Original article

Reflecting on mirrors

A. GILARDINI, M. MOZZONI*

BrainFactor, Milan, Italy
** Facoltà di Psicologia, Università degli Studi di Milano-Bicocca, Italy*

SUMMARY: *Since their discovery, mirror neurons have opened new avenues that may help us to discern the neural basis of many cognitive behaviours, like action understanding, imitation, language, theory of mind and "mentalism". Many articles have been published in support of or refuting the involvement of mirror neurons in these cognitive functions, from both anatomical and physiological perspectives. For example, the concept of "action understanding", a function ascribed to the mirror neuron system with which we are purportedly able to interpret and comprehend the actions of others, has been refuted on at least eight fundamental points, while, at the opposite end of the spectrum, other researchers are placing great faith in the mirror neuron hypothesis, convinced not only that it can explain human behaviour and abilities, but also postulating that the same cognitive processes in which mirror neurons are supposed to be involved could be affected in neurological disorders like autism and autistic spectrum disorders. They base this conviction on the fact that autism reflects the alteration of different nervous structures and activities in the brain, as well as information processing and synaptic connections. In particular, they say, the deficit in autistic subjects of affective and emotional behaviour, and their impaired ability to understand it in others could be due to an alteration of the mirror neuron system function. The potential connections between autism and the mirror neuron system functions are numerous, and could involve imitation, theory of mind, empathy and language. In this "broken mirror hypothesis", the mirror neuron system is used as an explanation for the mechanisms underlying autism, but this is hotly disputed. This review aims to give voice to both proponents of the mirror neuron system and those who oppose it to provide the reader with an overview of the situation as is, as well as an insight into the history of the mirror neurons and what their future may hold.*

KEY WORDS: *Autism, Broken mirror hypothesis, Imitation, Mirror neuron system.*

INTRODUCTION

The mirror neuron system was discovered by chance, just as Fleming happened upon penicillin in 1928, when a group of researchers led by Rizzolatti came across a particular set of neurons in the inferior frontal gyrus and the inferior parietal lobule able to activate whether the subject was performing or observing a motor action[41]. They made this discovery while they were studying the activity of specialised neurons active in the control of hand actions (object manipulation) in the ventral premotor cortex of the monkey. This prompted the publication of reams of literature documenting the search for an equivalent system in humans[6,20,40,42,44], but, since Rizzolatti's initial paper was rejected by a famous international research journal because of its "lack of general interest"[42], the MNS has been dogged by controversy[12,43].

Among the list of its theoretical functions, the MNS is reputed to be involved in "action understanding", where self-generated actions possess inherent meaning, which can also be accessed by observing the same

Correspondence: Prof. Marco Mozzoni, Facoltà di Psicologia, Università degli Studi di Milano-Bicocca, Edificio U6 Stanza, piazza dell'Ateneo Nuovo 1, 20126 Milan (MI), Italy, ph.(+39)-3389510592, e-mail: mozzoni@brainfactor.it
Progress in Neuroscience 2013; 1 (1-4): 45-49. *ISSN: 2240-5127*
Article received: 29 March 2013. doi: 10.14588/PiN.2013.Mozzoni.45

LIST OF ACRONYMS AND ABBREVIATIONS: **ASD** = Autistic Spectrum Disorder; **EMG** = ElectroMyoGraphy; **F5** = inferior frontal gyrus; **MNS** = Mirror Neuron System; **STS** = Superior Temporal Sulcus.

action in others[24]. Mirror neurons were hypothesized to support action understanding based on findings by Gallese et al.[18], who recorded neuronal activity from certain cells in the F5 area of the frontal cortex of macaques during action observation, but not when the objects where merely observed. To rule out any visually imperceptible movement, the neuronal activity of the hand area of the primary motor cortex and the electromyographic activity of several hand and mouth muscles were recorded during observation, which elicited no response in either case. This appeared to make it clear that something was going on in the brain when the monkey observed a "meaningful" action, i.e., someone picking up a banana, rather than just the piece of fruit itself, appearing to suggest that F5 is involved in sensorimotor associations. However, proving that this so-called action understanding actually exists is far easier said than done. In fact, as Fogassi et al.[15] stated, although knocking out the F5 area in macaques does in fact prevent them physically grasping the banana, it may be impossible to prove whether they are still able to "understand" the action performed by others. Furthermore, mirror neurons have since been found in the primary motor cortex of macaques, undermining Fogassi et al.'s control and suggesting that rather than being concerned with meaning, these cells in fact act as facilitators of the motor response through *learned response*[46].

Kohler tried to come at the issue in another way, hypothesizing that action understanding would also be triggered by the sound related to the action in question, and found that this was indeed the case in a small minority of F5 neurons, which fired when exposed to the sound of cracking peanut shells[29]. Umiltà also showed that while monkey mirror neurons do not respond to the act of picking up an imaginary banana, some of them do if the banana is real but hidden in some way (in this case behind a screen), provided, of course that the monkey knows it is there[47]. Both of these tests would appear to indicate that it is not the gesture itself that is important, but the meaning of the gesture. However, whether these responses are sensitive to the meaning or, once again, the working memory of the action, as many sceptics believe[24], is far less easy to demonstrate. That being said, the entire theory cannot be dismissed out of hand, particularly as Fogassi et al.[14], in another study, showed that some neurons in the simian inferior parietal lobule, another mirror-neuron-rich area, responded when the banana was picked up for the purposes of eating, but not when it was picked up to be put in a box in a similar location to the monkey's mouth. This led them to conclude that it was the purpose, or goal, of the action that was crucial, and that mirror neurons allow the monkey to understand the intention behind the action, although it may be the case that the monkey is responding to a feedback loop wherein the sensory event is merely associated with particular motor actions[24]. Indeed, non-mirror neurons in the STS of macaques respond to several observed gestures, but not when the act itself is performed[42], suggesting that mirror neurons are not in fact necessary for action understanding. Nevertheless, it is interesting to note that the STS is connected to the inferior parietal cortex, where mirror neurons projecting to the motor system F5 are present...

It is clear that further investigation, rather than heated debate, will be necessary to clarify the situation. In fact, as the methods used so far have been somewhat subjective[37], we are almost back to square one, and that is even before we come to discuss the question in humans, in whom the presence of mirror neurons has not even been definitively demonstrated[7,10,11]. If it does exist, however, it is starting to become evident that the human mirror system does not function in a similar way to that of macaques. Indeed, as Catmur et al. demonstrated[5] using motor-evoked potentials in the abductor muscles of the human hand, we can be trained to produce mirror effects by adaptive sensorimotor association, rather than action understanding[24]. What is more, according to a meta-analysis by Molenberghs[33], damaging the human F5 area provokes no correlated deficit in action understanding, and imitation of a meaningful action triggers regions in the superior and inferior parietal lobules and the dorsal premotor cortex instead of the F5 area.

Plus, Gallese[18] and Rizzolatti[39] et al.'s early hypothesis that mirroring is involved in speech perception, prompting a fervent revival of the motor theory, has also been disproved by the evidence, which suggests that although speech recognition may in some way be modulated by sensorimotor circuits, action under-

standing is not involved[24]. Nonetheless, it may be, say the advocates, that the mirror system is merely more complex, more evolved in humans than in monkeys. Indeed, although quite distinct in humans, a correlation between action understanding and action production has been found by several Authors[24].

This has led Casile and colleagues[4] to postulate the presence of two separate mirror systems underlying action understanding and imitation in humans. In this scenario, one adaptable system, already present at birth, may be involved in the development of an infant's ability to imitate facial expressions, creating a feedback loop about their own facial movements and thereby evolving according to experience. A different system, described as a perception-action coupling, would be used in the case of, say, hand movements, in which observation of the infant's own movements would be essential for their evolution.

Despite all the opposition, it is enormously enticing to associate the mirror neurons to human complex behaviour and disorders[34], explaining why many researchers have jumped on the MNS bandwagon. Indeed, the desire to provide debilitating neurological and psychological pathologies with such a simple explanation - and therefore a potential therapeutic target down the road - as MNS deficit or dysfunction is very strong, albeit furiously contested.

□ AUTISM IN THE MIRROR

One of the cognitive disorders most eagerly associated with a potential MNS disruption is autism[25,35,49], or autistic spectrum disorder. Indeed, ASD subjects, with their characteristic withdrawal from social interaction and their wide-ranging cognitive impairments in social skills, verbal and non-verbal communication, coupled with restricted and repetitive behaviours[1], and, above all, their apparent lack of empathy, or understanding of others' intentions, would seem to provide fertile ground for further research into the MNS. Indeed, autistic behaviours are known to reflect the alteration of different nervous structures and activities in the brain, involving the cerebellum and cerebral cortex[32], as well as information processing and the synaptic connections between neurons[31]. The affective and emotional deficit in ASD subjects[27], and their impaired ability to understand others has been tentatively ascribed to the "broken mirror hypothesis"[38], i.e., an alteration of the MNS function.

This hypothesis is backed up by results demonstrating structural abnormalities in the MNS regions of individuals with ASD, as well as a delay in the activation of the core circuit for imitation in individuals with Asperger syndrome, and a correlation between reduced MNS activity and severity of the syndrome in children with ASD[8,16]. Moreover, additional evidence for the involvement of MNS in autism derives from the resting-state suppression of the sensorimotor cortex (mu waves) during voluntary movement execution and the observation of the same movement made by others, which is absent in ASD[34].

The connections made between MNS function and autism are many, involving imitation, theory of mind, empathy and language[17,19,39]. During imitation, for instance, defined as the ability of a person to replicate an observed motor act or to observe, acquire and repeat using the same observed movements[9], the posterior part of the F5 area, which corresponds to the MNS, is more active during the repetition of an observed movement[2,3,23,26] and damage to these neurons can cause impairment in the imitations of some actions[25]. Encouragingly, the activity of mirror neurons involved in imitation has been found to be less extensive in ASD subjects[48].

However, people with autism also show an alteration in brain activity in regions outside the MNS[21], and the broken mirror hypothesis fails to explain the normal behaviour of autistic children when asked to perform goal-[22] or object-oriented imitation tasks[8, 45], not to mention their impeccable performance in imitation tasks when explicitly instructed to imitate[22]. This seems to suggest that in autistic subjects the apparent deficit may arise from not knowing what to imitate or when, due to their ignorance of less explicit social cues conveyed, for example, through eye contact[28,30]. The same involvement of visual processing could also explain the difference in mu wave suppression observed through electroencephalographic measurements in autistic subjects and controls[45].

Moreover, a recent study on movement selectivity showed that individuals with autism exhibited not only normal functional magnetic resonance imaging responses in MNS areas during observation and execution of hand movements, but they also exhibited typical movement-selective adaptation (repetition suppression) when observing or executing the same movement repeatedly, another blow to the broken mirror hypothesis[13].

Once again the experimental protocols thus far used in support of a link between MNS dysfunction and ASD are highly controversial[36]. For example, EMG

of the mylohyoid muscle during the execution of goal-oriented tasks has been used to determine the time relationship between the opening of the mouth and the beginning of the movement, and thereby show a difference between the behavior of the typical developing children and that of ASD individuals. Pascolo et al. also claim to provide evidence of a deficit in action chain organization in ASD subjects and bolster the hypothesis of a broken MNS for these individuals. However, the Authors later found that mylohyoid activation is unable to discriminate between typical development and ADS subjects, and therefore "there is not enough evidence to support a link between ASD and a broken MNS, and experimental results must be carefully interpreted before developing therapeutic or rehabilitative protocols"[36]. In the absence of more convincing evidence, we can only agree.

REFERENCES

1. American Psychiatric Association (APA). Diagnostic criteria for 299.00 Autistic Disorder (http://cdc.gov/ncbddd/autism/hcp-dsm.html) . Diagnostic and statistical manual of mental disorders: DSM-IV (4 edition). American Psychiatric Association, Washington (USA), 2000.
2. Buccino G, Vogt S, Ritzl A, Fink GR, Zilles K, Freund HJ et al. Neural circuits underlying imitation learning of hand actions: an event-related fMRI study. Neuron 2004; 42 (2): 323-334.
3. Buxbaum LJ, Kyle KM, Menon R. On beyond mirror neurons: internal representations subserving imitation and recognition of skilled object-related actions in humans. Brain Res Cogn Brain Res 2005; 25 (1): 226-239.
4. Casile A, Caggiano V, Ferrari PF. The mirror neuron system: a fresh view. Neuroscientist 2011; 17 (5): 524-538.
5. Catmur C, Walsh V, Heyes C. Sensorimotor learning configures the human mirror system. Curr Biol 2007; 17 (17): 1527-1531.
6. Cattaneo L, Rizzolatti G. The mirror neuron system. Arch Neurol 2009; 66 (5): 557-560.
7. Chong TT, Cunnington R, Williams MA, Kanwisher N, Mattingley JB. fMRI adaptation reveals mirror neurons in human inferior parietal cortex. Curr Biol 2008; 18 (20): 1576-1580.
8. Dapretto M, Davies MS, Pfeifer JH, Scott AA, Sigman M, Bookheimer SY et al. Understanding emotions in others: mirror neuron dysfunction in children with autism spectrum disorders. Nat Neurosci 2006; 9 (1): 28-30.
9. Decety J, Grezes J, Costes N, Perani D, Jeannerod M, Procyk E et al. Brain activity during observation of actions. Influence of action content and subject's strategy. Brain 1997; 120 (Pt 10) 1763-1777.
10. Dinstein I. Human cortex: reflections of mirror neurons. Curr Biol 2008; 18 (20): R956-R959.
11. Dinstein I, Hasson U, Rubin N, Heeger DJ. Brain areas selective for both observed and executed movements. J Neurophysiol 2007; 98 (3): 1415-1427.
12. Dinstein I, Thomas C, Behrmann M, Heeger DJ. A mirror up to nature. Curr Biol 2008; 18 (1): R13-R8.
13. Dinstein I, Thomas C, Humphreys K, Minshew N, Behrmann M, Heeger DJ. Normal movement selectivity in autism. Neuron 2010; 66 (3): 461-469.
14. Fogassi L, Ferrari PF, Gesierich B, Rozzi S, Chersi F, Rizzolatti G. Parietal lobe: from action organization to intention understanding. Science 2005; 308 (5722): 662-667.
15. Fogassi L, Gallese V, Buccino G, Craighero L, Fadiga L, Rizzolatti G. Cortical mechanism for the visual guidance of hand grasping movements in the monkey: A reversible inactivation study. Brain 2001; 124 (Pt 3): 571-586.
16. Frith U, Frith CD. Development and neurophysiology of mentalizing. Philos Trans R Soc Lond B Biol Sci 2003; 358 (1431): 459-473.
17. Gallese V. The manifold nature of interpersonal relations: the quest for a common mechanism. Philos Trans R Soc Lond B Biol Sci 2003; 358 (1431): 517-528.
18. Gallese V, Fadiga L, Fogassi L, Rizzolatti G. Action recognition in the premotor cortex. Brain 1996; 119 (Pt 2) 593-609.
19. Gallese V, Goldman A. Mirror neurons and the simulation theory of mind-reading. Trends Cogn Sci 1998; 2 (12): 493-501.
20. Grafton ST, Arbib MA, Fadiga L, Rizzolatti G. Localization of grasp representations in humans by positron emission tomography. 2. Observation compared with imagination. Exp Brain Res 1996; 112 (1): 103-111.
21. Hamilton AF. Emulation and mimicry for social interaction: a theoretical approach to imitation in autism. Q J Exp Psychol (Hove) 2008; 61 (1): 101-115.
22. Hamilton AF, Brindley RM, Frith U. Imitation and action understanding in autistic spectrum disorders: how valid is the hypothesis of a deficit in the mirror neuron system? Neuropsychologia 2007; 45 (8): 1859-1868.
23. Heiser M, Iacoboni M, Maeda F, Marcus J, Mazziotta JC. The essential role of Broca's area in imitation. Eur J Neurosci 2003; 17 (5): 1123-1128.
24. Hickok G. Eight problems for the mirror neuron theory of action understanding in monkeys and humans. J Cogn Neurosci 2009; 21 (7): 1229-1243.
25. Iacoboni M, Dapretto M. The mirror neuron system and the consequences of its dysfunction. Nat Rev Neurosci 2006; 7 (12): 942-951.
26. Iacoboni M, Woods RP, Brass M, Bekkering H, Mazziotta

JC, Rizzolatti G. Cortical mechanisms of human imitation. Science 1999; 286 (5449): 2526-2528.

27. Kanner L. Autistic disturbances of affective contact. Nerv Child 1943; 2: 217-225.
28. Klin A, Jones W, Schultz R, Volkmar F, Cohen D. Visual fixation patterns during viewing of naturalistic social situations as predictors of social competence in individuals with autism. Arch Gen Psychiatry 2002; 59 (9): 809-816.
29. Kohler E, Keysers C, Umiltà MA, Fogassi L, Gallese V, Rizzolatti G. Hearing sounds, understanding actions: action representation in mirror neurons. Science 2002; 297 (5582): 846-848.
30. Kuhl PK, Coffey-Corina S, Padden D, Dawson G. Links between social and linguistic processing of speech in preschool children with autism: behavioral and electrophysiological measures. Dev Sci 2005; 8 (1): F1-F12.
31. Levy SE, Mandell DS, Schultz RT. Autism. Lancet 2009; 374 (9701): 1627-1638.
32. Minshew NJ, Williams DL. The new neurobiology of autism: cortex, connectivity, and neuronal organization. Arch Neurol 2007; 64 (7): 945-950.
33. Molenberghs P, Cunnington R, Mattingley JB. Is the mirror neuron system involved in imitation? A short review and meta-analysis. Neurosci Biobehav Rev 2009; 33 (7): 975-980.
34. Oberman LM, Hubbard EM, McCleery JP, Altschuler EL, Ramachandran VS, Pineda JA. EEG evidence for mirror neuron dysfunction in autism spectrum disorders. Brain Res Cogn Brain Res 2005; 24 (2): 190-198.
35. Oberman LM, Ramachandran VS. The simulating social mind: the role of the mirror neuron system and simulation in the social and communicative deficits of autism spectrum disorders. Psychol Bull 2007; 133 (2): 310-327.
36. Pascolo PB, Cattarinussi A. On the relationship between mouth opening and “broken mirror neurons” in autistic individuals. J Electromyogr Kinesiol 2012; 22 (1): 98-102.
37. Pascolo PB, Pagnacco G. Subjectivity of typical experiments used to investigate the existence of mirror neurons - biomed 2011. Biomed Sci Instrum 2011; 47: 294-299.
38. Ramachandran VS, Oberman LM. Broken mirrors: a theory of autism. Sci Am 2006; 295 (5): 62-69.
39. Rizzolatti G, Arbib MA. Language within our grasp. Trends Neurosci 1998; 21 (5): 188-194.
40. Rizzolatti G, Fadiga L, Matelli M, Bettinardi V, Paulesu E, Perani D, Fazio F. Localization of grasp representations in humans by PET: 1. Observation versus execution. Exp Brain Res 1996; 111 (2): 246-252.
41. Rizzolatti G, Camarda R, Fogassi L, Gentilucci M, Luppino G, Matelli M. Functional organization of inferior area 6 in the macaque monkey. II. Area F5 and the control of distal movements. Exp Brain Res 1988; 71 (3): 491-507.
42. Rizzolatti G, Craighero L. The mirror-neuron system. Annu Rev Neurosci 2004; 27: 169-192.
43. Rizzolatti G, Fabbri-Destro M. Mirror neurons: from discovery to autism. Exp Brain Res 2010; 200 (3-4): 223-237.
44. Rizzolatti G, Fabbri-Destro M, Cattaneo L. Mirror neurons and their clinical relevance. Nat Clin Pract Neurol 2009; 5 (1): 24-34.
45. Southgate V, Hamilton AF. Unbroken mirrors: challenging a theory of Autism. Trends Cogn Sci 2008; 12 (6): 225-229.
46. Tkach D, Reimer J, Hatsopoulos NG. Congruent activity during action and action observation in motor cortex. J Neurosci 2007; 27 (48): 13241-13250.
47. Umiltà MA, Kohler E, Gallese V, Fogassi L, Fadiga L, Keysers C, Rizzolatti G. I know what you are doing. A neurophysiological study. Neuron 2001; 31 (1): 155-165.
48. Williams JH, Whiten A, Singh T. A systematic review of action imitation in autistic spectrum disorder. J Autism Dev Disord 2004; 34 (3): 285-299.
49. Williams JH, Whiten A, Suddendorf T, Perrett DI. Imitation, mirror neurons and autism. Neurosci Biobehav Rev 2001; 25 (4): 287-295.

Disclosure. *The Authors declare no conflicts of interest.*