014b). Compared to other studies investigating similar topics, the sample size of 26 participants was nevertheless average and for the coverage of the study (behavioral and functional data) sufficient (e.g. Derntl et al., 2010, Schulte-Ruther et al., 2008). Furthermore it should not go unmentioned, that we tried to compensated the small sample size by "[using] a high number of repetitions per condition in order to ensure sufficient experimental power of the fMRI data" (Prochnow et al., 2014b, p.6-7). Also, we would like to comment on the fact that the depersonalized expressions (the pictures appeared blurry due to the fact that they were "built" through the superimposement of many photographs) (see Lundqvist, 1998b) might present a certain ambiguousness and therefore have a negative impact on the empathic reasoning performance regarding the right labelling of the emotion as well as the activation of the areas comprising the hMNs (e.g. IFG). This might have been a particular challenge for the participating men, which could explain the frequent activation of the occipital areas. Taking a look at the results of this study, it becomes clear that there were several activations of the IFG during the trial, so apparently the blurry images of the ERP did not impair the empathic behavior severely. In addition, we tested prerequisites of empathic reasoning with four questionnaires that approach the topic of empathy from different angles (BFRT, MITE, TAS-20 and SPF) including self-reporting, as well as facial affect recognition and reading emotions from isolated pairs of eyes. Furthermore, we tested facial affect recognition with the DCERT covering all 6 basic emotions. The repeated use of the same faces for the four emotions might be a point of criticism since that might have led to repetitively wrong answers and thus deteriorate the outcome. As already mentioned in hypothesis 5 and 6 the ERP is a very challenging trial that requires a certain level of cognitive abilities and concentration. It could be queried, that the high cognitive load might have comprised the empathic reasoning abilities. However, several authors claim that a demanding cognitive task does not impair empathic reasoning performances (Schneider et al., 2012).

A possible "technical" limitation of the trial that has to be mentioned is the handling of the respond grips, meaning that under the time limitation and stress simply the wrong respond button was being chosen. The correct handling of the respond grips was practised in the test trial to avoid this constraint and if the handling was not done correctly, it led to an exclusion of the participant. It could be criticised that the forced choice answering menu influenced the outcome of the study since the results might have been worse if participants had to "freely" associate the emotions. A forced choice menu was a prerequisite for the following analysis, freely associating the emotions would have imposed a challenge to analyse. Unfortunately, the paradigm did not grant the possibility to analyse if there were any gender-differences in accurately recognizing the gender of the face presenting the emotion. Furthermore, regarding the data analysis it would have been interesting to conduct a more specific investigation of the wrong answers in order of the type of mistake to exclude perseverance. These two aspects might be interesting to investigate further in future research. Finally the topic of gender differences and empathy provides so much possibility of discussion and aspects that can be taken into account, that only a few of these aspects were approached in this disputation. For example the question of how education influences empathic behaviour is also interesting to take into account and might be of interest for further research. This reveals the depth and importance of the topic and that further research is worth to be conducted.

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10 Appendix

Appendix 1: Results of the behavioural data for women and men

Appendix 2: Anleitung zur Teilnahme an der fMRT-Studie

Appendix 1

		n	women mean/(SD)/*range*	n	men mean/(SD)/*range*	p
Age		12	**41.17** (13.91) *23.00-61.00*	14	**35.76** (10.04) *22.00-54.00*	0.264
Education		12	**13.92** (02.97) *10.00-17.00*	14	**13.86** (03.06) *10.00-17.00*	0.960
Handedness		12	**94.49** (08.15) *83.00-100.00*	14	**82.99** (11.00) *69.00-100.00*	0.265
BDI		12	**03.25** (03.82) *00.00-09.00*	14	**01.93** (02.53) *00.00-07.00*	0.302
TAS-20		12	**38.42** (06.68) *31.00-50.00*	14	**39.71** (09.53) *21.00-50.00*	0.696
SPF	**-empathy**	12	**15.92** (02.50) *11.00-20.00*	13	**14.08** (01.71) *34.00-50.00*	0.041
	-fantasy		**15.17** (02.29) *11.00-19.00*		**13.77** (02.05) *10.00-17.00*	0.121
	-pers. taking		**15.92** (02.84) *11.00-19.00*		**15.62** (01.98) *12.00-20.00*	0.760
	-total		**44.75** (07.24) *34.00-53.00*		**43.46** (04.20) *34.00-50.00*	0.588
		n	**mean**/(SD)/*range*	**n**	**mean**/(SD)/*range*	**p**

		n	mean/(SD)/*range*	n	mean/(SD)/*range*	p
BFRT		12	**47.67** (02.61) *44.00-54.00*	14	**48.21** (02.58) *45.00-53.00*	0.596
		n	**mean**/(SD)/*range*	**n**	**mean**/(SD)/*range*	**p**
MITE		12	**82.27** (09.43) *70.80-100.00*	14	**79.06** (10.76) *58.00-96.00*	0.432
	-happiness		**100.00** (00.00) *100.00-100.00*		**99.07** (03.48) *87.00-100.00*	0.365
	-anger		**97.92** (07.22) *75.00-100.00*		**97.29** (07.29) *75.00-100.00*	0.827
	-sadness		**94.58** (06.69) *87.00-100.00*		**91.86** (23.46) *12.00-100.00*	0.701
DCERT	**-disgust**	12	**93.67** (10.03) *75.00-100.00*	14	**90.00** (12.31) *62.00-100.00*	0.418
	-surprise		**93.58** (08.56) *75.00-100.00*		**95.57** (10.23) *64.00-100.00*	0.600
	-fear		**63.33** (28.90) *00.00-100.00*		**60.50** (34.69) *00.00-100.00*	0.825
	-total		**90.00** (05.08) *79.00-97.00*		**89.07** (09.36) *64.00-100.00*	0.762

Note: Results of the behavioral data for women and men, showing the number of participants (n) mean results and the corresponding standard deviation (SD), as well as the range and probability (p). Presenting results for the categories of age, education, handedness, BDI= Beck´s depression inventory, BFRT= Benton Facial Recognition Test, DCERT= difficulty controlled emotion recognition test, MITE= Mind in the eye test, SPF= Saarbrückener Persönlichkeits Fragebogen and TAS-20= Toronto alexithymia scale 20;

Appendix 2

Anleitung zur Teilnahme an der fMRT-Studie

Liebe/r Patient/in,
lieber Proband/in,

herzlichen Dank für die Bereitschaft an dieser wissenschaftlichen fMRT-Studie teilzunehmen.

Es ist für das Gelingen der Studie wichtig, dass Sie diese Information genau lesen.

Während Sie gleich im MRT liegen, werden Ihnen entweder Bilder von Gesichtern oder grauen Mustern präsentiert. Bitte schauen sie sich die Bilder genau an und stellen Sie sich bei den Gesichtern vor, dass Ihnen diese Person im Alltag begegnet.

Auf jedes Gesicht folgen 4 Sätze, die jeweils Ereignisse beschreiben, die der Person passiert sein könnten.

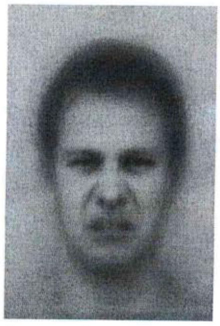
Wählen Sie bitte durch Drücken der entsprechenden Taste den Satz aus, der Ihrer Meinung nach am Besten auf die Person zutrifft. Orientieren Sie sich bei Ihrer Einschätzung nicht an sich selbst, sondern daran was der Person auf dem Bild passiert sein könnte.

Haben Sie ein graues Muster gesehen, lesen Sie bitte die Sätze und drücken Sie die jeweilige Taste, an deren Stelle der Satz "Die Taste drücken" steht.

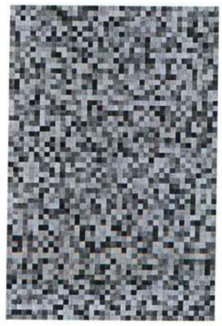
Bilder und Sätze können sich mehrfach wiederholen, dies ist von uns beabsichtigt. Bei beiden Aufgaben kommt es darauf an, möglichst den am Besten passendsten Satz zu finden. Dennoch wird auch Ihre Reaktionsgeschwindigkeit erfasst und nach einigen Sekunden geht es automatisch weiter. Dies ist nicht weiter schlimm.

Bevor die eigentliche Messung startet, machen Sie ein kleines Training, um mit der Aufgabe vertraut zu werden. Sollten danach noch Fragen offen sein, zögern Sie bitte nicht den Untersucher anzusprechen. Er kann Sie über die Sprechanlage hören.

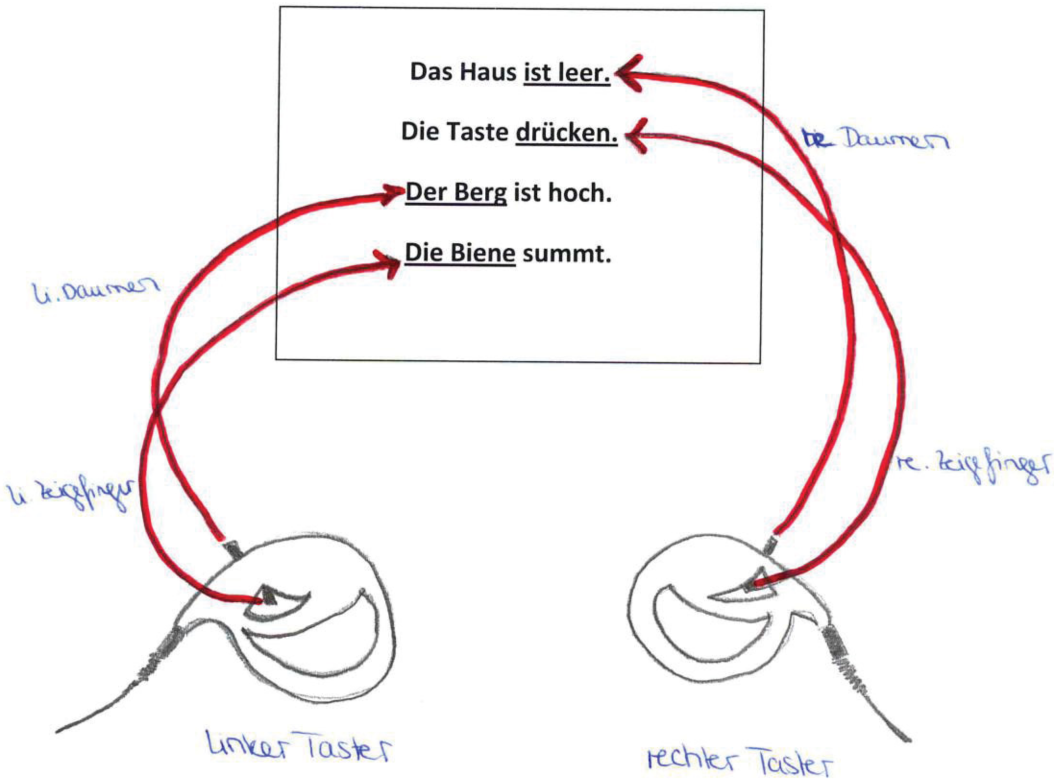
<u>Beispiel für den Umgang mit den im MRT verwendeten Antworttasten</u>



Beispiel für ein Gesicht



Beispiel für ein graues Muster



<u>Fragebogen für Probanden</u>

<u>Generelle Informationen:</u>

Name:

Alter:

Gewicht:

Kontaktnummer:

<u>Fragen zu Einschlusskriterien für die Studie:</u>

1) Hatten Sie schon einmal eine Kernspintomographie (Ja / Nein)?

2) Für Frauen: Besteht die Möglichkeit einer Schwangerschaft (Ja / Nein)?

3) Für Frauen: Verhüten Sie mit der Spirale (Ja / Nein)?

4) Leiden Sie unter Platzangst (Ja / Nein)?

5) Befinden Sie sich aktuell in einer emotionalen Ausnahmesituation (Ja / Nein)?

6) Sind Sie Rechtshänder, d.h. benutzen Sie bei den meisten Tätigkeiten bevorzugt die rechte Hand (z.B. Zähne putzen, schreiben, zeichnen, einen Ball werfen,...) (Ja / Nein)?

7) Sind Sie als Linkshänder geboren und wurden auf rechts umgelernt (Ja / Nein)?

8) Ist Deutsch Ihre Muttersprache bzw. sind Sie mit der deutschen Sprache aufgewachsen (Ja / Nein)?

9) Leiden Sie an neurologischen oder seelischen Erkrankungen (Ja / Nein)?

10) Nehmen Sie Medikamente ein? Falls ja, welche?

11) Benötigen Sie eine Sehhilfe? Bitte angeben welcher Art (Brille / Kontaktlinsen) und welche Stärke.

12) Tragen Sie Piercings oder sind Sie tätowiert?

13) Haben Sie Metalle im Körper (z.B. Implantate, Aneurysmenclips, Schrauben, Herzschrittmacher,...)? Falls ja, welcher Art, in welchem Körperteil und wann wurden diese etwa eingesetzt?

Danksagung

Für die Unterstützung folgender Personen möchte ich mich herzlich Bedanken.

Prof. Dr. Rüdiger J. Seitz

Dr. Denise Potthoff

Dr. Katharina Koch

Herr Sascha Brunheim

Frau Erika Rädisch

Frau Kimberly Steinhäuser

Herr Julian Reale