

***Master Thesis Neuroscience and Cognition***

# **The role of self-agency and facial mimicry in normal human empathy**

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## **- Preface -**

Although this is my master's thesis, and I have had about 5 years to exercise writing on an academic level, it remains difficult to write a master thesis all on your own. Therefore I would like to thank my supervisor at Utrecht University, Kirsten Ruys, who has supported me and gave helpful comments during my writing process and has helped me to improve my thesis.

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Erlen Bruls, March 2010

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## **-Abstract-**

Philosophers in early human history already noticed that we humans are able to empathize, as the term for this phenomenon roots in ancient Greek. Although the existence of empathy has been noticed long ago, it is only recently that scientific researchers have become interested in this phenomenon. Reason for this is not the lack of interest but because it is difficult to investigate this phenomenon. Many factors seem to be contributing to our empathic ability.

Two of these factors that have been found important for experiencing empathic feelings on a normal level, are a sense of self-agency and facial mimicry. Psychiatric disorders with a distortion in empathy have often been related to a deficiency in self-agency (Autistic Spectrum Disorders, Alexithymia, schizophrenia/schizotypy, social phobia/Social Anxiety Disorder) or facial mimicry (Autistic Spectrum Disorders). In this thesis the importance of self-agency and facial mimicry for normal empathy was determined. This was done by investigating whether a deficiency in empathy could be related to a deficiency in the sense of self-agency or facial mimicry.

The studies discussed in this thesis provide evidence that both self-agency and facial mimicry are important factors contributing to the empathic ability. The deficiency in empathy of individuals with psychiatric disorders was found to be related to deficiencies in facial mimicry and/or to deficiencies in a sense of self-agency

# **Chapter 1 Introduction to empathy, self-agency and facial mimicry**

## **Empathy and the shared representation theory**

Philosophers in early human history already noticed that we humans are able to empathize. The term for this phenomenon roots in ancient Greek—from *empathia* (passion), which is composed of “en” (in) and “pathos” (feeling) (Singer and Lamm, 2009). Although the existence of empathy has been noticed long ago, it is only recently that scientific researchers have become interested in this phenomenon. Reason for the lack of previous attention to this phenomenon is not due to the lack of interest, but because empathy has been difficult to investigate properly and it still is. Even the description of empathy varies across different scientific papers, because its hard to capture the true essence of empathy. However what is quite clear from all these different definitions, is that empathy is about “feeling what another feels”. What is still not clear in recent literature is whether empathy is the result of imagining how the subject itself would feel like in similar situation (self-perspective taking) or imagining how the other feels like (other-perspective taking).

Many research papers investigating empathy, start with giving different definitions of the phenomenon empathy. I will not discuss all these definitions of empathy again. I will take one of the recent definitions for empathy and when I use the term empathy in this thesis it refers back to that definition. The definition of empathy, I will use is given by Singer and Lamm (2009) in their recent paper, and states the following: “empathy occurs when an observer perceives or imagines someone else’s (i.e., the target’s) affect and this triggers a response such that the observer partially feels what the target is feeling”. Thus when the subject perceives another’s emotion, the observer empathizes automatically. It seems that detection of the other’s emotion (via facial expression), changes the observers brain and bodily state to that of the target, causing the observer to share the emotion of the target.

Evidence for this automaticity has indeed been found (Carr et al., 2003]. This automatic sharing is a bottom-up approach where perceptual input is followed by automatic sharing of emotions. However that this sharing goes automatically, does not mean that the individual has no further influence on what he or she is feeling after this automatic process. Top-down regulation, from brain areas involved in

executive functions, make it possible to regulate the extent of the emotional sharing (Singer et al., 2004).

There are several theories that explain how the observer is able to empathize with the target. There is a theory, that of embodied emotion, which states that we empathize by activating brain networks, that were made after we had a similar experience as the target in the past. (Niedenthal et al., 2007). This was one of the theories that already existed before research was done on the neurobiology of empathy. Another theory, the shared representation theory, is based on more recent findings of studies investigating the neurobiology of empathy (Decety and Jackson, 2006; de Vignemont and Singer, 2006; Singer and Lamm, 2009). The shared representation theory states that the observer mentally simulates the target when it takes the target's perspective. So when you empathize with someone, your brain simulates the activations of the other person's brain. This is possible because we all share the same autonomic nervous (and motoric) system. [Decety and Jackson, 2006]. The shared representation theory differs from the embodied emotion theory, as regards to whether an experience of the same emotion in the past, is necessary to feel what the other is feeling. This seems to be important in the embodied emotion theory, but whether this is also important in the shared representation theory is not discussed explicitly in the literature. Because in this thesis I will focus on the neurobiology of empathy, I shall discuss the role of self-agency and facial mimicry from the theory of shared representation point of view.

### **When do we empathize: measuring empathy**

Batson (2008) states there are two different ways to perceive the other's situation:

1) you can imagine how another person sees his or her situation and feels as a result (imagine-other perspective) or,

2) you can imagine how you would see the situation were you in the other person's position and how you would feel as a result (imagine-self perspective).

According to Batson's analysis it is important to make a distinction between other- and self-perspective taking, as only the other-perspective will evoke empathic concern in the observer, while the self-perspective can lead to personal distress and will not evoke empathic concern. Empathic concern is thought to be related to altruistic behaviour [Rameson and Lieberman, 2009], or in simpler words helping someone in need. Taking the self perspective, and the accompanying personal

distress would probably not invoke this empathic concern and helping behaviour. In this thesis I will take Batson's view on empathy. Only when the other's perspective is taken empathy is possible, and both self-experience of an emotion as taking the self-perspective when observing another's emotion can be seen as control situations, where true empathy is absent.

Studies investigating empathy have also used both self-experience of an emotion as self-perspective taking as a control situation. Although some studies do use the self versus the other perspective to investigate empathy, others do not make this distinction. A reason for this could be that recent studies investigating empathy and its base in the brain, have used one emotion frequently : pain [Jackson et al., 2005; Jackson et al., 2006; Bufalari et al., 2007; Lamm et al., 2007; Danziger et al., 2009]. These studies do not always explicitly take these two perspectives into account. Using the emotion pain, does not necessarily require the experimenters to make this distinction in the observer's perspective because the self-experience of emotions is used as the control situation. So the control situation is when the subjects feel the pain themselves and the experimental situation is when the subjects watches another experience pain and then the perspective the observer takes is not mentioned (Bufalari et al., 2007; Singer et al., 2004).

Studies that do take in account these different perspective, take the self-perspective as a control situation (Jackson et al., 2006; Lamm et al., 2007) and taking the other's perspective is the experimental situation which is associated with empathy (Batson., 2008).

Because in the current literature studies with both paradigms are present, I will use studies with both paradigms.

### **The importance of self-agency and facial mimicry in normal human empathy**

Two things that seem to be important for a human that is capable of experiencing empathic feelings on a normal level are:

- 1) mimicry of facial expressions of the target and,
- 2) the capability to know that what you feel is not really what you feel but it's the result of observing a target with that emotion. When you trigger your own emotion and you are aware of this, this is called "emotional awareness" or "self-agency". (Decety and Jackson, 2006).

Normal is always vague word, also in the context of normal empathy. You could consider the empathic ability normal when it allows you to function well in current society. When self-agency and facial mimicry do not function properly, this goes together with a deficiency in the empathic capability of the individual which is problematic in current society. So a deficiency in those factors could lead to abnormal empathy. The current society, requires the individual to have high levels of communication skills. Being present in such huge numbers on the planet today, and living so close next to each other, we humans must be able to understand each other's mental and affective states. Not only it enables us to communicate and interact with each other in effective and pleasant ways, it also enables us to predict the actions, intentions, and feelings of others. [Singer and Lamm, 2009] Especially predicting another's emotional state is important to know how to react (for example help) when necessary.

How important our capability to understand someone else's emotion and to react properly is only becomes evident when this capability is deficient. People that have deficiencies in self agency and facial mimicry seem to have problems with empathy which in turn could lead to bigger problems like social exclusion. To help individuals deal with their deficiency in empathy and also to learn more about how empathy is generated in normal individuals, it is important to determine in whether these factors are important for empathizing.

### **Self-agency and empathy**

According to the shared representation theory the observer simulates the brain activation patterns of the target. But if there would be a complete overlap between self- and other representations this would induce emotional distress and anxiety [Decety and Jackson, 2006], which could cause the observer to move away from the target. Of course this is not the function of empathy, as empathic concern is thought to be related to altruistic behavior [Rameson and Lieberman, 2009], and therefore approach behavior would be a more logical consequence. To prevent this avoidance behavior, when experiencing someone else's emotions, the observer must somehow distinguish his or her feelings from those of the target. It is necessary that there is a mechanism in the brain controlling the emotional input triggered by merely observation of the targets emotion. The term self-agency has been used for the individual being aware that an action finds its origin in the self. Agency is a well-known definition for the origin of an action. It is called self-agency when the origin of the action lies or is thought to lie within the self.. A broader



description was is the awareness of oneself as an agent who is the initiator of actions, desires, thoughts, and feelings (ref). Thus the term self-agency can also be used to describe when one thinks the origin of an emotional response lies within the self. Different is that the term used in studies investigating empathy, is not always self-agency but also “emotional awareness (of the self)” is used. A possible description of the phenomenon self-agency (emotional awareness) in emotion research could be ‘knowing that the emotional experience was generated as a response to an emotional stimulus or an emotional event, and consequently knowing the emotional experience is not a the results empathizing with another (via other-perspective taking caused by another’s emotional expression)’.

In the brain there is thought to be an inferential mechanism that allows distinguishing whether or not a sensory event has been self-produced. This distinction is made by comparing the actual sensory information with the consequences of one’s action as predicted on the basis of internal action related signals such as efference copies (Haggard and Tsakiris, 2009; Synofzik et al., 2010). A similar mechanism might be responsible for a sense of self-agency in emotional events.

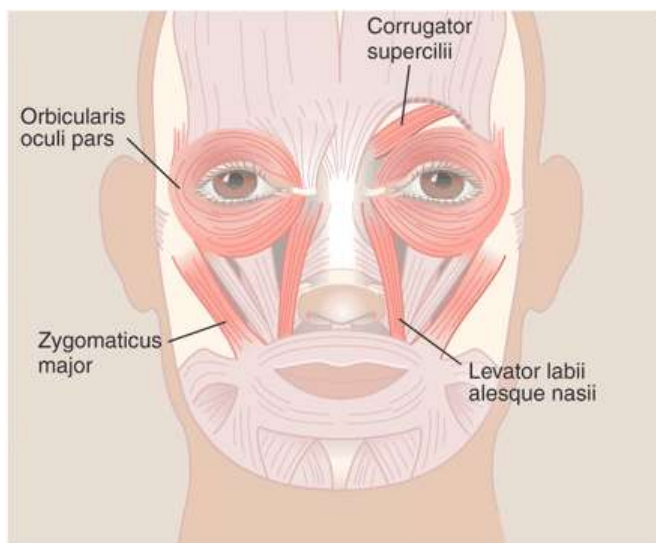
Individuals with psychiatric disorders, that have been related to a distorted sense of self-agency (emotional awareness), seem to have trouble with empathizing. Therefore it is interesting to investigate how deficiencies in self-agency are related to empathic abilities.

### **Facial mimicry and empathy**

Observing the emotional state of another individual happens for a great part via observation of another’s facial expression. Automatic mimicking of another’s facial expression is thought to cause the observer to share the brain activations of the target. Evidence for this was found in a study by Hennenlotter et al. (2008). Here *botulinum toxin* (BTX) was used to reduce the feedback from muscle activity in the face to the brain. The application of BTX indeed attenuated activity in brain regions important for empathy, during observation of facial expressions.

Before you can *feel* how the other is feeling, you should of course first *recognize what* the other is feeling. It seems that the way our face is build up, it is designed for expressing emotions, regarding the large amount of facial muscles present in the human face. All these facial muscles make it possible to express many kinds of

emotions, merely with our face. [Niedenthal et al., 2007]. Some muscles that are used in facial mimicry research are shown in Figure 1. The *corrugator supercilii* (CS), knits the eyebrows when frowning, and the *zygomaticus major* (ZM), elevates the lips when smiling. [Achaibou et al., 2008]. Especially these facial muscles are important for us to “read” another’s emotion. That we can read another’s emotional state correctly by merely looking at another’s facial expression is suggested by a study done by Carrol and Russel [1996]. Subjects were asked to look at different facial expressions, which the experimenters had beforehand labelled with a specific emotion. The subjects judged the emotional state the other were in correctly ; their answer matched with the label.



**Figure 1** : Some of the facial muscles that are frequently used in experiments, examining facial mimicry [Niedenthal et al., 2007]

Humans have been found to automatically mimic each other’s facial expressions are [Sato and Yoshikawa, 2007]. Automatic mimicry is defined as the tendency to automatically synchronize affective expressions, vocalizations, postures, and movements with those of another person (Hatfield et al. 1994). That mimicking is called automatic does not yet mean that it can not be controlled by top-down processes, like for example inhibitory processes [Singer and Lamm, 2009; Bien et al., 2009].

Only some studies investigate facial mimicry of positive emotions, studies investigating empathy give more attention is given to facial mimicry of negative emotions, like pain and disgust. A reason for this could be that it is more likely that these emotions will evoke emphatic concern, because people experiencing

negative emotions might need your help more than people experiencing positive emotions. The idea behind this is that when you see someone with an expression of pain on his face, empathizing is needed more, compared to when someone is smiling excessively because he or she just won the lottery.

But it is questionable whether the function of facial mimicry of negative emotions has a function in creating empathic concern, and not merely has a more primitive function in creating an avoidance response [Yamada and Decety, 2009]. Although this is not clear yet, several studies do suggest that mimicry is an important component of the capability to feel empathy.

Sonnby-Borgstrom (2002) measured the degree of automatic mimicking of facial expressions of emotion in two groups, a low-empathy group and a high-empathy group. Individuals were divided into these two groups, according to their score on a questionnaire measuring empathy. The degree of facial mimicry, was measured with electromyographic (EMG) activity of the face muscles. It was found that the high-empathy group had a higher degree of mimicking activity, than the low empathy group. This suggests that individuals that mimic facial expressions more, might have a higher empathic ability. A study done with children also showed that activity in parts of the brain that are thought to be involved in empathy - the mirror neuron system [MNS]- was elicited by observation and imitation of emotional expressions. So observing and mimicking the expressions, caused the observer subjects to activate their brain also. More importantly this study showed that activations in the MNS were positively correlated with empathic behavior of the children.[Pfeifer et al., 2007].

Carr et al. (2003) found that both observation and imitation of facial expressions activated the same network, however imitation led to greater activations in some parts of this network. They suggested that a representation of the action of the target which expressing the emotion, in the observer allows us to feel empathy.

That mimicry is related to empathy is clear from these studies. That mimicry also leads to prosocial behavior is pointed out by a study done by van Baaren et al (2004). This study demonstrated that participants who had been mimicked by the experimenter were more helpful and generous toward other people than non-mimicked participants. Thus these beneficial consequences of mimicry were not restricted to behaviour directed toward the mimicker, but included behaviour directed towards people not directly involved in the mimicry situation [Decety and Moriguchi, 2007].

These studies together indicate that mimicking of facial expressions, is an important factor contributing to the empathic abilities and prosocial behaviors in healthy individuals. Summarizing the results discussed above we are able to recognize each other's emotional state by merely observing another's facial expression, we automatically mimic each others emotions and mimicking of another's emotion causes the observer to share the emotional state of the target. Therefore it would be very interesting to determine whether individuals who have a deficiency in facial mimicry, also have deficiencies in empathy. This subject will be, next to the importance of self-agency, the second focus in this thesis.

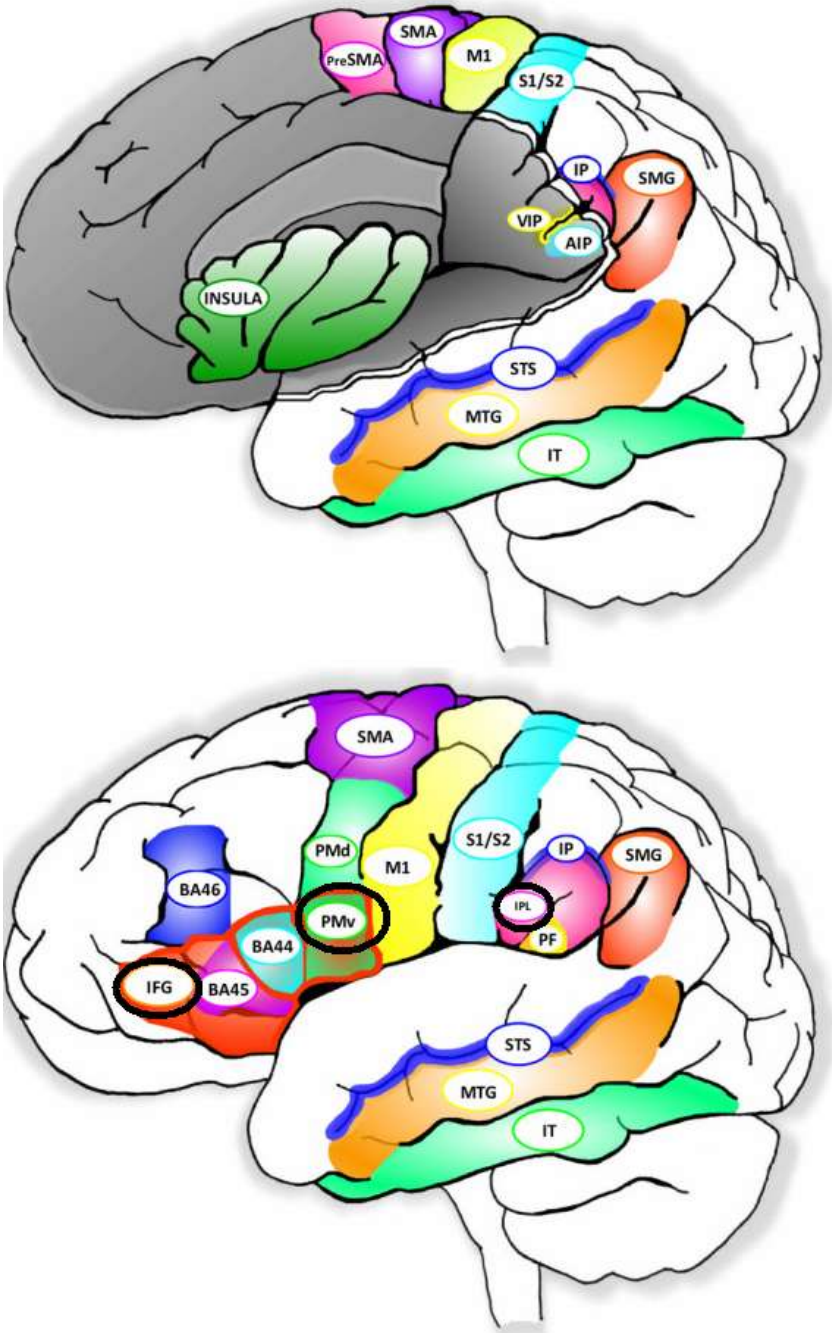
## **Chapter 2 The neural base of empathy and self-agency**

### **The neural base of empathy**

According to the current hypothesis about the neural base of empathy, the shared network hypothesis, to empathize with another individual, we simulate the brain activation of the other. So we use our own brain as a model to understand the emotions of others. (Rameson and Lieberman, 2009). The finding that first gave evidence for this shared network hypothesis for empathy theory, came from a study done with macaque monkeys (Rizzolatti et al., 1981). Certain neurons within the area F5 did not only fire when the monkey grasped and manipulated an object but also when the monkey was only observing someone else performing the same or a similar action. (Rizzolatti et al., 1981). Cells with these properties, which suggest that the monkey is observing its own actions reflected by a mirror, have become known as the mirror neurons. (Iacoboni, 2009). Since the existence of these mirror neuron cells was discovered in monkeys, researchers have been searching for these cells in the human brain, because these cells could explain why we humans are able to empathize. Indeed humans also seem to have a mirror neuron system (MNS). Areas in the human brain which contain mirror neurons are the ventral premotor cortex (PMv) and the inferior parietal lobule (IPL) and the posterior part of the inferior frontal gyrus (IFG) (Iacoboni, 2009). Areas that contain mirror neurons are circled black in the schematic anatomical view in Figure 2.

The core neural circuitry of imitation is composed of this fronto-parietal mirror neuron system but also of a higher-order visual system; the posterior part of the superior temporal sulcus. (Iacoboni, 2009). According to Iacoboni (2009) also regions that may themselves not contain mirror neurons per se, such as the superior temporal sulcus (Pineda, 2008), are part of the neural circuitry for imitation. The MNS can therefore also be considered to be more extended. Besides involving the STS this “extended” Mirror Neuron System (MNSe) has been suggested to involve many other brain areas and regions that do not contain mirror neurons. The reason that these areas could also be considered to be part of the MNS, is because the core circuitry for imitation interacts with different areas in the brain to support different forms of imitative behavior (Iacoboni, 2009). Because of these interactions they could be considered critical for imitative behavior which makes them part of an extended mirroring process. (Pineda, 2008)

In Figure 2 the brain areas that are suggested to be involved in this extended MNS are shown in a schematic anatomical view of the human brain. A summary of all the brain areas, their abbreviations and their suggested function is given in table 1.



**Figure 2:** Schematic anatomical view of a human brain, showing areas involved in the extended mirror neuron system (MNSe). The areas circled in black- the PMv, IPL and the IFG- have found to contain mirror neuron cells. (Image adapted from Pineda, 2008).

**Table 1:** Abbreviations and functional descriptions of anatomical brain areas of the extended mirror neuron system (Pineda, 2008).

<b>Abbreviation</b>	<b>Name</b>	<b>Function</b>
AIP	Anterior intraparietal	visually guided grasping; comparable to monkey area F5
BA44	Brodmann's area 44	Broca's area; language production
BA46	Brodmann's area 46	rostral portion of the IFG; sustained attention and working memory
IFG	Inferior frontal gyrus	action observation and imitation
Insula	Insular cortex	body representation and subjective emotional experience
IP	Intraparietal sulcus	guidance of limb and eye movement
IPL	Inferior parietal lobule	post-central sulcus/anterior border, intraparietal sulcus/superior border, and the lateral fissure/ anterior inferior border.
IT	Inferotemporal cortex	identification and categorization of objects
M1	Primary motor cortex	patterns of muscle activation
MTG	Middle temporal gyrus	subserves language and semantic memory processing, visual perception, and multimodal sensory integration
PF	Parietal frontal	rostral convexity of IPL
PMd	Dorsal premotor	simultaneous encoding of multiple movement
PMv	Ventral premotor	monkey area F5; analogous to BA 44; pars opercularis of IFG
S1	Primary somatosensory	kinematics
S2	Secondary somatosensory	integrating across body parts; frontoparietal operculum and lateral convexity of IPL
SMA	Supplementary motor	planning motor actions
SMG	Supramarginal gyrus	spatial orientation and semantic representation
STS	Superior temporal sulcus	visual information entry area
VIP	Ventral intraparietal	comparable to monkey area F4

The system for imitation is suggested to be a part of the network involved in empathy. However the MNSe on its own, does not yet makes it possible for us to empathize with each other. Carr at al. (2003) suggested that the fronto-parietal mirror neuron system is connected to the limbic system via the insula. [Carr at al, 2003]. We can feel what others feel by a mechanism of action representation (MNS) and a subsequent modulation of our emotional content (in the limbic system) via the insula. Here the insula seems to play an important role in relaying action representation to emotion.

### **Evidence for the shared network hypothesis from studies investigating empathy of pain**

The emotion pain is frequently used in empathy research [Jackson et al., 2005; Jackson et al., 2006; Bufalari et al., 2007; Lamm et al., 2007; Danziger et al., 2009]. To test the shared network hypothesis, it is interesting to determine whether experiencing pain yourself and seeing another experiencing pain, both lead to similar activation patterns in the brain. Indeed, subjects activated the anterior cingulate cortex (ACC) and the anterior insula (AI), when watching someone else experiencing pain. These regions are part of the pain affective system which is activated when the subject self experiences pain. (Jackson et al., 2005). During a task where subjects observed a facial pain expression or an event that would be experienced painful, patients with congenital insensitivity to pain (CIP) activated the ACC and AI, which the healthy controls also activated. (Danziger et al., 2009). These findings support the idea that simulation of brain activity of the observed target plays an important role in human's ability to empathize. Also this suggests that previous personal sensory experience of pain might not be necessary for this system to be active. (Danziger et al., 2009). This study also showed that the degree of empathic ability in the CIP patients, which was measured with an empathy scale questionnaires, correlated positively with activations in the medial prefrontal cortex (mPFC) and the posterior cingulate cortex (PCC), which are involved in other-perspective taking. (Danziger et al., 2009).

### **Empathy versus Theory of Mind?**

Theory of mind (ToM), also called mentalizing, is the capacity to know the beliefs and thoughts of others, and empathy is the capacity to feel what another feels. The difference between these two phenomena is that in ToM, affective states can also be



represented in the observer so the observer understands the state the target is in, but the emotion is not felt like when the observer empathizes with the target. This idea is based on studies where empathy can function normally while ToM is deficient or vice versa. (Singer, 2008)

Singer (2008) makes a distinction between brain areas involved in theory of mind and brain areas involved in empathy based on fMRI studies investigating ToM and empathy. Areas that are suggested to be involved in empathy are the ACC, AI and S2 and areas that are thought to be involved in ToM are MFC, TPJ and STS.

Singer (2008) makes it clear that there still is a discussion about which brain areas are involved in empathy, and that possibly a distinction in the function of these areas should be made. However important for this thesis is that both cognitive perspective taking (ToM) and emotional perspective taking (empathy) have a role in

understanding others and because the uncertainty in the distinction between these two, areas involved in both phenomena will be taken into account..

### **Brain areas involved in a sense of self-agency: don't lose yourself in empathy**

Here I will discuss how the brain creates a sense self-agency. Different brain areas are thought to be involved in a sense of self-agency. Decety and Meyer (2008) argue that two of the main components contributing to the experience of empathy are the (bottom-up) process of affective sharing (via perception action coupling in the MNS) and a sense of self-agency to differentiate oneself from the other (which likely involves fronto-parietal and prefrontal circuits). (Decety and Meyer, 2008). The first component of empathy that the observation of an emotion elicits the activation of analogous motor representation in healthy observers, begs the question why there is not complete overlap between internally generated and externally engendered motor representations. (Decety and Meyer, 2008).

### ***A clear distinction the brain between self- and other-perspective taking***

In a study by D'Argembeau et al. (2007) it was found that the mPFC is possibly involved in both self-perspective (dorsal anterior mPFC) and other-perspective taking (posterior dorsal mPFC). They suggested that the left dorsal mPFC may be

involved in decoupling one's own from other people's perspectives on the self: the interaction between the two dimensions yielded activation in the left dorsal mPFC. It seems that different parts of this brain area are involved in different functions. Possibly because these activations lie so close to each other, this distinction was not detected in studies which found activations in the medial prefrontal cortex as a whole region, during both the self- as the other-perspective (Ruby and Decety, 2003, 2004; Seger et al., 2004). That even within a certain area a distinction between functions can be made is supported by another study. Here it was found that the insula was activated in both the other- as the self-perspective, however different subregions of the insula were responsible for each form of perspective taking. Taking the other-perspective activated the anterior part of the insula and taking the self-perspective activated the more posterior part is activated (Jackson et al., 2006). This was supported by a finding of Decety and Moriguchi et al., (2007). Here it was found that when subjects experienced the pain themselves this was associated with more caudal activations. The perception of pain in others is represented in more rostral (and dorsal) regions. This caudal part also receives input from spino-thalamic nociceptive projections (Decety and Moriguchi., 2007)

Other studies have suggested that some brain areas are activated only during other perspective taking, and could in this way contribute to a sense of self-agency. According to Decety et al., (2006) areas that seem to be involved in the other perspective selectively are the posterior cingulate cortex (PCC), the frontopolar cortex, and right temporo-parietal junction. (TPJ).

These studies together suggest that a sense of self-agency is generated by certain subregions within a brain area, which are responsible for either the self- or the other-perspective. And another way in which a sense of self-agency might be generated is because certain brain areas are selectively activated during other-perspective taking.

### ***Same brain areas responsible for distinction between self- and other-perspective taking***

In their paper Decety and Moriguchi (2007), tried to detangle the brain areas involved in self- and other-perspective taking. In contrast with the studies discussed above, these studies together suggest that whole brain areas are

responsible for both the self- as the other-perspective taking. I will now discuss these studies.

In one study, participants were scanned while they were asked to either imagine themselves or someone else performing a variety of everyday actions. Both conditions were associated with common activation in the supplementary motor area (SMA), premotor cortex, and the occipito-temporal region. This neural network corresponds to the shared motor representations between the self- and the other. Taking the perspective of the other to simulate his or her behaviour resulted in selective activation of the frontopolar cortex and right inferior parietal lobule (IPL) (Ruby and Decety., 2001).

In a second study it was investigated how truthful students found a sentence on a topic of their study (medicine), while adopting the self or another's (in this case a lay's) perspective. The set of activated regions recruited when the participants put themselves in the shoes of a lay-person included the medial prefrontal cortex, the frontopolar cortex and the right inferior parietal lobule (IPL) (Ruby and Decety, 2003).

In a third study, the participants had to take a self-perspective or the perspective of another (their mother), when reading a sentence that described an emotional-laden situation (e.g., someone opens the toilet door that you have forgotten to lock). When taking their mothers perspective neurodynamic changes were detected in the frontopolar cortex, the ventromedial prefrontal cortex (vmPFC), the medial prefrontal cortex (mPFC), and the right inferior parietal lobule (right IPL). The affective content of the situations depicted did not matter. When reading the emotional-laden situations the amygdala and the temporal poles, were found activated. (Ruby and Decety, 2004).

In a fourth study participants had to make food preference judgements for themselves or for someone else they knew fairly well. When they judged for themselves activations in the medial prefrontal cortex (mPFC), anterior insula (AI) and secondary somatosensory areas (SII) were found. When they judged for the other person, activations in the medial prefrontal cortex (mPFC), the frontopolar cortex and the posterior cingulated cortex (PCC) were found.(Seger et al., 2004).

A recent study by Benoit et al. (2010) adds an interesting finding above these findings. Here it was found that the (rostral) mPFC was activated both during retrieval of information about the self as during thinking about another. The interesting new finding was that the degree to which this areas was activated, while processing others, correlated with the degree of perceived similarity between the

self and the other (the degree of shared personality traits). This suggests that the (rostral) mPFC is involved in both making judgments about the self as in making judgments about persons very similar to themselves

Summarizing the studies that investigated self- versus other's perspective it seems that brain areas thought to be involved in a sense of self-agency are activated during both self- as other perspective taking. The mPFC and right IPL and some other areas (frontopolar cortex, occipito-temporal regions, SMA, premotor cortex) were activated both when one reflects on oneself, but also when individuals intentionally adopt the subjective perspective of others (Decety and Moriguchi., 2007). Interestingly areas that could possibly be divided in subregions, like the mPFC, are found active as a whole during both the self- as the other-perspective taking in the five studies discussed above.

Adding to this brain areas, like the PCC and the frontopolar cortex, that were suggested to be involved in other-perspective taking selectively (Decety et al., 2006), have also been found activate during awareness of one's own emotional state. This was found for the PCC, which was found active during both evaluation of one's own emotional state and in self focused attention (Saxe et al., 2006) and for the frontopolar cortex (Christoff et al., 2000) which was found activate during a task where monitoring and manipulating information that was internally represented was required.

Next to the finding that some areas (mPFC, PCC) are important for both self- as other- perspective taking, other brain areas are found to be more involved in self-processing: the TPJ and the IPC. Schulte-Rüther et al. (2007) suggested that the posterior TPJ and inferior parietal regions mediate the distinction between the self- and the other-perspective in emotional interpersonal cognition. The temporoparietal junction (TPJ) is a heteromodal association cortex, which integrates input from the lateral and posterior thalamus, as well as visual, auditory, somesthetic, and limbic areas. It has reciprocal connections to the PFC and to the temporal lobes. Because of these anatomical characteristics, this region is a key neural locus for self processing that is involved in multisensory body related information processing, as well as in the processing of phenomenological and cognitive aspects of the self (Blanke & Arzy, 2005) Another study showed that the TPJ not only processes sensory events from the self, but it is also active when predictions about own actions are incongruent with what the body gets as an input from the environment. (Spengler et. al., 2009) supporting the idea that this area is

important for a sense of self-agency. The right inferior cortex holds an image of the body in space and time and seems to have a similar function as the TPJ, as it is found active when subjects compared others-perspective with their own perspective. (Decety and Moriguchi, 2007).

It seems that separating areas involved in self- and other-perspective taking, might not be so easy, as this distinction in subregions was not found in these studies. Also areas that were suggested to be involved in other-perspective taking selectively, were activated during emotional awareness of the self.

However it was also found that some brain areas seem to be more involved in emotional processing in the self or self-perspective taking.

### ***How is the sense of self-agency generated in the brain?***

Possibly taking the self- or the other-perspective is not so differently represented in the brain. Maybe the function of taking the self or the other perspectives is too closely related, and consequently the same brain areas are used. This makes sense when it is considered that both taking the self- as the other-perspective can lead to the understanding of another's feelings. According to the shared representation hypothesis this leads to an internal activation similar to the activation in the individual really experiencing the emotion. Both might be a self-generated process which is created by the same brain regions or brain regions very close to each other.

All the aforementioned evidence strongly suggests that it probably does not rely on a specific brain region, rather it arises from the interaction between areas distributed over the brain. the TPJ and IPL/IPC, in conjunction with the mPFC, PCC and the AI, play an important role in the sense of self, by comparing the source of sensory signals; whether they originate from the self or from the environment. Such a function is crucial for empathy in order to maintain a minimal distinction between the self and the other and to keep track of the origin of the feelings. This sense of self-agency or emotional awareness of the self is crucial to keeping track of which emotions belong to whom, when using a mechanism of shared representations in the brain.

A summary of brain areas found to be involved in generating a sense of self-agency and their abbreviations and their suggested function is given in table 2.

**Table 2:** Brain areas that have been suggested to be involved in generating a sense of self-agency (emotional awareness of the self) by distinguishing emotions of the self from emotions of the other (Blanke & Arzy, 2005; Singer et al., 2004; Singer, 2008; Decety and Meyer 2008; Decety and Moriguchi, 2007)

<b>Abbreviation</b>	<b>Name</b>	<b>Function</b>
mPFC	Medial prefrontal cortex	Helps integrate information about the internal state of the body with higher-level mental state knowledge needed to categorize one's own as well as others' emotions (Singer et al., 2008)
ACC	Anterior cingulate cortex	Representation of bodily states of arousal and awareness of these bodily states. (Singer, 2008)
PCC	Posterior cingulate cortex	Has also has been associated with emotional evaluation and perspective taking (Singer et al., 2004)
Right TPJ	(Right ) Temporo-Parietal Junction	This region is a key neural locus for selfprocessing that is involved in multisensory body related information processing, as well as in the processing of phenomenological and cognitive aspects of the self (Blanke & Arzy, 2005)Plays a critical role in the distinction between self-produced actions and actions generated by others (Decety and Meyer, 2008)
Right IPC/ IPL	Right Inferior Parietal Cortex/ Inferior Parietal Lobule	Distinguishing the self from the other and therefore in navigating shared representations (Decety and Moriguchi, 2007)

## **Chapter 3 Distortions in empathy and the importance of self-agency and facial mimicry**

### **From normal to deficient empathy**

That certain brain areas are involved in the ability to experience empathy is clear (see Figure 2). If we consider empathy as a brain function it is logical that - like other brain functions- it differs between individuals. For example the ability to understand mathematics or learn foreign languages also differs between individuals, some individuals are better than others. Thus having more or less empathy than another, does not consequently mean your empathic ability is abnormal. This is supported by a study done by Pfeifer et al (2008) where activations in the MNS -involved in empathy- correlated with empathic abilities in normal children, which shows that empathic abilities also vary across a normal population of individuals. The empathic ability of an individual could be defined as abnormal in several psychiatric disorders. I will define the empathic ability of these individuals as abnormal because these individuals have problems in everyday life because of their empathic ability. Take for example a situation on the playground of a school. A child with a deficiency in empathy (Child A) accidentally causes another child (Child B) to fall down during a game. Child A does not understand that the other child is crying because it is in pain, and will not help the other child. When other children see this, this child A could be considered as not caring if it does not care about others. Consequently the other children don't want to play with the child anymore.

In this chapter I will focus on individuals with psychiatric disorders in which empathy has been found impaired. Goal of this chapter is to determine how the two factors, facial mimicry and self-agency, are important for normal empathy.

First I will focus on psychiatric disorders which have frequently been related to a deficiency in facial mimicry : Autistic Spectrum Disorders (ASD). Here it will be determined whether a deficiency in facial mimicry makes individuals with ASD less empathic than normal control individuals.

Secondly I will focus on two psychiatric disorders and a personal trait which have frequently been related to a deficiency in self-agency : ASD, Schizophrenia, social phobia/anxiety disorder (SAD) and Alexythymia. For these populations it will be

determined whether there is relationship between the impaired empathic ability and a deficiency in self-agency.

### **Deficiencies in facial mimicry and empathy**

As discussed in Chapter 1, facial mimicry seems an important factor contributing to empathic abilities in normal children and adults. Therefore it would be interesting to determine whether individuals with a deficiency in facial mimicry are also less empathic.

ASD is a psychiatric disorder of which a core deficit is suggested to be the reduced imitative behavior. (Pelligrino et al., 1992). In the shared representation hypothesis copying the facial expressions of another induces the same emotion in the observer (see Chapter 1). Imitation deficits have therefore been proposed as an explanation for the difficulty of autistic children in establishing social relationships and identifying with others (Rogers et al., 1999).

Evidence that facial mimicry in ASD is deficient comes from several studies.

Compared to developmentally delayed children, 20-month infants with autism were found to be specifically impaired on an empathy task and imitation (Charman et al., 1997). Another study done by Dawson et al. (1999) found that 30 to 70 month-old autistic never smiled when their mother was smiling. Young individuals with autism thus do not seem to automatically mimic facial expression when they observe them. This was also found in adolescents and adults with ASD. While they did mimic facial expressions voluntarily (which is effortful and slow), they did not spontaneously mimic (which goes quickly) others facial expressions (McIntosh et al., 2006). This could indicate that their perception-action coupling is deficient (Decety and Moriguchi., 2007).

In the MNS perception and action are coupled, as mirror neurons get activated when observing or executing an action. Maybe findings of the studies above could indicate that the MNS does not function properly in individuals with ASD.

The MNS normally involved in imitative behavior, has been found deficient in individuals with ASD. The MNS enables the modelling of the behaviour of other people through a mechanism of embodied simulation. Embodied simulation could provide 'intentional attunement', a direct form of experiential understanding of others. A disruption of MNS activity would preclude such experiential



understanding of others, leading to the social deficits of autism. A disruption of MNS activity would preclude such experiential understanding of others, leading to the social deficits of autism. (Iacoboni and Dapretto, 2006).

During observation and imitation of facial expressions of emotion, less activity was found in the inferior frontal gyrus (IFG), an area which is part of the mirror neuron system, in children with ASD compared to control children. The MNS activity in children with ASD inversely correlates with the severity of disease: the higher the severity of disease, the lower the MNS activity. (Dapretto et al., 2006).

Other studies which investigated activity of the MNS during observation and imitation of hand movements found reduced activity in the MNS in the ASD groups compared to the normal control group.

A study investigated MNS functioning in normal and ASD children and adults with EEG activity over the sensorimotor cortex, which is thought to reflect mirror neuron activity. One method for testing the integrity of this system is to measure mu responsiveness to actual and observed movement. In normal control individuals mu activity was found suppressed during both observation and execution of a movement, which was found before in typically developing individuals. In the ASD individuals this mu suppression was found during execution of the movement, but not during observation of the movement. (Oberman et al., 2005).

Another study investigated activity in the MNS with fMRI in adolescents with ASD compared to a normal control group. One of the main findings in this study was that activity of the right posterior middle temporal gyrus at the temporo-parietal junction (TPJ) was reduced in the ASD group. This area was found active in controls during imitation of the hand movement, which indicates it is important for imitative behaviour. Activity in the amygdale also differed between the ASD and the control group. During imitation activity of the left amygdale was higher in the ASD group compared to the control group. But the variance of amygdale activity was higher in the control. Williams et al. (2006) suggested that imitation and emotional circuits are not properly connected in ASD individuals, and therefore amygdale activation does not give the motivation to imitate. (Williams et al., 2006).

Thus it seems that in individuals with ASD facial mimicry is deficient and there also seem to be deficiencies in the MNS. This possibly reflects that perception and

action are not properly linked in the brain, which could contribute to the symptoms of ASD.

### **Deficiencies in self-agency and empathy**

As discussed in Chapter 1, self-agency seems an important factor contributing to empathic abilities in normal children and adults. Therefore it would be interesting to determine whether individuals with a deficiency in self-agency are less empathic.

### **ASD**

A recent fMRI study investigated whether representation of the self in the brain is the same in individuals with ASD as in normal control individuals. The subjects made reflective mentalizing or physical judgements about themselves (e.g. 'How likely are you to think that keeping a diary is important') or about the British Queen (e.g. 'How likely is the Queen to think that keeping a diary is important'). A familiar but non-close other (the Queen) was used as the 'other' condition in this study to increase the chance of finding regions involved in the self-other distinction. (Lombardo et al., 2010). While controls significantly recruited the ventromedial prefrontal cortex more for self than other, individuals with autism did not. Interestingly ASD-individuals with the greatest social impairments in early childhood showed the least ventromedial prefrontal cortex self-other mentalizing distinction, while the least socially impaired individuals showed the largest ventromedial prefrontal cortex self-other mentalizing distinction. (Lombardo et al., 2010). This suggests that the ventromedial PFC is involved in self-agency in normal controls and that it might be impaired in individuals with ASD, leading to social impairments, including a deficiency in empathy.

### **Alexithymia**

Alexithymia is not a psychiatric disorder on its own, but it has been a term for describing a set of deficiencies in the emotional processing system, since Sifneos (1972) introduced it. Alexithymia (ALEX) is a term for describing individuals who appear to have deficiencies in understanding, processing, or describing their emotions (Moriguchi et al., 2009). The deficiency in emotional self-awareness also extends to not being able to understand the emotions of others. These problems that individuals with ALEX have with recognizing their own emotions and those of others, indicates that the involved neurological system, might be dysfunctional.

Different levels of activity in the MNS have indeed been found in individuals with ALEX compared to normal controls, suggesting abnormal functioning.

Moriguchi et al. (2006) investigated neural activity during a task where subjects had to take the perspective of an animation figure performing a certain action. They found no group differences in cerebral activity in the TPJ and the TP, areas normally thought to be involved in self-agency of emotion. That these areas are important for self-agency was supported by the finding that the activity in the right TP had a positive correlation with perspective-taking scores. However it was found that perspective taking was deficient. First they found scores of perspective-taking were lower in the ALEX group, compared to the non-ALEX group. Second they found reduced activity of the right mPFC in the ALEX group. This suggest that the deficiency of the individuals with ALEX in perspective-taking is related to a deficiency in the underlying neural system, the MNS. These results point to common components in the recognition of the self and others; therefore, ALEX involves impairments both in self-awareness and also in understanding the perspective of others at a higher cognitive level. (Moriguchi et al., 2006).

Another fMRI study compared activity in the brain in an ALEX and a non-ALEX group, when looking at pictures depicting human hands and feet in painful situations. The individuals with alexythimia estimated the pain the targets were in, lower than the individuals without alexythimia and furthermore scores on a empathy scale were also lower in this group giving evidence for a deficiency of in the empathic ability of individuals with ALEX as it suggests they cannot estimate emotions (pain in this case) of other normally. The ALEX group showed reduced activation in dorsolateral prefrontal cortex (DLPFC) and the left caudal anterior cingulate cortex (ACC) within the pain matrix. As discussed in chapter 2 regions of the PFC and ACC have been found important for normal self-agency. Thus the symptoms of individuals with ALEX related to impaired self-agency -unawareness of their own and others emotions- could indeed be caused by a deficiency in the neurological system involved in empathy. It is also necessary to report that other areas involved in empathy were found hyper activate in individuals with ALEX. Greater activation in the ALEX group was found in the right insula and inferior frontal gyrus. The increased activation of these area might suggest that parts of the empathy network are also functioning inefficient. (Moriguchi et al., 2007)

Adding to the previous finding that individuals with ALEX showed activity reduced in areas important for self-agency a recent study showed that during a task were subjects had to observe hand movements, activity in the MNS was greater for the

individuals with ALEX than for those without ALEX (Moriguchi et al., 2009). Neural activity was found higher in the premotor and the parietal cortices. But this over activation seems to be related to a dysfunctional MNS, because activity of the left premotor area correlated negatively with perspective taking, and activity of the right superior parietal region correlated with severity of ALEX measured with an interview. These results suggest that the stronger MNS-related neural response in individuals scoring high on ALEX is associated with their insufficient self-other differentiation.

### ***Schizophrenia and schizotypy***

Studies that investigated the empathic ability of individuals with schizophrenia directly are not very numerous. Still the psychiatric disorder schizophrenia has often been related to a deficit in empathy. One study that has investigated directly whether individuals with schizophrenia are impaired in their empathic abilities compared to normal control individuals was done by Bora et al. (2008). The empathic ability of the subjects in this study was determined by how they scored on several tasks which tapped (appropriate) empathic responses. It was found that individuals with schizophrenia had severe empathy dysfunction, based on their scores on these tasks. Thus the generally expected existence of an empathy deficit in individuals with schizophrenia, is supported by this study which investigated it directly.

The reason why empathy might be dysfunctional in this group could be related to a weaker sense of self-agency which characterizes people with schizophrenia. A sense of self-agency is thought to be very important for normal empathy, as it makes it possible to know whether you are experiencing an emotion of the self or that of another. A study investigated the sense of self-agency in a highly and low schizotypal group of students. Schizotypy can be seen as an indicator of a predisposition to schizophrenia (Asai et al., 2008). It was found that the highly schizotypal group, judged the sense of self-agency according to the temporal delay between hearing a tone and pressing a button. The low schizotypy group had a stronger sense of self-agency, as they sometimes felt a sense of self-agency while a temporal delay was perceived between the tone and the button being pressed. (Asai et al., 2008). According to the results of this study highly schizotypal individuals have a weaker sense of self-agency than low schizotypal individuals. Synofzik et al. (2010) give a possible explanation for this weaker sense of self-agency in these

patients, based on two experiments. The weaker sense of self-agency might be caused by a poorer ability to make predictions about the sensory consequences of self-action- which is important to determine the agent of an action- when presuming the mechanism underlying a sense of self-agency is true (see chapter 1). Indeed in the first experiment, the variability of predictions about sensory consequence of self-action was found correlate with delusions of influence in individuals with schizophrenia. This deficiency in making internal predictions could have caused individuals with schizophrenia to rely more on external cues about self-action. The stronger weighting of external cues could help to avoid misattributions of agency for self-produced sensory events due to imprecise internal predictions. This hypothesis was tested in a second experiment where visual feedback of the consequence of a certain action was or was not given. When feedback was absent patients did not see themselves as the agents more often than the normal controls. This supports the hypothesis as when external cues are temporarily not attended or unavailable patients might fail to attribute self-produced sensory events to their own agency and assume external causal forces are the cause. (Sysnofzik et al., 2010).

A preliminary study by Harrison et al. (2007) investigated if abnormal patterns of brain activations of individuals with schizophrenia might be contributing to their empathy deficit. Task-induced deactivations (TIDs) were determined during a task where emotional awareness of others in individuals with and without schizophrenia. This was done in brain areas associated with empathy. Relative to control subjects, schizophrenia patients showed significantly greater TID of the medial prefrontal cortex (mPFC) and posterior cingulate cortex (PCC). The mPFC and the PCC are probably involved in a sense of self-agency as these areas have been found activated during self-experience of emotions (see chapter 2). That individuals with schizophrenia deactivated these areas more during a task in which they were instructed to think about what another was feeling, suggests that a sense of self-agency might be lacking.

### ***Social Phobia***

Individuals with social phobia, also known as Social Anxiety Disorder (SAD), have a marked and persistent fear for social situations, where they are exposed to unfamiliar people. They fear that they will stand out because of the way they act (showing anxiety), which will be humiliating and embarrassing. (Spurr et al., 2002). That individuals with social phobia/SAD fear social situations is probably caused

by their abnormally high self-focussed attention (Spurr et al., 2002). This abnormally high self-focussed attention is probably related to a sense of self-agency. Social phobics are highly aware of their emotion fear (anxiety), which makes them more self-focussed. This was shown in a study by Wells and Papageorgiou (2001) subjects were either told that their heart rate was low or that their heart rate was high, before they were exposed to a social situation. When they were told their heart rate was high, the subjects were more anxious in the social situation, and the self-focus was also higher. The focus on your own emotion, probably goes together with a sense of self-agency and in this way the two might be related.

A fMRI study investigated brain activity during a trust game. In this trust game subjects thought that they had to work together with either a human or a computer to gain as much money as possible. To make the right decisions taking the perspective of the other was required during the condition where the other player was thought to be human. Brain activity was determined for both the individuals with social phobia as the normal controls for the human minus the computer condition. Activity of the mPFC in individuals with social anxiety was found reduced compared to normal controls. (Sripada et al., 2009). This finding was supported by another study where reduced activity in the dorsomedial and dorsolateral PFC was found in the social phobia group, when they were exposed to faces expressing negative emotions. (Goldin et al., 2009).

An fMRI study found that during observation of faces expressing an emotion, deactivation of the PCC was lower in individuals with social phobia than in normal controls. The PCC is thought to be involved in a sense of self-agency suggesting that self-agency might be lower in this group. (Gentili et al., 2009)

## **Chapter 4 Discussion; Are self-agency and facial mimicry important factors contributing to the empathic ability?**

There are many psychiatric disorders that have been related to a deficiency in empathy. Interestingly studies investigating the empathic ability of individuals with these psychiatric disorders have often found deficiencies in facial mimicry and in a sense of self agency. So by investigating whether this deficiency in empathy could be related to a distorted sense of self-agency and a deficiency in facial mimicry could give us the answer to the main question of this thesis. The main question in this thesis was whether facial mimicry and a sense of self-agency were important factors contributing to normal empathy.

To answer the main question, the thesis was divided into three chapters.

In Chapter 1, I started with shortly discussed the importance of self-agency and facial mimicry in normal control individuals. In this chapter it was concluded that self-agency must be important for normal empathy as it enables us to separate an emotional experience caused by empathizing from emotional experience not caused by empathizing. This sense of self-agency makes it possible for us to know that what you feel is not your own emotion and by this empathizing causes us to help another when needed instead of avoiding the other because experiencing the other's emotion causes distress. Besides this it was also concluded that facial mimicry is an important factor contributing to empathy in normal individuals, as several studies have found correlations between the degree of facial mimicry and scores of empathizing ability. Also when facial mimicry was made impossible, reduced activity was found in brain areas involved in empathy.

In Chapter 2 the neural base of empathy in normal control individuals was determined. Here it became clear that the neural network involved in empathizing includes various brain areas, distributed all over the brain. It was concluded that the an extended mirror neuron system together with the insula and limbic areas underlie our ability to experience our own emotions but also those of others.

A second issue in this chapter was how a sense of self-agency was generated by the brain. It was determined whether there was a distinction could be made, between brain areas involved in self- or other-perspective taking. This distinction could be responsible for generating a sense of self-agency during empathizing. The answer

to this question remains unclear. It was found that certain sub regions of brain areas were indeed found selectively active during either self- or other-perspective taking. However most studies found that the some brain areas, were involved in taking both the other as the self-perspective. Still a sense of self-agency could be generated, but this would then probably be generated by the interaction between different parts of the empathy network, some parts more involved in emotional awareness of the self and other more involved in emotional awareness of others. Thus a sense of self-agency is probably generated by brain area communicating with each other.

In Chapter 3 it was determined whether individuals with certain psychiatric disorders, which are marked by a deficit in empathic ability, could be related to deficits in facial mimicry (for ASD) or a deficit in a sense of self-agency (ASD, Schizophrenia/Schizotypy, Apathy and social phobia/SAD). Determining whether brain areas involved in a sense of self-agency in normal controls are differently activated in individuals with a deficiency in empathy, could give us more information about the importance of a sense of self-agency. Also determining whether facial mimicry is done less by individuals with a deficiency in empathy, could give us information about the importance of facial mimicry.

Now I will focus on answering the question asked in this thesis: Do the factors self-agency and facial mimicry have an important role in normal empathy?

### **Is facial mimicry important for normal empathy?**

In ASD individuals more general imitation of an action was found impaired (Charman et al., 1997). Next to this more general deficiency in imitation of actions more specific impairments in the imitation of facial expressions were found. Young individuals were found impaired in mimicry of facial expressions (Dawson et al., 1999), and in adolescents automatic facial mimicry was found impaired (McIntosh et al., 2006). It was suggested that perception-action coupling was deficient in ASD (Decety and Moriguchi, 2007). As the perception action coupling takes place in the MNSe, a deficiency in the MNSe was expected. Indeed reduced activity was found in areas that are part of the MNSe. Dapretto et al.(2006) found reduced activity in the IFG and this also correlated with severity of the ASD symptoms. Oberman et al. (2005) also found differential activation patterns in the MNS in individuals with ASD, compared to normal controls. Williams et al. (2006) found activity to be



reduced in the MTG, part of the MNS, in individuals with ASD. Also it was found that activity in the limbic system, the amygdala, varied more in normal controls. It was suggested that the amygdala activity was not properly modulated by the imitation network (MNS).

Summarizing these findings individuals with a deficiency in empathy (ASD individuals) have been found impaired in facial mimicry. According to the shared representation hypothesis facial mimicry, would normally activate the MNS. Activation of the MNS is then thought to modulate our emotional experience in the limbic system (See chapter 1). The studies investigating whether the deficiency in imitative behavior (including facial mimicry) could be related to deficiencies in the empathy network, have indeed found that reduced activity in this network in individuals with ASD. A dysfunctional MNS and limbic system, might be responsible for deficiencies in facial mimicry and empathy.

### **Is a sense of self-agency important for normal empathy?**

Studies discussed in this thesis have shown that certain brain areas play an important role in generating a sense of self-agency. In chapter 2 it was concluded that the TPJ and IPC, in conjunction with the mPFC, PCC and the AI, play an important role in experiencing a sense of self, by comparing the source of sensory signals; whether these signals originate from the self or from the environment. However how exactly these areas generate a sense of self-agency is not really clear yet. In Chapter 1 it was suggested that total overlapping of circuits during other-perspective taking was not possible, because then the individual could lose a sense of the self in experiencing another's emotion. However many studies found certain brain regions involved in both the self- as the other perspective. So how can these areas generate a sense of self-agency? It was suggested that this was created by a network of brain areas, distributed all over the brain. In this network some brain areas seemed to be more involved in processing sensory signals from the self (TPJ and IPC) while others were more involved in processing signals from the environment (mPFC and PCC) The distinction between the self-perspective and others-perspective results from interaction between these areas.

Although most studies that were discussed found that certain brain areas are involved in both forms of perspective taking, evidence was also found that, a distinction can be made within these brain areas. Thus, some parts within these

brain areas are devoted to self-perspective taking, whereas other parts within these brain areas are devoted to other-perspective taking.

Possibly studies which found the whole region to be involved in both perspectives might not have found this distinction, because these sub regions lie so close to each other.

In this thesis, it has been investigated whether a deficiency in empathy, that is found in several psychiatric disorders, could be related to a distorted sense of self-agency. Evidence supporting the idea that a sense of self-agency plays an important role in a normal sense of self-agency has indeed been found. Activity in areas suggested to be involved in a normal sense of self-agency, has been found reduced in individuals with psychiatric disorders compared to normal control individuals. Activity is found reduced in the ventro MPFC in individuals with ASD compared to normal controls (Lombardo et al., 2010). MPFC activity has also been found reduced in individuals with ALEX (Moriguchi et al., 2006). Another study that showed individuals with ALEX could not estimate the pain others were in properly compared to normal controls, and also scored lower on an empathy scale than normal controls (Moriguchi et al., 2007). Also activity in the ACC and dorso lateral PFC was found reduced. Next to these functional abnormalities in individuals with ALEX, activity in the MNS has was also found increased in individuals with ALEX, however this was positively related to impaired perspective taking abilities and also to severity of the ALEX symptoms, suggesting that MNS functioning might have been dysfunctional.

Individuals suffering from schizophrenia have been found severely impaired in their empathic ability (Bora et al., 2008). Also individuals with a predisposition to develop schizophrenia (highly schizotypal individuals) seem to have a lower sense of self-agency, than low schizotypal individuals (Asai et al., 2008). Sysnofzik et al. (2010) gave a possible explanation for this lower sense of self-agency of individuals with schizophrenia. It was found that individuals with schizophrenia varied more in their predictions about what kind of consequence their own action would have, this greater variability correlated positively with their delusions of influence (misattributions of agency to their environment). Also environmental feedback was found very important in generating a sense of self-agency in these patients. The explanation for the weaker sense of self-agency might therefore be related to the difficulty these patients had with attributing self-produced sensory events to the self and the assumption that they were caused by the environment (especially

feedback from the environments was not given or they were unaware of this feedback). A study by Harrison et al (2007) gave evidence supporting this explanation. Here it was found the mPFC and the PCC were deactivated more in individuals with schizophrenia compared to normal controls, when they were instructed to think about what another was feeling.

Individuals with social phobia are suggested to be abnormally high self-focused, they are more aware of their own emotional state than normal controls. So this could mean that their sense of self-agency might be abnormal. Activity in the mPFC/dorsolateral PFC has been found reduced in individuals with social phobia (Sripada et al., 2009; Goldin et al., 2009). Also deactivation of the PCC during a task where other-perspective taking was required was found lower in the PCC in individuals with social phobia (Gentili et al., 2009).

Summarizing results from these studies, functional abnormalities in the mPFC and the PCC are often found in psychiatric disorders that have been associated with a deficit in empathy. These areas have been found activated during self- but also other-perspective taking. An important question that still remains to be answered is how the mPFC and PCC can generate a sense of self-agency, when these areas are active during both self- and other-perspective-taking. Strangely in all discussed studies no functional abnormalities were found in the TPJ and IPC, while these areas are thought to be more involved in self-experience of an emotion or self-perspective taking.

But possibly only parts of the network involved in generating a sense of self-agency are functioning abnormally (mPFC and PCC), which would probably also result in impaired interactions with the other areas (TPJ, IPC) and consequently causing distortions in the sense of self-agency.

Certain brain areas that are found active during both self-and other- perspective taking (like the mPFC), could be divided in different sub regions, with each sub region being responsible for either self- or other perspective taking. Therefore it would be interesting, for future research to also focus on whether differential activations within brain areas (subregions) between individuals with psychiatric disorders and normal controls can be found.

This thesis has shown that we can learn more about the role of facial mimicry and self-agency in empathy by investigating psychiatric disorders in which deficiencies in empathy have been found. However next to doing research with individuals with

psychiatric disorders, it remains important to also investigate how a sense of self-agency and facial mimicry are important for normal control individuals. A reason why this is important, is because individuals with psychiatric disorders vary in their symptoms or the severity of their symptoms. This variability within a group of patients could influence in which brain areas reduced activations are found. For example different results were found when individuals with schizophrenia are divided in groups, based on their symptoms. For example schizophrenia patients with psychosis were more impaired in their sense of self-agency than individuals without psychosis (Kircher et al., 2003). Therefore for future research I would advise to take a very specific group of individuals, all with similar (severity of) symptoms.

That sense of self-agency and facial mimicry are both important factors contributing to the empathic ability in humans has been supported by studies discussed in this thesis. Deficiencies in empathy were indeed associated with deficiencies in both self-agency and facial mimicry. This thesis has given some insights in how a sense of self-agency and facial mimicry are important for normal empathy. However some issues remain unclear. For example how can the network of brain areas involved in empathy, generate a sense of self-agency precisely? Is there really a similar mechanism in the brain like the one used for generating self-agency in action? And why have some studies found a distinction within brain areas between areas involved in either the self- or the other-perspective while most other's have not? Further research is necessary to answer these questions.

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