# Mirror images

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# Autism and the mirror neuron system

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Autism spectrum disorders and the putative mirror neuron system
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## Abstract

The idea that the core symptoms of autism could have originated from a dysfunctional mirror neuron system has received much attention from the media in the past five years. In this review, we evaluate this controversial claim by examining a wide array of behavioral, neurophysiological, and neuroimaging studies on imitation, action perception, and face perception in Autism Spectrum Disorder. We observe that the available evidence for a disruption of the mirror neuron system in autism is quite inconsistent. Several factors that could contribute to an explanation of these inconsistencies are: the nature of the stimuli, the degree of identification with the actor, and the attention paid to the actor's movements. Furthermore, the age of the participants may play an important role, since there are indications that in autism functioning of the mirror neuron system might improve with age. The available evidence does not support the claim that a dysfunctional mirror neuron system can explain the whole constellation of autistic symptoms, but does instigate an interesting modified hypothesis. Autism might be characterized by a developmental delay that predominantly affects the functioning of strictly congruent mirror neurons, which are rarer than broadly congruent ones and are necessary to represent the precise body kinematics of observed actions. Such a specific and transient difficulty might be the consequence of differences in synaptic plasticity and/or early deficits in orienting attention towards biological motion and faces, and could account for some of the imitation difficulties found in autism.

## 5.1 Introduction

Mirror neurons were discovered in the ventral premotor cortex of the monkey (area F5), which was studied for its involvement in action preparation. Mirror neurons have the astonishing property of firing not only when the monkey performs an action, but also when the monkey observes or hears another individual perform a similar action (di Pellegrino et al., 1992; Fujii et al., 2008; Gallese et al., 1996; Keysers et al., 2003; Kohler et al., 2002; Umiltà et al., 2001). With the firing of these neurons, the monkey can be said to 'simulate' the actions of others: it activates premotor neurons *as if* it were performing a similar action. More recently, neurons with the same property were also found in the inferior parietal cortex (area PF/PFG) of the monkey (Fogassi et al., 2005; Fujii et al., 2008; Rozzi, Ferrari, Bonini, Rizzolatti, & Fogassi, 2008). A continuum of response properties has been uncovered, which ranges between the features of two types of prototypical mirror neurons. On one end of the continuum there are strictly congruent mirror neurons, which only fire when the observed action is performed with the same effector and in the same manner as the action they serve to execute. On the other end there are broadly congruent mirror neurons, which fire during the observation of a range of actions that share the same goal as the one they serve to execute, irrespective of the effector used by the other individual (Gallese et al., 1996; Keysers, Thioux, & Gazzola, 2011; Rizzolatti & Craighero, 2004). For example, a mirror neuron that responds selectively to the observation and the execution of a precision grip is classified as strictly congruent. A mirror neuron that is responsible for the observation and execution of a precision grip, but that also fires to the observation of another individual grasping with the whole hand, the foot, or the mouth, is classified as broadly congruent. Strictly congruent mirror neurons may encode the specific details of *how* an observed action is performed, while broadly congruent mirror neurons are well-positioned to encode the goal of the action, that is *what* it tries to achieve, irrespective of *how* it is achieved –with the hand, with the mouth, or even with the foot (Keysers et al., 2011; Thioux et al., 2008).



### 5.1.1 The human mirror neuron system

Humans also 'simulate' the actions of others in their action execution system: activity in the parietal and premotor regions increases when a subject observes someone else performing an action (Buccino et al., 2001; Gazzola & Keysers, 2009; Gazzola et al., 2007; Grèzes et al., 2003; Iacoboni et al., 1999; Shmuelof & Zohary, 2005; Tai, Scherfler, Brooks, Sawamoto, & Castiello, 2004), or hears the sound of an action (Gazzola et al., 2006). Furthermore, action perception facilitates congruent motor output as measured using motor evoked potentials (Aziz-Zadeh, Iacoboni, Zaidel, Wilson, & Mazziotta, 2004; Urgesi et al., 2006) and reaction times (Brass, Bekkering, Wohlschlager, & Prinz, 2000). Recently, several research teams have used functional magnetic resonance imaging (fMRI) to examine more closely whether the same neuronal populations in the parietal and premotor cortices are recruited during both action execution and observation. Two experiments have confirmed this by showing cross-modal adaptation: the blood-oxygen-level- dependent (BOLD) signal in the parietal and premotor cortices is diminished during action observation when it is preceded by the execution of the same action, relative to a different action (Chong, Cunnington, Williams, Kanwisher, & Mattingley, 2008; Kilner, Neal, Weiskopf, Friston, & Frith, 2009). Two other studies

have demonstrated that a pattern classification algorithm, which has learned to discriminate brain activity corresponding to the participants listening or watching actions A and B, can also discriminate above chance whether on different trials the participants executed action A or B (Etzel et al., 2008; Oosterhof, Wiggett, Diedrichsen, Tipper, & Downing, 2010). The cross-modal adaptation of the BOLD signal and the successful pattern classification across execution and perception suggest that the activity across the premotor and parietal regions during action observation reflects the firing of neuronal populations that encode information about the actions (*what* and *how*) in the same manner as when executing similar actions.

In humans, mirror neurons are thought to play an important role in imitation and in understanding the goal behind the actions of others (Iacoboni, 2009; Keysers, 2009; Rizzolatti & Craighero, 2004; Rizzolatti & Luppino, 2001). In addition, a subset of mirror neurons encoding mouth and face movements may contribute to the perception of facial expressions (Ferrari et al., 2003; Mukamel et al., 2010). The observation of facial expressions is associated with increased activity in regions of the inferior precentral and inferior frontal gyri that are also involved in producing similar expressions (Carr et al., 2003; Leslie et al., 2004; van der Gaag et al., 2007). This activity is thought to trigger congruent activity in emotional brain regions such as the insula and the amygdala (Carr et al., 2003; Jabbi & Keysers, 2008), which are involved in experiencing similar emotions (Jabbi et al., 2007; Wicker et al., 2003). According to this hypothesis motor simulation could also contribute to decoding the emotional value of facial expressions (Bastiaansen et al., 2009; Iacoboni & Dapretto, 2006; Jabbi & Keysers, 2008).

The same network, comprising the inferior frontal gyrus (IFG), the insula, and the amygdala, is also likely to be active during 'facial mimicry' (Carr et al., 2003; Lee et al., 2008). Electromyography (EMG) recordings during the observation of facial expressions demonstrate the occurrence of spontaneous reactions in those muscles of the face that are also involved in the production of that facial expression –for instance in the zygomaticus major muscle when viewing a series of happy faces (Dimberg et al., 2000). These spontaneous reactions of the facial muscles occur approximately 500 ms after stimulus onset. The fact that witnessing an angry expression is often associated with activity in the frontalis muscle, which is involved when producing a fearful expression (Beall et al., 2008), and the fact that viewing body postures can also trigger an emotionally congruent reaction in the muscles of the face (Magnée, Stekelenburg, Kemner, & De Gelder, 2007; Tamietto et al., 2009), suggest that these facial reactions may occur following an emotional response. The reader is, however, also seems to be true: sometimes facial reactions influence the way emotions are perceived (Niedenthal, 2007). In fact, blocking facial mimicry affects the perception of the boundary between different emotional expressions (Niedenthal et al., 2001), as well as the perceived duration of an emotional expression (Effron et al., 2006). Taken together, these observations indicate that motor simulation and emotional processing interact reciprocally during the perception of facial expressions.

### 5.1.2 Development of the human mirror neuron system

Little is known about the early development of the mirror neuron system (MNS). Two studies have collected indirect measurements of mirror neuron activity in infants using electroencephalography (EEG, Lepage & Théoret, 2006) and Near-Infrared Spectroscopy (Shimada & Hiraki, 2006). The

results suggest that activation of the (pre)motor cortex during action observation is present by the age of 6 months. At this age, infants show a propensity to encode the goal of the actions they observe (Woodward, 1998), which might reflect the work of the MNS. The tendency to encode the goal of observed actions is not present earlier in life, but seems to develop together with the infant's ability to execute the same actions (Sommerville & Woodward, 2005; Sommerville, Woodward, & Needham, 2005, but see Csibra, 2008; Kamewari, Kato, Kanda, & Ishiguro, 2005; Southgate, Johnson, & Csibra, 2008). Therefore, the MNS might gradually develop between 0 and 6 months, hand in hand with the child's ability to execute goal-directed actions.

According to Keysers and Perrett (2004), Hebbian learning could explain the development of the MNS. Since during grasping the child is also spectator of her own hand actions, parietal and premotor neurons fire at the same time as some neurons in the posterior superior temporal sulcus (pSTS), which respond to the observation of hand actions irrespective of the viewpoint. Those neurons that fire at the same moment strengthen their connections through Hebbian synaptic potentiation. This increases the specificity of the connections between the pSTS neurons, which are involved in the perception of body movements, and the grasping circuits of the parietal and premotor cortex, where mirror neurons will acquire their property. The same pairing between execution and observation also occurs in situations where one is being imitated (Brass & Heyes, 2005; Del Giudice et al., 2009; Heyes, 2001). For instance, a child cannot observe its own facial expressions, but the adult who imitates the child's expression can serve as a mirror. This could trigger an activation in the child's pSTS that becomes associated with the premotor cortex activity corresponding to the expressed emotion (for a different perspective see Meltzoff & Decety, 2003). Recently, Del Giudice et al. (2009) proposed that the early development of the MNS could be canalized by several genetic factors such as the spontaneous and cyclical movements present in childhood between 0 and 6 months, and a hard-wired preference for biological motion and for perfect contingencies between perception and sensation. Spontaneous movements occurring cyclically could help develop stable neuronal circuits in the (pre)motor cortex. At the same time, a child's preference for biological motion and perfect contingencies could guide their attention towards their own movements and optimize Hebbian learning.



### 5.1.3 The mirror neuron theory of autism

Some researchers have proposed that the core symptoms of autism could result from an impairment of the MNS. The central idea is that if mirror neurons support the ability to imitate others and to understand the goal behind their actions, the disruption of this system might also impair the later development of the ability to understand the state of mind of other people (Iacoboni & Dapretto, 2006; Meltzoff & Decety, 2003; Oberman & Ramachandran, 2007; Rizzolatti & Fabbri-Destro, 2008; Rizzolatti et al., 2009). To examine this hypothesis in detail, we review studies that have investigated the cerebral substrate of imitation and action perception in Autism Spectrum Disorder (ASD) in the following sections. We begin with studies where participants were explicitly requested to imitate the observed actions and then turn to studies investigating the observation of hand action without imitation, which can be regarded as automatic imitation or action simulation from a MNS perspective. Before concluding, the penultimate section will examine in detail automatic facial reactions and the involvement of simulation mechanisms during the perception of emotional

expressions, which seems to constitute an area of particular weakness in autism.

## 5.2 On Imitation

### 5.2.1 Neuroimaging findings on imitation

Three studies have compared brain activity in individuals with ASD and controls during tasks that explicitly required the imitation of facial expressions or hand/finger movements. One study used magnetoencephalography (MEG) to test imitation in eight adults with ASD and 10 control participants (Nishitani, Avikainen, & Hari, 2004). Subjects had to reproduce three different mouth configurations that corresponded to the ones seen on pictures of a face. Source analysis revealed that the active brain circuit during imitation, comprising occipital cortex, STS, inferior parietal lobule, IFG, and primary motor cortex (MI), was similar in the two groups. However, in the ASD group activation of the IFG was delayed approximately 50 ms. In addition, the activation of the IFG and MI was weaker compared to controls. In both groups, MI activation was observed approximately 50 ms after activation of the IFG. The two other experiments used fMRI to investigate the cerebral network involved during imitation in autism. In the first study, Dapretto et al. (2006) scanned children with autism and matched controls (12 ± 2 y.-o.) while they were imitating and observing emotional facial expressions. In contrast to the typically developing children, the children with ASD did not activate the pars opercularis of the inferior frontal gyrus (BA44) during imitation. This difference was found both in the contrast between imitation and rest within the ASD group, and in the direct comparison between the groups. In addition, BA44 was also less active in the ASD group compared to controls during the passive observation of emotional expressions. Finally, activity in the pars opercularis was negatively correlated with symptom severity in the ASD group during imitation. These results are unlikely to be attributable to a failure in attending to the faces: the children in the ASD group showed reliable activity in the fusiform gyrus and amygdala, and their imitation performance did not differ from that of control participants. The authors conclude that the failure to activate BA44 denotes a deficit of the mirror neuron system in autism. In the second fMRI study, Williams et al. (2006) tested the imitation of finger movements in 16 adolescents with ASD and 15 matched controls (15 ± 2 y.-o.). In this experiment (adapted from Iacoboni et al., 1999), the subjects had to move their right index or middle finger in response to a stimulus, which was either a movie of the finger movement, a still picture of a hand with a cross over the finger that had to be moved, or a grey background with only the cross that indicated which finger to move. The direct comparison between groups showed that several areas were less active in the participants with autism during the imitation of finger movements (- rest), including the inferior parietal cortex. The authors interpreted this as a deficit of the MNS. This conclusion is weakened, however, by the fact that for the same contrast several areas were hyper-active in participants with autism, including the left precentral gyrus, which is a major component of the human MNS. Furthermore, there was no significant group difference in the network of brain areas that was more active during the imitation condition compared to the simple execution of the finger movement (in front of a still hand or a grey background). Moreover, in contrast with previous research (Iacoboni et al., 1999), differences in activity were not seen in the inferior frontal gyrus (BA44) for this contrast, not even in the control group.

Although the three aforementioned studies suggest that the cerebral network involved in the imitation of hand actions and facial expressions might be abnormal in autism, they do not reveal consistent differences in MNS activity. One study found a delayed and weaker activation of the IFG, one reported a complete absence of activity in BA44, and one study found a hypo-activation of the inferior parietal lobe, along with many other areas of hypo- and hyper-activation. These inconsistencies may largely result from the different stimuli used in the three experiments. Participants had to imitate non-meaningful mouth movements in the first study (Nishitani et al., 2004), meaningful emotional expressions in the second study (Dapretto et al., 2006), and non-meaningful finger movements in the third study (Williams et al., 2006). These findings suggest that imitation of facial expressions may be particularly challenging for children with ASD. Before drawing any conclusions about the role of mirror neurons in imitation difficulties and in the etiology of ASD, the nature and severity of the imitation difficulties in autism should be carefully considered.

### 5.2.2 Nature of imitation difficulties in autism

The most carefully designed studies on imitation performance have included a control group of children that is matched to the ASD group on the basis of mental age and verbal IQ. These studies have shown that the overall level of development explains most of the interindividual variability in imitation performance, and that the overlap of performance between groups is large (e.g. Beadle-Brown & Whiten, 2004; Charman & Baron-Cohen, 1994; Charman et al., 1997; Perra et al., 2008; Rogers, Hepburn, Stackhouse, & Wehner, 2003). Part of the imitation difficulties may even be accounted for by factors that are not specific to imitation or action perception-execution matching. For instance, Vivanti and collaborators (2008) recently showed that the low performance of their ASD group in imitating non-meaningful gestures could be explained by the amount of time these individuals spent fixating the demonstrated action. This important finding suggests that the performance of subjects with ASD on imitation tests may suffer from their difficulties in the perception of biological motion more generally (Blake, Turner, Smoski, Pozdol, & Stone, 2003; Klin, Lin, Gorrindo, Ramsay, & Jones, 2009). This ability involves the pSTS, a cortical area that is considered to be the main source of input to the MNS, in which decreased grey matter volume has been reported in autism (e.g. Boddaert et al., 2004; Hadjikhani, Joseph, Snyder, & Tager-Flusberg, 2006). The contention that imitation can be impaired in autism for reasons other than a dysfunction of the observation-execution matching mechanism was tested by Leighton et al. (2008). The authors studied a group of 16 adults with ASD, who displayed a deficit for both mirror and non-mirror imitation compared to well-matched controls. They gave the participants two new variations of the imitation task the ASD group had performed poorly on. In one version, the to-be-performed action was indicated by the movements of geometrical shapes on the screen, instead of the human hand movement. In another condition, the execution aspect of the task was removed, and the participants had to describe what the human agent was doing. Participants with autism were impaired on the two alternative versions of the test as well. Therefore, the authors concluded that the imitative nature of the main task was not responsible for the low performance in this group. It should be noted, however, that the origin of the difficulties observed in the two alternative versions of the imitation task remains unexplained. Following the instructions indicated by the movements of the shapes might, for instance, be accomplished in controls by using the same neuronal ensembles

as those used for action perception-execution matching (Schubotz, 2007). Furthermore, a deficit in the processing of biological motion could contribute to the imitation deficit in the other test (i.e. verbal description of hand actions). The merit of this study is that it stresses the importance of testing more precisely what aspects of the imitation task are fundamental to the difficulties experienced by individuals with ASD, as the problem might not be restricted to matching action perception with execution, but might occur 'upstream' (Tessari, Canessa, Ukmar, & Rumiati, 2007).

When examining the role of the MNS in the imitation difficulties evidenced in ASD, it is also important to realize that not all aspects of imitation performance are equally affected. The difficulties experienced by individuals with autism seem much greater when they have to understand the beliefs of someone else than when they have to imitate hand actions (Hamilton, Brindley, & Frith, 2007). Critical for the mirror neuron hypothesis, children with autism do not seem to have much difficulty reproducing the goal of an action that was demonstrated by an experimenter (Aldridge, Stone, Sweeney, & Bower, 2000; Carpenter, Pennington, & Rogers, 2001). Carpenter et al. (2001) tested infants between two and five years old on a task in which children were shown an action performed on an object, and were then given the opportunity to manipulate the object themselves (Meltzoff, 1995). Both children with autism and mentally retarded children accomplished the target actions more often after being shown a failed attempt to perform the action than after witnessing a non-purposeful action or during prior spontaneous interaction with the objects. Furthermore, in both groups children performed the expected target action after viewing a failed attempt as often as after the experimenter showed the correct end state. In this experiment, children with autism were perfectly able to interpret actions in the context of their goals. According to Hobson and collaborators (2008; 1999), one aspect that seems more problematic for these children is the reproduction of the style of an action –for instance, throwing a ball into a trashcan gently (underhand toss) or more forcefully (overhand throw). The authors showed that the style in which an action is performed is unlikely to be reproduced by children with autism, especially when the style is not necessary for the successful accomplishment of the action. Children with autism did perform similarly as controls in the imitation of goal-directed actions demonstrated on unfamiliar objects. According to Hobson and Hobson (2008), the specific difficulty imitating the style of an action might indicate a difference in the quality of the intersubjective engagement during the test (Hobson & Meyer, 2006; see also Carpenter, 2006). From our own perspective, the dissociation between goal and style is reminiscent of the distinction between strictly and broadly congruent mirror neurons. While both strictly and broadly congruent mirror neurons respond to the sight of the action they serve to execute, broadly, but not strictly, congruent mirror neurons also discharge during the observation of other actions that achieve the same goal using different means (or styles, following the denomination of Hobson and collaborators). Given that strictly congruent mirror neurons make up only one third of the MNS (Gallese et al., 1996), the accurate encoding of the style that depends on this subpopulation should be three times more vulnerable to neural dysfunctions than the encoding of the action goal, which might explain the dissociation between goal and style replication found in autism.

### 5.2.3 Comments

In conclusion, evidence for an impairment of imitation skills in autism as a result of a dysfunction of

the MNS is still scarce and inconsistent. Recent investigations that try to characterize more precisely the nature of the imitation difficulties help clarify the possible role of the MNS. The dissociation between the imitation of goal and style (Hobson & Hobson, 2008) suggests that the MNS might function sufficiently well to successfully match the goal of observed actions, but not well enough for the more vulnerable reproduction of style. At the same time, the finding that the time spent looking at the action can explain the performance on the imitation of meaningless gestures (Vivanti et al., 2008) suggests that an impairment of the pSTS, upstream of the MNS proper, may also play a critical role in imitation difficulties. The pSTS is implicated in the perception of biological motion and is the main source of input of the MNS. Any deficit at this level can be expected to have serious effects on the functioning and development of this system. Finally, the participation of the MNS in the processing of emotional facial expressions might be critically impaired in children with autism, which may contribute to some of the social difficulties evident in ASD as we shall discuss later.

## 5.3 Observation of hand actions

Other researchers have looked for evidence for a dysfunction of the MNS in autism in the simulation of observed actions without an explicit action imitation requirement. Here again, studies that have looked at the neural response during action perception have produced relatively inconsistent results.



### 5.3.1 MEG, EEG, and fMRI investigations

One early study used MEG (2x61 channels) to record the response of the motor cortex during action execution and action observation in five adults with autism and eight controls (Avikainen, Kulomaki, & Hari, 1999). The left and right median nerves (running the length of the arm) of the subjects were stimulated alternatively, while the rolandic oscillations in the Beta frequency range (~20 Hz) were used as an indicator of MI activity. During rest, stimulation of the median nerve is followed by a 20Hz-rolandic rebound. This induced rebound is abolished when the participant executes an action, and is also greatly reduced during action observation. The same action-observation-induced suppression of the rolandic rebound was found in controls and participants with autism. This indicates that in this group of young adults with autism, the motor cortex activity was modulated during action observation in a similar way as in controls. The groups were, however, small and the variability between individuals with autism was large.

In addition to this MEG study, several research groups have used EEG to measure the suppression of *mu* rhythms over the central electrodes during action execution and action observation in individuals with ASD. Mu rhythms are EEG oscillations recorded over the sensorimotor cortex in (or slightly above) the alpha frequency range (8.5–10.5 Hz), which are suppressed during movement execution and observation in typically developing subjects; a phenomenon that is thought to indirectly reflect the firing of neurons in the (pre)motor cortex (Pineda, 2005). In one experiment, Oberman et al. (2005) found a complete absence of mu rhythm suppression during the observation of hand actions in autism. In this experiment, participants opened and closed their hand, watched a movie of the same action, watched a movie with two bouncing balls, and watched

a display consisting of background white noise. In controls, significant mu suppression was observed for both the action execution and action observation conditions relative to baseline, but not during the observation of bouncing balls. In ASD, mu suppression was present during execution, but it was completely absent for the observation of hand movements. In a complementary experiment with a group of children between eight and 12 years of age, Oberman et al. (2008) found that the mu wave suppression was significant in the autism group if the hand performing the action in the movie was familiar, but not when it was unfamiliar. The absence of mu wave suppression in ASD during the observation of hand actions has, however, not been replicated by three other research teams. In one study, Bernier and collaborators (2007) asked young adults with and without ASD to watch a grasping action, execute the same action, and imitate the action. Significant mu suppression was found in all three conditions in participants with ASD, though the effect was less pronounced compared to controls. In another study, Fan and collaborators (2010) had their participants (n=20 ASD, 11-26 y.-.o, n=20 matched controls) observe videos of a hand manipulating a small object, and execute the same action. Significant mu suppression was found in both groups during imitation as well as passive observation of hand actions. Furthermore, in both groups mu suppression was larger for the observation of hand actions than for the observation of a moving dot. Finally, Raymaekers and collaborators (2009) reported significant mu wave suppression in two groups of children aged between eight and 13 years, who observed and executed a meaningless hand movement (i.e. closing and opening of the hand). Here also, mu suppression was larger in both groups during the observation of hand movements than during the observation of a bouncing ball (non-biological motion). Interestingly, in this study involving younger children the authors found a significant correlation between the index of mu suppression and the age of the participants in the ASD group only. Similar to the original studies by Oberman and collaborators (2005; 2008), this study tested meaningless hand movements that are usually less accurately imitated than meaningful ones in autism (Rogers, Cook, & Meryl, 2005; Vivanti et al., 2008; Williams, Whiten, & Singh, 2004). Therefore, normal mu suppression in this experiment demonstrates that the use of meaningless movements may not explain the absence of effect found in the original study. The more recent study by Oberman et al. (2008) suggests that instead the engagement of ASD individuals in the task may be a major determinant of the amount of simulation. In the familiar hand condition the children were shown a picture of the actor (family member or self) before the movie depicting the hand action, which might have helped those with ASD to identify with the actor.

Further research is needed to reveal the effects of different experimental variables on mu wave suppression in ASD. Since autistic symptoms appear early in life and may change over the course of development, the presence of mu wave suppression should ideally be tested in very young children. Mu rhythms are, however, not always easy to find using EEG. For instance, testing children between five and seven years of age, Martineau and collaborators (2008) failed to find a modulation of the mu rhythms that they had previously found in adults (Cochin, Barthelemy, Roux, & Martineau, 1999). In this experiment, children watched complex dance movements or control stimuli representing landscapes. Interestingly, a modulation of theta rhythms (1 – 5.5 Hz) was found in typically developing children that was absent in children with ASD (Martineau et al., 2008). As there was no execution condition in the experiment, it is impossible to know whether this difference in theta rhythms modulation should be attributed to a dysfunction of the MNS. This finding indicates, however, that exploring other frequency bands might be necessary to capture mirror neuron activity

in younger children.

Surprisingly, only a couple of studies have used fMRI to investigate the passive observation of hand actions in ASD. The results of these two studies are rather straightforward: there seems to be no major deficit in the cerebral network involved in simulating hand actions. Martineau and her colleagues (2010) compared the cerebral activity of seven adults with ASD and eight control participants while they observed and executed flexion-extension hand movements. No cerebral area was hypo-active in the ASD group. On the contrary, relative to controls, the ASD participants showed hyperactivation of the inferior frontal gyrus pars opercularis (BA44) in both hemispheres during the observation of meaningless hand movements compared to the observation of a hand at rest. In a sophisticated experiment, Dinstein et al. (2010) used a repetition suppression technique to investigate the response of the MNS during action execution and observation. Thirteen adults with ASD and 10 controls observed meaningful hand postures and performed the same gestures. For action execution, the same reduction in BOLD signal was observed in both groups in the premotor cortex and the intraparietal region for repeated relative to novel finger movements. During observation, the reduction of the signal with stimulus repetition was also observed in both groups, but only in the intraparietal region. The direct comparison between groups also did not reveal major differences in mirror neuron areas. In both groups, the intraparietal region and the ventral premotor cortex were active during both action observation and execution. Interestingly, a supplementary analysis of the within-subject variability (across blocks) showed that the variability of the BOLD response was higher in individuals with autism, despite similar average levels of whole-brain hemodynamic responses.



### 5.3.2 Measuring interference from observed actions

A behavioral interference paradigm makes it possible to obtain an indirect measurement of the motor cortex activity elicited by action observation. In a simple but powerful experiment, Bird et al. (2007) asked adult participants with and without ASD (n=15 in each group) to watch short movies of a human or a robotic hand changing from a neutral intermediary position to an open or closed position. The participant's task was to open or close their dominant hand as soon as the stimulus started to move. The onset of the visual stimulus served as a go signal, but whether the stimulus was of the open or closed type was irrelevant to the action of the participant. Participants performed blocks of the same movement in which the observed action could be either congruent or incongruent with the executed movement. Similar to controls, participants with autism were slower when the action was performed while viewing an incongruent stimulus. This is suggestive of normal automatic activation of the (pre)motor cortex during action observation. Furthermore, in both groups the interference effect was more pronounced when the observed action was performed by a human than by a robot, which is in agreement with the idea that mirror neurons are preferentially tuned to react to biological motion (Dayan et al., 2007). In the same vein, Spengler et al. (2010) recently reported significant interference of observed actions on the executed actions of adult participants, who were requested to lift a finger in response to a number that appeared superimposed on a movie of a hand performing a congruent or incongruent finger movement. Although these results suggest normal interference from observed actions in autism, an interesting observation from another research group provides some support to the idea that individuals with

autism *sometimes* fail to simulate other people's action in their (pre)motor cortex. Welsh and collaborators (2009) asked the participants in their experiment to reach for a target position on the left or on the right side of a table, alternating turns with another subject, who was sitting in front of them. In the course of each turn, the subjects performed two consecutive reaching actions. When reaching twice for the same location, both controls and participants with ASD showed an inhibition of return, which means that they were slower reaching for a location when they had reached for the same location just before (within-subject IOR). Interestingly, an inhibition of return was also found when the subjects had to reach for a location just after the other participant had reached for the same location (between-subjects IOR). Here, an interesting difference emerged between the groups. Participants with ASD showed a between-subjects IOR if, and only if, the LED that triggered the other's response was visible. When the LED could not be seen, and the subjects could only see the end of the other participant's movements, the inhibition of return disappeared in the group with autism, but remained in the control group. This suggests that in contrast to controls, participants with ASD were not influenced by a representation of the action of the other individual in their motor cortex. At first glance, these results seem to contradict the two other studies' reports of normal interference (Bird et al., 2007; Spengler et al., 2010). One explanation could be that in the context of this game, participants with ASD looked at the LED and paid little attention to the hand of the other player, since it was not required by the task. If this interpretation is correct, it would support the idea that individuals with ASD are somehow less likely to automatically orient their attention towards the movements of other humans (Klin et al., 2009).

### 5.3.3 Monitoring hand muscles activity

Two additional studies must be described before closing this section on the simulation of hand actions. Both studies found significant group differences when looking at muscle-specific reactions triggered by action observation. In an experiment involving 10 adults with ASD and 10 controls, Théoret et al. (2005) used transcranial magnetic stimulation (TMS) over the motor cortex to measure the modulation of motor evoked potential (MEP) by the observation of finger movements. The hand on the video was presented either in egocentric or allocentric view (i.e. fingers facing away or towards the observer, respectively). During action observation, MEPs of control participants increased in the muscle involved in executing the observed movement (relative to the other muscles). In autism, MEP facilitation was found for hands in an allocentric orientation, but not for hands in an egocentric orientation. This may indicate a specific difficulty in identifying with the actor when the hand is seen from an egocentric perspective. A more drastic difference was described in another study. Cattaneo et al. (2007) used EMG to record the activity of the mouth-opening mylohyoid muscle while participants were grasping or were observing someone grasping an object with the purpose of either eating it or placing it in a container The participants were seven children with ASD and eight controls between five and nine years old. In anticipation of the subsequent action, children in the control group already activated the mylohyoid muscle during the reaching phase of the "grasping to eat" action. The same was true when they observed the same action being performed by the experimenter. During execution, children with ASD failed to show preparatory activity of the mylohyoid muscle before the bringing-to-the-mouth phase of the action. Moreover, they showed no activation of this muscle during observation, not even during the last

phase, when the experimenter was moving the food to his or her mouth. In a complementary experiment, the execution of a chain of hand-foot actions was tested. Participants were asked to reach and grasp a piece of food and throw it in a garbage can, which could be opened using a foot pedal. Activity was recorded from the ankle dorsiflexor muscle. Control participants anticipated the pedal opening during the grasping phase, whereas the children with ASD did not. These results suggest that children with ASD fail to anticipate the next action they are going to perform in their motor cortex, while typically developing children do (see also Fabbri-Destro, Cattaneo, Boria, & Rizzolatti, 2009). In addition, while typically developing children showed a modulation of the ankle muscle during and shortly before observing that of the demonstrator, children with ASD failed to show any evidence of simulating the observed actions in their motor cortices. Naturally, simulation need not occur if the subject is unable to execute the observed action. Therefore, if the children with ASD did not anticipate the next action they were going to perform themselves, they may not have anticipated the action of the experimenter in their motor cortex. The results indicate, however, a complete absence of motor activity during observation in the group with ASD, while they were capable of performing the action themselves –albeit without the typical sequential anticipation (Fabbri-Destro et al., 2009).

### 5.3.4 Comments

In summary, concerning the automatic simulation of hand actions/finger movements, three studies reported abnormal motor simulation (Cattaneo et al., 2007; Oberman et al., 2005; Welsh et al., 2009), three studies found partial support for a simulation deficit (Bernier et al., 2007; Oberman et al., 2008; Théoret et al., 2005), and seven studies reported normal (or enhanced) motor simulation (Avikainen et al., 1999; Bird et al., 2007; Dinstein et al., 2010; Fan et al., 2010; Martineau et al., 2010; Raymaekers et al., 2009; Spengler et al., 2010). It is often argued that negative findings should be considered with caution, because the study may have simply lacked the statistical power to detect the hypothesized effect. However, in the case of the studies failing to find a group difference between controls and participants with ASD, this argument is much more difficult to apply. Given that those studies that failed to find group differences are those that did demonstrate significant evidence for action simulation within the ASD group, and given that those that did find group differences are those that failed to find evidence for simulation in ASD, it is unclear which of the two groups of studies should be discarded as possible ‘false negatives’. Instead, it seems more promising and important to examine the factors that could explain why some studies failed to find significant motor simulation in their cohort of participants with autism. The results of the three experiments that reported an interference effect of observed actions suggest that, while the automatic activation of motor simulation circuits may be preserved (Bird et al., 2007; Spengler et al., 2010), orientation towards biological motion is probably an important variable (Welsh et al., 2009). Furthermore, mu wave suppression and MEP experiments show that the familiarity or level of identification with the actor is also likely to influence the amount of motor simulation in autism (Oberman et al., 2008; Théoret et al., 2005). These factors (attention to biological motion and familiarity/identification with the actor) may contribute to the high variability of BOLD response described in individuals with ASD (Dinstein et al., 2010). Finally, most experiments investigating the simulation of hand actions have tested adult participants. Those that tested children between seven

and 12 years of age have reported either a significant difference between groups (Cattaneo et al., 2007; Oberman et al., 2008) or a positive effect of age on action simulation in the ASD group (Raymaekers et al., 2009).

## 5.4 Facial and bodily expressions

Facial expressions constitute a very particular class of stimuli for individuals with autism, who tend to look less at the eye region or even at the face as a whole (e.g. Corden, Chilvers, & Skuse, 2008; Warren Jones, Carr, & Klin, 2008; Klin & Jones, 2008; Klin, Jones, Schultz, Volkmar, & Cohen, 2002; Pelphrey et al., 2002; Spezio, Adolphs, Hurley, & Piven, 2007a, 2007b), and who as a group tend to demonstrate difficulties in discriminating emotions from facial expressions (e.g. Ashwin, Chapman, Colle, & Baron-Cohen, 2006; Corden et al., 2008).

### 5.4.1 Inferior frontal gyrus pars opercularis and face perception

Although early fMRI studies of face perception in autism often concentrated on the functioning of the fusiform face area, several teams of investigators have now reported whole-brain group comparisons during passive observation of emotional or neutral faces (Ashwin et al., 2007; Dapretto et al., 2006; Hadjikhani et al., 2007), and also during perceptual tasks requiring the participants to detect female faces (Pierce et al., 2004), detect their own face in morphed pictures (Uddin et al., 2008), or match upright and inverted faces (Bookheimer et al., 2008). As far as potential differences in motor simulation are concerned, it is difficult to draw any straightforward conclusion from these experiments. Two out of three studies involving adult participants failed to find any group differences in mirror neuron areas (Ashwin et al., 2007; Pierce et al., 2004). The third study found a hypo-activity of the pre- and post-central regions, and the inferior frontal gyrus during passive viewing of neutral faces (Hadjikhani et al., 2007). However, in this case, the difference could also be attributed to the greater proportion of female participants in the control group, as women are thought to be more empathic and simulate more than males (Baron-Cohen, Knickmeyer, & Belmonte, 2005). Three studies, which tested younger participants between eight and 18 years of age, revealed significant hypo-activation of the inferior frontal cortex (Bookheimer et al., 2008; Dapretto et al., 2006; Uddin et al., 2008). The areas of hypo-activity are, however, scattered over the inferior frontal region; some areas with group differences are more than 25 mm apart from each other (Marc Thioux & Keysers, 2010). Unquestionably, these studies used very different tasks and stimuli. It is still unclear whether all these tasks and stimuli are equally well-suited for investigating the simulation of facial expressions.

We recently obtained fMRI data from a relatively large group of 21 adult participants with ASD and 21 controls while they watched short movie clips of actors displaying neutral, pleased, and disgusted facial expressions (Bastiaansen et al., 2011a). We did not find any group difference between participants with and without ASD, even when focusing the analysis on a region of interest in the inferior frontal gyrus (BA44), where Dapretto et al. (2006) found a significant reduction of activity in a group of (only 12) children with ASD. However, in our study involving adults between 18 and 55 years of age, activity in pars opercularis (BA44) increased significantly with age in participants with ASD, but not in controls. While the youngest adults with autism showed significant

hypo-activation of BA44, by age 30 activity in this region was indistinguishable between the two groups. Importantly, this age-related increase of activity in BA44 in autism was associated with improvements in social functioning. The same relationships between BA44, age, and social functioning were not found in the control group of participants, who were pairwise-matched with the participants with autism on age, gender and full-scale IQ. Furthermore, these correlations were not found in another control group that was scanned using the same protocol. This group consisted of individuals with a diagnosis of schizophrenia, who had scores that were comparable to the ASD group on a social functioning questionnaire. Therefore, the increase of activity in BA44 with age might be specific to the developmental trajectory of ASD, and may have a significant impact on the social functioning of these individuals. One possible explanation for the observed age-related increase in BA44 activity could be a change in the way older individuals look at the face. Analysis of the participants "points of regard" during the experiment showed that older participants, ASD and controls alike, had a tendency to look longer at the mouth region, which contained most of the relevant information about the displayed emotion in the movie clips. In a seminal study involving adolescents, Klin et al. (2002) also found that social competencies in ASD were significantly correlated with the time spent looking at the mouth region. These observations suggest that the pattern of gaze behaviors in children with ASD might be responsible for a delay in the development of the neural circuits supporting the motor simulation of facial expressions, which in turn would have direct consequences on the ability to share others' emotions and on the development of social competences (Bastiaansen et al., 2011a).

### 5.4.2 Monitoring facial muscles activity



Recording facial muscle reactions with EMG is another approach for investigating (pre)motor cortex activity that is triggered by the perception of facial expressions. The results of three studies that compared individuals with and without ASD seem to confirm that age matters. In one study, McIntosh and collaborators (2006) recorded the EMG response of the cheek and brow muscles in 11 individuals with ASD and 14 controls between 13 and 64 years of age, who watched displays of happy and angry facial expressions. The authors looked at the rate of automatic EMG responses, and found no difference between the groups. However, while in the control group the muscle responses were most often congruent with the observed facial expression (e.g. activity in the zygomaticus for happy faces), in participants with ASD there were as many incongruent as congruent responses. In a supplementary task, the authors also asked the participants to voluntarily imitate the expressions they observed. In this condition, more activity was recorded in the congruent than in the incongruent muscle in both groups. In a subsequent study, Beall et al. (2008) recorded the EMG activity of three different facial muscles while children between seven and 12 years of age watched displays of happy, fearful, and angry facial expressions. In the typically developing children, the experiment revealed muscle-specific reactions to happy and angry facial expressions, but not to fearful faces. In children with autism, the pattern was very different; there was no response for happiness and anger, and an undifferentiated response to fearful faces. Interestingly, there was a relationship between age and muscle activity in autism, with older children showing a higher rate of congruent responses to happy faces. Finally, in a study involving only adults, Magnée et al. (2007) found that the EMG response was actually larger in participants with ASD, and was perfectly

congruent with the displayed happy or fearful emotion.

Taken together, the results of these three EMG investigations are consistent with the hypothesis that motor simulation of facial expressions improves with age in ASD. Importantly, these studies also highlight the fact that facial motor reactions can be of normal overall intensity in autism, but at the same time lack the congruence observed in typically developing individuals (McIntosh et al., 2006). Translated to the limited resolution of fMRI, which still struggles to discriminate motor activity patterns across emotions (van der Gaag et al., 2007), such an abnormal pattern of activity in motor cortices could masquerade as BOLD activity of normal overall intensity. One possibility could be that the pattern of normal overall intensity coupled with a lack of specificity in facial reactions is an intermediate state between a total absence of simulation in children (Beall et al., 2008; Dapretto et al., 2006), and a perfectly normal or even enhanced simulation of facial expressions in adults (Bastiaansen et al., 2011a; Magnée, De Gelder, van Engeland, & Kemner, 2007). Further studies will be necessary to validate this hypothesis, and to investigate the relationship between empathy (i.e. sharing the feelings and the emotions of others) and motor simulation of facial expressions throughout the lifespan, both in ASD and typically developing individuals.

### 5.4.3 Empathy and motor simulation

Two recent publications have offered a first glimpse on the fragile relationship between empathy and motor simulation in individuals with autism. Avoiding the use of faces as stimuli, Grèzes et al. (2009) scanned 10 adults with ASD and 10 controls during the observation of neutral and fearful body postures. The authors concluded that there were no major group differences in the pattern of parietal and premotor activity related to the observation of dynamic body postures (neutral and fearful together). Group differences were found, however, for the processing of fearful compared to neutral stimuli, with the ASD group showing hypo-activation of the dorsal premotor cortex and the pars triangularis of the inferior frontal gyrus in the right hemisphere, hypo-activation of the amygdala, and an absence of modulation of the connectivity between the amygdala and the other regions. Therefore, this experiment suggests the presence of a problem (much likely pervasive) in the relationships between mirror neuron functioning and activity in emotional/affective centers of the brain. The second study conducted by Minio-Paluello and collaborators (2009) supports this conclusion. In this experiment, 16 adults with ASD and 20 well-matched controls underwent single-pulse TMS while they observed pictures of a hand that was affected in a painful or non-painful manner. The painful stimuli depicted a static image of the hand being pricked by a needle. Three types of control stimuli were used that showed the hand being touched with a cotton stick, the hand alone, or a tomato being pricked with the needle. The TMS-induced MEPs were recorded in two hand muscles: the pain-affected muscle and an unaffected control muscle. In line with the results of a previous study (Avenanti et al., 2005), MEPs in controls decreased in the muscle receiving pain when the participants watched the painful movie condition (relative to the three other conditions). The same modulation was not found in the group of participants with ASD. Moreover, the amount of MEP modulation for the painful condition correlated with the imagined sensory qualities of pain in control participants, but with reports of self-arousal experience in individuals with ASD. These interesting results suggest that individuals with ASD do not share the

sensory and motor components of the pain experienced by others to the same extent as typically developing individuals do.

### 5.4.4 Comments

In summary, the available evidence indicates that motor simulation of facial expressions may improve with age in ASD (Bastiaansen et al., 2011a; Beall et al., 2008; Dapretto et al., 2006). This phenomenon may be related to changes in gaze behaviors and may have important consequences for social functioning (Bastiaansen et al., 2011a; Klin et al., 2002). Interestingly, the investigation of facial muscle reactions suggests that the activation of the (pre)motor cortex, even if present, may not always match the observed emotion faithfully (McIntosh et al., 2006). This pattern of facial reactions with normal intensity, but lack of normal muscle-specificity, may represent an intermediate stage between a complete absence of facial simulation in children (<12 y.-o.), and a normal or enhanced simulation in adults (>30 y.-o). Such a developmental delay, if verified, could originate from two complementary sources. First, the autistic brain may be characterized by abnormal activity-dependent synaptic plasticity due to abnormalities in synaptic proteins such as neurexins, neuroligins, and Shank3 (Bourgeron, 2009; Pardo & Eberhart, 2007). In a Hebbian learning framework (Del Giudice et al., 2009; Keysers & Perrett, 2004), this reduced plasticity would imply that infants diagnosed with ASD need more frequent pairings of their own facial expressions with those of others in order to develop strictly congruent mirror neurons and muscle-specific facial mimicry. Infants with autism, however, seem to preferentially orient towards non-social contingencies and to lack the normal propensity to look at others (Warren Jones et al., 2008; Klin & Jones, 2008; Klin et al., 2009; Osterling, Dawson, & Munson, 2002; Volkmar, Chawarska, & Klin, 2005). This second factor could lead to a deprivation of the congruent visual signals that are necessary in ASD to form Hebbian associations between their own facial expressions and those of others, which could lead to a retarded development of congruent mirror neurons for facial expressions.



There is empirical evidence that links the abnormal pattern of gaze behaviors in ASD to a hyper-reactivity of the amygdala (Dalton et al., 2005). According to some researchers, individuals with ASD actively avoid looking at the face and the eyes of other people to prevent aversive over-arousal (Corden et al., 2008; Dalton et al., 2005; Nacewicz et al., 2006). Therefore, a dysfunction of the amygdala could, through its influence on gaze behaviors, contribute to an explanation of the delay in the maturation of strictly congruent mirror neurons and the late appearance of congruent facial muscle reactions. In contrast, the communication between emotional centers of the brain and motor simulation mechanisms may remain quite problematic in ASD throughout adulthood (Grèzes, Wicker, Berthoz, & De Gelder, 2009; Minio-Paluello et al., 2009). The relationships between motor reactions, emotion recognition, and emotional empathy, and the changes that may occur during development in autism, should be further investigated.

## 5.5 Conclusion

In this review, we critically examined the claim that Autism Spectrum Disorder could result from a dysfunction of the mirror neuron system. The available evidence indicates that action perception

can trigger a motor response in individuals with ASD, albeit not as consistent as in typically developing individuals. In this concluding section, we will summarize the factors that likely influence motor simulation in ASD and discuss their possible impact on the development of the mirror neuron system. We will finish this section with a brief comment on the possible relationship between understanding action goals and understanding other people's state of mind.

### 5.5.1 Factors that influence motor simulation in autism

The reason why some researchers have failed to find evidence of motor simulation whilst others have might be partly due to the heterogeneity within and across studies of the recruited ASD groups. Simulation mechanisms may, for instance, not be affected to the same extent in every individual, and measurement errors may be larger in groups of participants with ASD (Dinstein et al., 2010; Fan et al., 2010). Multiple differences between studies may also account for the discrepancies in the reported results. The present review of the literature identified several potential candidates that seem to influence the amount and quality of motor simulation in autism: the age of the participant, the nature of the stimuli, the degree of identification (or familiarity) with the actor, and the participant's tendency to orient towards biological motion.

Automatic orientation towards biological motion is thought to be disrupted in toddlers with ASD, who tend to orient towards non-social contingencies instead (Klin et al., 2009). Such a deficit early on is likely to have negative consequences on the maturation of the pSTS circuits supporting the processing of biological motion (Blake et al., 2003; Boddaert et al., 2004), and consecutively on the development of the mirror neuron system. Furthermore, it could explain why the amount of time children with ASD spend looking at the demonstrator is a good predictor of imitation accuracy for meaningless gestures (Vivanti et al., 2008). In addition, it could explain the occasional lack of action simulation that is observed in adults with ASD when explicitly attending to the movement of another individual is not required by the task (Welsh et al., 2009).

The influence that the degree of identification with an actor has on motor simulation in ASD is suggested by the results of two experiments. The first showed typical patterns of mu rhythms suppression only when a picture of the child (or a family member) was presented prior to the hand stimulus (Oberman et al., 2008). The second found simulation for hands shown in an allocentric, but not egocentric viewpoint (Théoret et al., 2005), –as if individuals with ASD were prevented from simulating in the condition where the hand looks like their own.

The nature of the stimulus is also likely to have an influence on motor simulation in ASD. Emotional faces might, for instance, be more challenging (Beall et al., 2008; Dapretto et al., 2006; McIntosh et al., 2006), than goal-directed meaningful hand actions (Avikainen et al., 1999; Bernier et al., 2007; Bird et al., 2007; Dinstein et al., 2010; Fan et al., 2010; Raymaekers et al., 2009).

Finally, age seems to be an important factor. Three studies have reported a significant relationship between age and the amount of motor simulation in ASD (Bastiaansen et al., 2011a; Beall et al., 2008; Raymaekers et al., 2009). In addition, those studies that have found a complete absence of (pre)motor cortex activity during the observation of hand actions (Cattaneo et al., 2007) or facial expressions (Dapretto et al., 2006) have all tested ASD groups comprising young participants (under 14 y.-o). The recruitment of the simulation network may normalize with age in ASD, which might positively affect social adjustment in adulthood (Bastiaansen et al., 2011a). This

finding is in agreement with the results of clinical studies demonstrating social improvements throughout adolescence and adulthood (e.g. McGovern & Sigman, 2005; Shattuck et al., 2007; for a review of earlier studies see Seltzer, Shattuck, Abbeduto, & Greenberg, 2004). If the associations between age, social functioning, and increased motor simulation are confirmed by new studies, it could have a very positive consequence for interventions in ASD, as it suggests that promoting the simulation of facial and bodily expressions at an early age might improve social functioning in ASD. The MNS is actually plastic, and a good deal of experiments have shown that expertise in a motor domain is associated with increased activity in the simulation network during the observation of similar movements (e.g. Calvo-Merino, Glaser, Grezes, Passingham, & Haggard, 2005; Cross, Hamilton, & Grafton, 2006; Haslinger et al., 2005). In the same vein, training one specific finger movement in reaction to a stimulus representing a different movement, can create a muscle-specific response in the trained finger that occurs when the stimulus is presented again for passive observation (Catmur et al., 2007). This indicates that it should be possible to promote muscle-specific facial reactions while viewing various emotional stimuli. The hope is that this will help improve decoding emotions in ambiguous situations and ultimately enable sharing others' emotions "on the fly". We believe this sort of intervention may have positive effects even if the primary deficit lies outside the mirror neuron system, as for instance in the tendency to orient towards biological motion, in the reactivity of the amygdala to emotional stimuli, or in the communication between emotional centers of the brain and the (pre)motor cortex.

### 5.5.2 Broadly versus strictly congruent mirror neurons



Regarding the possible involvement of the MNS proper in Autism Spectrum Disorder, the report of a dissociation between imitation of goal and style (Hobson & Hobson, 2008) seems to be critical. This finding, namely, suggests that the MNS may work well enough to match the goal, but not the style of an observed action. This is consistent with the literature on autism and facial mimicry, which suggests that even when there is a response at the muscle level, this response is not always congruent with the observed emotion (McIntosh et al., 2006). Furthermore, this idea is consistent with two studies that have found an impairment of hand action simulation in autism based on the measurement of muscle activity (Cattaneo et al., 2007; Théoret et al., 2005). Muscle activity in response to hand action observation means that the result of the simulation in the premotor cortex is sent all the way down to the body muscles that are specifically involved in executing the same action with the same effector. This process requires more than the simulation of the goal, which can be accomplished by broadly congruent mirror neurons. It probably also requires the participation of the rarer strictly congruent mirror neurons and output from this premotor system to the spine (probably through MI). In sum, a new hypothesis may be tentatively advanced stating that simulation difficulties in autism may result from a partial dysfunction or delay in the maturation of MNS that specifically affects the less numerous, and therefore more vulnerable, strictly congruent mirror neurons.

### 5.5.3 Mirror neurons and theory of mind

Several researchers (e.g. Iacoboni & Dapretto, 2006; Oberman & Ramachandran, 2007; Rizzolatti & Fabbri-Destro, 2008; Rizzolatti et al., 2009; Williams et al., 2001) have argued that a dysfunction of the MNS could impair both the comprehension of the immediate goal of observed actions (e.g. she is going to grasp the pencil), and the later development of the ability to read the mind of others (e.g. she wants to draw a sketch of the new lab facilities for us to see). The causal link between the integrity of the MNS and the development of a capacity to reflect upon the state of mind of others has, however, not been established (de Lange, Spronk, Willems, Toni, & Bekkering, 2008; Spunt, Satpute, & Lieberman, 2011). Reflecting upon the state of mind of someone else is known to engage structures outside the MNS, including the medial prefrontal cortex, the superior temporal sulcus, the temporal poles, and the temporo-parietal junction (Amodio & Frith, 2006; Gallagher & Frith, 2003; Saxe, 2006). There is evidence suggesting that these brain regions might be hypo-active when individuals with ASD are engaged in theory of mind tasks (Castelli, Frith, Happé, & Frith, 2002; Happe et al., 1996). Investigating the relationships between the MNS and those regions that support mind reading will be necessary for a thorough assessment of the mirror neuron theory of autism. The present review demonstrates that individuals with Autism Spectrum Disorder do not suffer from major difficulties in understanding the immediate intentions of others, and are capable of re-enacting others' actions in their (pre)motor cortices. Given the comparatively greater difficulties they seem to experience in theory of mind tasks (Hamilton et al., 2007), it seems very unlikely that a properly functioning mirror neuron system would be sufficient to independently enable mind reading.

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