



Introduction

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Mirror neuron research: the past and the future

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This special issue is, in large part, based on the presentations given at a workshop held at the 'Ettore Majorana' Centre in Erice (Sicily) to celebrate the discovery of mirror neurons, 20 years after the first report on their discovery [1]. All articles in this issue have been updated and deal with the present state of the art of mirror research in different fields.

It was certainly difficult to predict from the note published in 1992 how profoundly the discovery of mirror neurons would influence cognitive neuroscience in the next 20 years. Even more difficult was to forecast that the discovery of mirror neurons would have an impact on disciplines outside neurosciences, such as psychology, ethology, sociology and philosophy, or that they would interest novelists (e.g. *The elegance of the hedgehog* [2]) and laymen.

Why has the notion of mirror neurons had such a wide impact on cognitive disciplines? Two reasons are the most likely. The first is that their discovery put the problem of how we understand others at the forefront of neuroscience. The second is that, by showing that mirror neurons were basically motor neurons, they suggested a rather unexpected solution to this problem: the motor system is involved in understanding the actions and intentions of others.

This problem of how we understand others is not new in philosophical debates. One of the most accepted views is that the capacity to understand the intentions of others is based on the observer's capacity to *infer* others' internal mental states and to ascribe to them a causal role in generating the observed behaviour [3,4]. This view is in line with the analytical tradition based on the propositional account of others' minds. An alternative view, put forward by phenomenologists, is that we understand others by *comparing* an action done by others with our own behaviour in a similar situation [5]. The discovery of mirror neurons did not disprove the conventional analytical view, but demonstrated the validity of the phenomenological stance, at least in most everyday life conditions. It is important to stress that action understanding through the mirror mechanism is a *direct* activation of motor representation. It does not require a cognitive simulation of others' behaviour as suggested by simulation theory of action understanding [6].

Interest in the direct understanding of others' actions increased enormously when it was found that the mirror mechanism is also present in the emotional brain centres. Although there is no doubt that one can understand others' emotions via inferential mental processes (as during the observation of emotions), there is clear evidence that brain structures involved in the integration and control of emotions, like the insula and the anterior cingulate, respond both when one feels an emotion (e.g. pain or disgust) owing to natural stimuli, or when one observes that emotion in others [7–10]. This mechanism allows a direct first-person understanding of others' emotion. 'Your pain is my pain'.

Some authors previously questioned the presence of mirror neurons in humans [11]. This is not, however, a current issue, given the overwhelming evidence for the existence of mirror neurons in humans from hundreds of experiments [12] carried out with a variety of techniques (positron emission tomography, functional magnetic resonance imaging, transcranial magnetic stimulation, magnetoencephalography and electroencephalography), as well as from a few single neuron studies [13]. It is, nevertheless, of some interest to examine the reasons why this somehow surprising debate took place. In fact, traditionally, the mechanisms discovered in primates as well as in other species

of animals are considered, at least *prima facie*, to exist also in humans. Nobody questioned, for example, the existence of 'simple' and 'complex' neurons in the visual cortex of humans, despite the fact that they were first discovered in the cat and then studied in detail in the monkey [14,15].

One reason for the opposition of some neuropsychologists to accept the existence of mirror neurons in humans is probably due to the fact that the mirror mechanism was discovered when it was not completely clear whether damage to the areas endowed with this mechanism determines deficits in understanding others' actions (for evidence for the causative role of mirror neurons in action understanding, see [12,16]). Typically, the opposite series of events occurs, that is experimental and/or clinical studies indicate that a certain cortical region is involved in a particular function (e.g. occipital cortex in vision) and then single neuron recordings in animals reveal the mechanism underlying this function.

The second reason is that the motor system has been traditionally considered not to be involved in cognitive functions [17]. Its role was thought to be limited to the control and production of movements. The discovery of mirror neurons as well as of other motor neurons involved in cognition, such as neurons coding peripersonal space or neurons transforming object affordances into potential motor acts (canonical neurons), radically changed this view. Yet, as often occurs in science, there was some resistance to changing consolidated points of view.

An exciting and not fully explored field is the origin of mirror neurons and how the development of social-cognitive skills in infancy may rely on the maturation of the motor system. We gave ample space in this special issue to this topic [18–22]. It is highly debated whether the mirror system arose as the consequence of association learning or an evolutionary process that endowed a population of neurons with a mechanism necessary for accomplishing a specific function [20,23].

According to the associative account, mirror neurons emerge during development as the result of strengthening sensorimotor connections that originally evolved for visuomotor control [20]. From this perspective, for example, the motor command for reaching/grasping made by the infant is associated with the sight of his/her own hand. The simultaneous firing of motor and visual neurons can strengthen their connections (see also [24,25]). The further step would be to generalize the visual description of the agent's action to that of others and therefore the observation of others' actions is sufficient to trigger the observer's motor neurons.

The alternative account maintains that at least part of the mirror neuron system is genetically determined and adapted to serve one function as the consequence of the natural selection process ([20], but also see [26,27]). More recently, models have been proposed which avoid pitting one view against the other, thus escaping an old fruitless nature–nurture divide. Rather, these models integrate learning processes into a more realistic theoretical framework on how the brain develops in the peri- and post-natal period, and on how some brain mechanisms do not need to be specified by strict genetic rules. It is known that plastic changes *do* occur in the brain during ontogeny and involve a complex interaction between the environment and gene expression in different brain networks. Nobody could deny, for example, that the development of vision and the organization of the visual cortex in primates and cats, and of human language and song learning in birds, are examples of adaptations that, in

order to develop, require genetic instructions as well as specific environmental inputs.

One should also consider that neural circuits very rarely evolved for one purpose only. They are often co-opted for other purposes as well; that is, they are *exapted* to serve additional functions. Thus, the brain networks that are involved in sensorimotor transformation can be recruited to support additional functions such as action understanding and imitation.

The key role of epigenetic events in driving neuronal development has recently been emphasized [26]. These epigenetic events might facilitate and stabilize, in the course of phylogeny, sensorimotor mechanisms involved in the coding of others' actions (i.e. mirror neurons). The markers of this gene expression can consistently emerge in each generation, when infants face specific and predictable environmental conditions [28], thus leading to long-lasting changes in the phenotype. In fact, in all individuals of our species, infants experience the vision of their own hand and benefit from universal forms of face-to-face interactions with the caregiver. These behavioural events affect those brain mechanisms (including the mirror mechanism) that have been referred as to experience-expectant, which actively 'seek out' specific environmental inputs. If the elements of this 'expectable' environment are either lacking, or else markedly disturbed, then the immature nervous system is likely to be profoundly affected, thus requiring alternative strategies for rewiring the networks. According to the epigenetic hypothesis, new emergent neuronal responses and the related epigenetic mechanisms yielded some advantages for the organism (e.g. faster or more accurate capacity to recognize others' actions through mapping the actions onto one's own motor knowledge), and natural selection would have favoured their stabilization and facilitation of expression [26].

An important field for future research studies will be to assess the sensitivity of mirror neurons to early perturbations of the social environment and whether there are critical periods necessary for the wiring of the sensorimotor connections responsible for mirror neuron construction and functioning. Clinical investigations of disturbances of early social interactions, such as in children who experience a severe lack of early social stimulation or who, for genetic reasons, have deficits in social communication, could represent an interesting challenge to explore the ontogeny of this mechanism and its functional role.

Another important issue that will be fundamental for understanding the mirror mechanism more deeply is to elucidate its neurochemical and molecular bases. This appears very difficult to address with macaques due to the limitation in applying biomolecular techniques in a species with low reproductive efficiency (one infant per year, long gestation period and delivery interval) and which requires high costs in terms of housing and experiments performing. By contrast, other animal models, such as marmosets or birds, appear to be suitable for investigating complex social-cognitive skills and their neural underpinnings.

Marmosets, for example, have been used with success in biomedical research, not only because of the reduced costs involved, but also because of the possibility of using them in neuroscience research both with invasive and non-invasive techniques (to use them in neuroscience research both with invasive and non-invasive techniques [29–31]). The results of these and other studies clearly showed that marmosets display remarkable similarities with humans in terms of brain networks, immune response and endocrinological profile.

The recent studies on transgenic techniques [31] and on the embryonic stem cells of marmosets indicate that this species may be a more suitable model for genome research and bio-molecular investigation than the macaque. These new areas of research, together with the recent discovery of mirror neurons in the ventral premotor cortex of marmosets [32], represent therefore a first critical step in paving the way to new investigations aimed at clarifying the molecular basis and the evolutionary origins of this mechanism in primates.

Studies in songbirds are another example of how mirror neuron research has expanded and stimulated the field. Given the complex interactions occurring during development between parents and their offspring which are so critical for song learning, it is not surprising that in songbirds, neurons with mirror properties (audio–motor mirroring) have been found. The work by Mooney and co-workers ([33], see also [34]) clearly demonstrates that, in songbirds, areas involved in song production and learning (i.e. area HVC) do have neurons with mirror properties for audio–motor matching. Lesions in the HVC impair song production and song recognition, as well as the capacity to learn new contingencies. These authors suggest that audio–motor mirror neurons in songbirds may be involved in song learning and communication [34], thus making a striking parallel between the functional role of humans' Broca

area in speech production and perception [35] and the HVC in birds. The possibility of investigating the molecular basis of song production and learning in different species of birds makes this model extremely promising in investigating the development and functional role of the mirror mechanism and its molecular basis.

Finally, this new information should be extremely useful not only for a better comprehension of the mirror mechanism itself, but also for its practical application in psychiatric and neurological disorders. There is indeed evidence, although still preliminary, of possible underdevelopment or impairment of the mirror system in autism [12] and in those psychiatric disorders [36] in which social competence is compromised [12]. A better knowledge of the molecular and neurochemical basis of this mechanism will represent a breakthrough for establishing new therapies and interventions based on solid experimental findings.

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