

Mirror Neurons and Mirror-Touch Synesthesia

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Abstract

Since mirror neurons were introduced to the neuroscientific community more than 20 years ago, they have become an elegant and intuitive account for different cognitive mechanisms (e.g., empathy, goal understanding) and conditions (e.g., autism spectrum disorders). Recently, mirror neurons were suggested to be the mechanism underlying a specific type of synesthesia. Mirror-touch synesthesia is a phenomenon in which individuals experience somatosensory sensations when seeing someone else being touched. Appealing as it is, careful delineation is required when applying this mechanism. Using the mirror-touch synesthesia case, we put forward theoretical and methodological issues that should be addressed before relying on the mirror-neurons account.

Keywords

mirror neurons, synesthesia, mirror touch, motor cortex, F5, threshold theory

More than 20 years ago, a seminal article from Rizzolatti's laboratory (di Pellegrino and others 1992) revealed a population of neurons in monkeys' premotor regions that exhibited a similar pattern of activity when monkeys viewed an action and when they conducted the action. Rizzolatti named these neurons "mirror neurons". Since then, mirror neurons have been found in monkeys, in humans, and even in birds (Rizzolatti and Fabbri-Destro 2008; Rizzolatti and others 2014). This staggering finding became one of the most exciting discoveries in neuroscience.

Mirror neurons have been extensively researched in monkeys, utilizing invasive techniques such as single cell recordings as well as imaging techniques. Results of these studies revealed a parieto-frontal mirror circuit (see Fig. 1), with an abundance of mirror neurons in the ventral premotor region of F5, the primary motor cortex (F1) and in supplementary visual regions in the parietal lobe (i.e., inferior parietal area [PFG] and the anterior intraparietal area [AIP]). The visual input to these regions stems from the superior temporal sulcus (STS), which is active during action observation but not during actions themselves. Other research (Fogassi and others 1996) implicated an inferior premotor region (i.e., F4) as crucial in distinguishing between viewing actions performed within reach of the monkey and viewing actions performed further away from it. Different mirror neurons have been demonstrated to code action goal (Umiltà and others 2008), action intention (Rizzolatti and others 2014), the perspective of the viewed action (Caggiano and others 2011) and recently, even the value of the action (Caggiano

and others 2012) (i.e., some F5 neurons fire more rapidly when a monkey views a different monkey grabbing food compared with viewing a monkey grabbing a neutral object).

The invasive techniques used with nonhuman primates are very rare in human subjects and are reserved for epilepsy patients awaiting a surgical procedure (Mukamel and others 2010). This raises a challenge for identifying and locating mirror neurons in humans. Furthermore, studies need to differentiate mirror neurons activity from simple action-preparation. In spite of the limitations, there is evidence demonstrating the existence of mirror neurons in humans. They have been exhibited in partially homologous locations to the ones found in monkeys in the parietal and frontal lobes, and specifically in the caudal inferior frontal gyrus (IFGc), the ventral premotor cortex (PMv), and in the inferior parietal lobule (IPL) (Rizzolatti and others 2014; see Fig. 2).

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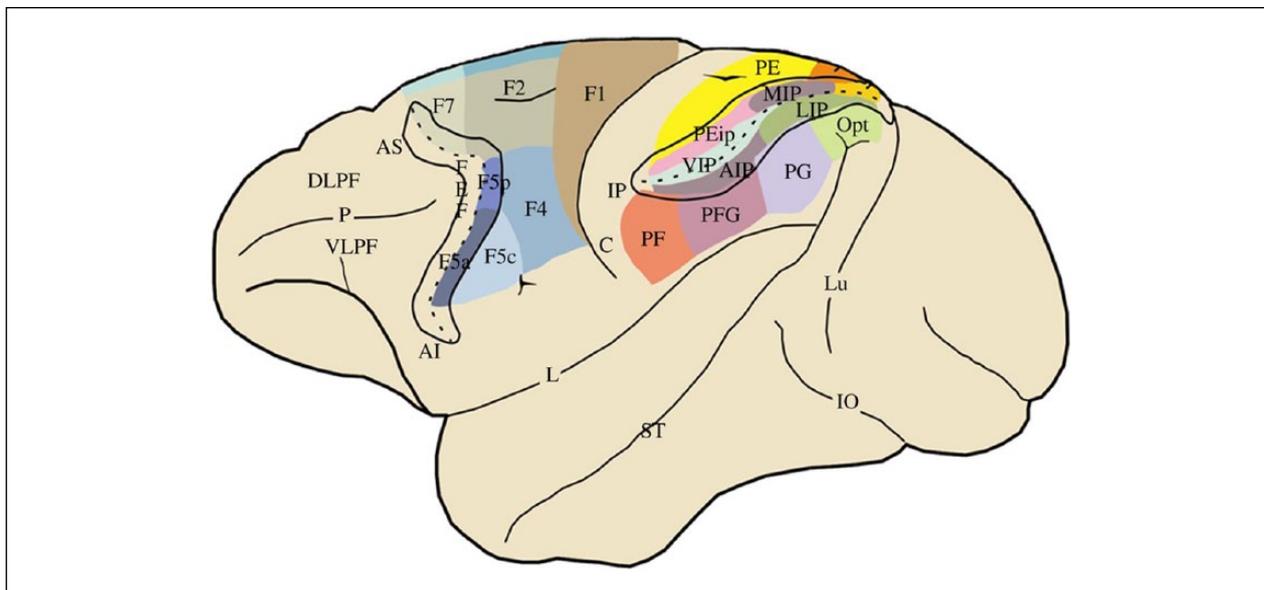


Figure 1. Anatomy of monkey fronto-parietal cortex, including regions that pertain to mirror neurons. The intraparietal and arcuate sulci have been opened to show the areas buried inside them. AI = inferior arcuate sulcus; AIP = anterior intraparietal area; AS = superior arcuate sulcus; C = central sulcus; DLPF = dorsolateral prefrontal cortex; FEF = frontal eye field; IO = inferior occipital sulcus; L = lateral fissure; LIP = lateral intraparietal area; Lu = lunate sulcus; MIP = medial intraparietal area; P = principal sulcus; ST = superior temporal sulcus; VIP = ventral intraparietal area; VLPF = ventrolateral prefrontal cortex. Reprinted with approval from Rizzolatti G, Fogassi L. 2014. The mirror mechanism: recent findings and perspectives. *Philos Trans R Soc B* 369(1644):20130420. Copyright (2014), with permission from the Royal Society.

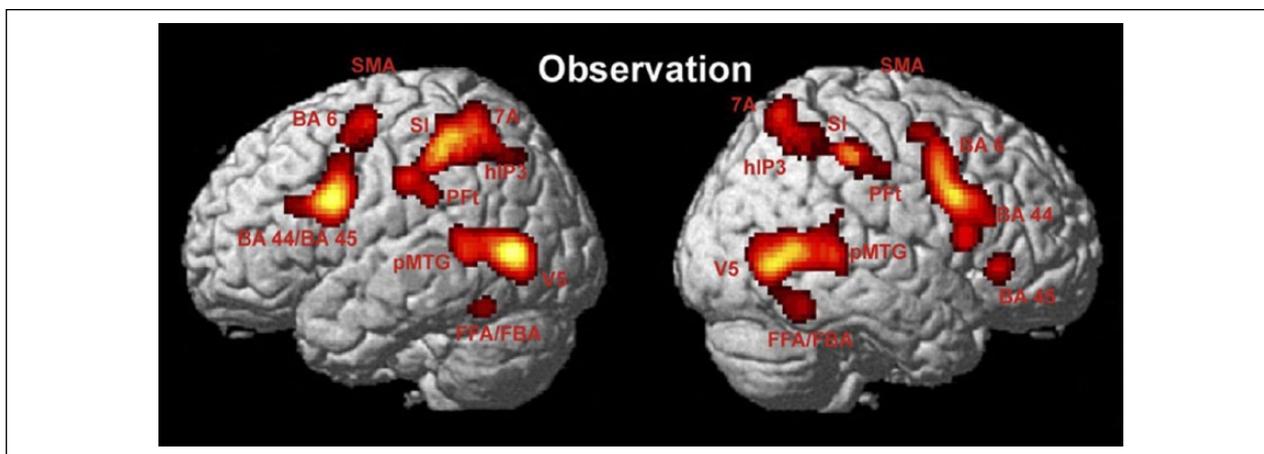


Figure 2. Graphical summary of meta-analysis of anatomy of human brain regions that are active during viewing of actions. Results from meta-analysis are displayed on the left and right lateral surface view of the Montreal Neurological Institute (MNI) single subject template. pMTG = posterior middle temporal gyrus; SMA = supplementary motor area (hidden within the interhemispheric fissure); BA44/45 = Broca's area; BA6 = lateral premotor cortex; SI = primary somatosensory cortex (BA2); 7A = superior parietal area; Pft = inferior parietal area; hIP3 = intraparietal area; V5 = extrastriate visual area; FFA/FBA = fusiform face area/ fusiform body area. Reprinted with approval from Caspers S, Zilles K, Laird AR, Eickhoff SB. 2010. ALE meta-analysis of action observation and imitation in the human brain. *Neuroimage* 50(3):1148–67. Copyright (2010), with permission from Elsevier.

The concept of mirror neurons provides a parsimonious mechanism that might underlie action understanding (Rizzolatti and others 2014), social cognition (Rizzolatti and Fabbri-Destro 2008), empathy, and theory of mind

(Gallese 2001). These suggestions and basic research have already led to translational science in clinical populations that struggle in these fields. It has been shown, for example, that patients suffering from impaired social

functioning as a result of schizophrenia or schizoaffective disorders exhibit a selective reduction in mirror neuron activity (Enticott and others 2008). It has even been speculated that avoidance symptoms and reduced social interactions in individuals suffering from autism spectrum disorders stem from dysfunction in the mirror system. This dysfunction and associated symptoms could be reduced through targeted developmental intervention using associative learning and monitored social interactions (Vivanti and Rogers 2014).

However, it seems that there is some distance between the experimental procedures and the theoretical generalizations. For example, studies on mirror neurons of individuals suffering from schizophrenia (e.g., Enticott and others 2008; McCormick and others 2012) do not report a correlation between social dysfunction severity and the abnormality of mirror neurons. Furthermore, individuals suffering from schizophrenia possess multiple anatomical and functional differences (Goghari and others 2010). These two elements combined burden the possibility to infer that mirror-neurons deficit is the cause for social difficulties in patients suffering from schizophrenia. A reliable conclusion regarding mirror system's involvement in a cognitive ability or deficit pends explicit theorizing and meticulous testing. We now turn to assess the utilization of mirror neurons in different cognitive functions through its recently suggested account for a specific type of synesthesia (see Box 1).

Box 1. Synesthesia.

Synesthesia is a portmanteau word composed from the Latin word "syn," meaning together, and "aesthesia" meaning sensation. Synesthesia is a phenomenon in which one experiences merging of senses, that is, stimulation of one sense (i.e., "inducer") leads to an additional, automatic, and involuntary experience (i.e., "concurrent"; Cytowic 2002). For example, in grapheme-color synesthesia, a certain grapheme induces a specific color ("the numeral 1 is red"). Since Sir Francis Galton's first scientific documentation of synesthesia (1880), various forms of synesthesia have been found; currently more than 40 types of synesthesia are documented. The most prevalent is synesthesia that involves color as a concurrent (e.g., grapheme-color, smell-color, touch-color, taste-color), but there are rarer types like touch-taste or sound-touch (Cytowic 2002). Although synesthesia may seem to be a peculiar phenomenon, its prevalence is ~4% (Simner and others 2006).

Apart from being an interesting phenomenon that deserves scientific attention, the study of synesthesia is utilized for understanding normal perception and cognition. Numerous studies demonstrate that synesthetes exhibit heightened activity in regions that are associated with the concurrent percepts when exposed to the inducer (Fig. 3). The underlying neuronal mechanism is debated. There are two competing explanations in the literature.

The hyper-connectivity hypothesis suggests that this excessive neuronal activity stems from over-connectivity between inducer and concurrent associated brain regions (Bargary and Mitchell 2008). The disinhibition hypothesis, on the other hand, asserts that synesthetes and non-synesthetes do not differ in connectivity. Instead, it attributes synesthesia to reduced neuronal inhibition in the concurrent-associated substrate (Grossenbacher and Lovelace 2001).

Mirror-touch synesthesia (MTS) is a phenomenon in which people describe somatosensory sensations when watching someone else being touched (Blakemore and others 2005; Holle and others 2013). The threshold theory is a prominent model of MTS (Blakemore and others 2005; Ward & Banissy 2015), stipulating that mirror-touch neurons are the somatic extension of mirror neurons and they exist in all humans. Accordingly, MTS is an extreme endpoint of a normal mirror-touch mechanism. In these synesthetes, activity of mirror neurons reaches a certain threshold that facilitates the perception of touch even when only viewing it (see Fig. 3 for functional differences in MTS compared with control participants).

A notable caveat in the threshold theory relates to excess activation of mirror neurons within primary and associative somatosensory cortices. Rizzolatti (2014) argues that the purpose of the mirror neuron system is to transform sensory information into motor actions. Rizzolatti stresses that the "parieto-frontal mirror neurons are motor" (p. 218). Therefore, if MTS results from an abnormality in the mirror neuron system, we would expect it would result in excessive activation in brain regions that are associated with motor activation (e.g., premotor cortex, primary motor cortex). However, viewing a person being touched produces similar motor activation in MTS and control participants (Holle and others 2013). That is, the excessive somatosensory activation does not yield different motor activation that is the hallmark of mirror neuron activity. A more radical alternative is that the threshold theory is accurate and that mirror-touch synesthetes inform science on a novel kind of somatosensory "mirror-like" neurons, whose existence had been previously hypothesized (Keysers and Gazzola 2009). This hypothesis could be tested via basic research in monkeys by probing single cells in the somatosensory cortices while monkeys view others being touched. Some support of this latter alternative comes from a meta-analysis of human mirror neuron research (Caspers and others 2010) that found segments of the somatosensory cortex exhibited modified activation when humans viewed motor actions (see Fig. 2).

Another theoretical incompatibility between the mirror-neuron framework and threshold theory lies in the non-semantic/perceptual nature of MTS. Ramachandran

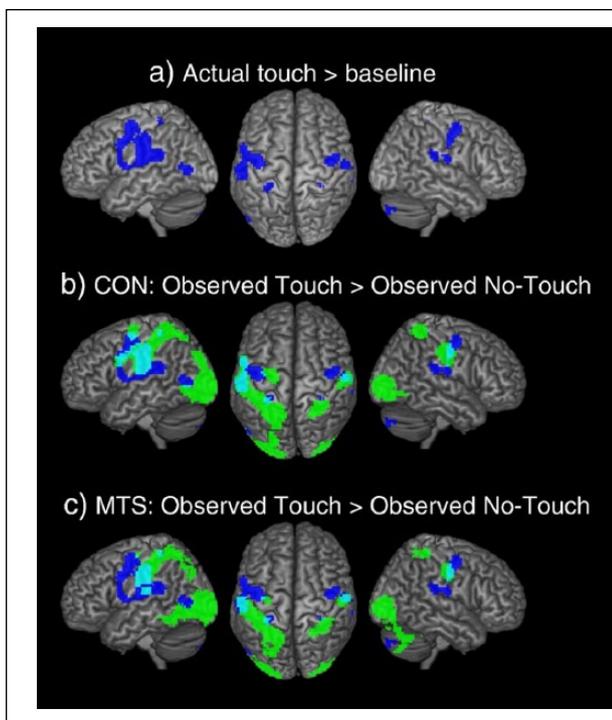


Figure 3. Summary of Holle and others (2013) contrasting mirror-touch synesthetes and control participants. (a) Results from an actual touch localizer task (the experimenter touched one cheek of the participant for periods of 20 seconds while the participant underwent a functional magnetic resonance imaging [fMRI]), shown in dark blue. (b) Contrast of observed touch vs. observed no-touch (in green) as well as its conjunction (cyan) with actual touch in controls. (c) Observed touch versus observed no-touch (green) and its conjunction (cyan) with actual touch in mirror-touch synesthesia (MTS). Reprinted with approval from Holle H, Banissy MJ, Ward J. 2013. Functional and structural brain differences associated with mirror-touch synaesthesia. *Neuroimage* 83:1041–50. Copyright (2013), with permission from Elsevier.

and Hubbard (2001) suggested two classes of synesthesia. In low-level synesthesia, the *perceptual processing* of the inducer elicits the concurrent sensation; in high-level synesthesia, the *concept of the inducer* elicits the concurrent sensation. The current literature on MTS covers exclusively vision of touch as the inducer (Ward and Banissy 2015), thus categorizing MTS as a low-level synesthesia. Conversely, Rizzolatti and Craighero (2004) suggest that mirror neurons are sensitive to the semantic level — monkey mirror neurons are activated with different modalities of the same action; for example, a hand moving toward a nut as well as hearing an auditory cracking sound would produce similar activation of mirror neurons (Kohler and others 2002). Given this semantic nature of mirror neurons, we would expect mirror-touch synesthetes to feel touch when presented with the concept of touch in different modalities and perhaps in symbolic

presentations (e.g., visual presentation of the sentence “he touched her hand”).

Finally, another basic assumption of the threshold theory is that synesthetes experience tactile sensations when they watch others being touched, in an equivalent way as do non-synesthetes when they are physically touched. This, however, was never directly tested. In order to do so, one would need to contrast actual touch with viewing touch in MTS and in control participants. If the threshold theory is accurate, then we would expect to see an interaction in which control participants would display greater somatosensory activation when being touched compared to when viewing someone being touched and that MTS synesthetes would display smaller or insignificant differences between the two conditions (see Fig. 3). Holle and others (2013) did contrast individuals with MTS and control participants while they underwent functional magnetic resonance imaging (fMRI); however, their design utilized actual touch only in a localizer task prior to the “no-touch” conditions. Holle and colleagues did not contrast “touch” and “no-touch” (see Box 2 for testing similarities in fMRI).

Box 2. Testing for Similarities.

The core idea underlying the concept of mirror neurons is that they correspond in a similar manner when one observes an action or executes one oneself. Therefore, an fMRI study designed to reveal “mirror activity” in neurons would have to establish similarity between the hemodynamic response associated with executing an action and observing it. However, the conventional inferential statistics used to fit a general linear model (GLM) to the fMRI blood oxygen level-dependent (BOLD) signal are not suitable to test for similarities; instead, they are designed to test differences between conditions. Accordingly, the activity in each individual voxel (in a region of interest, or in the whole brain) is characterized for every experimental condition and statistical tests are executed to test whether the activity in these voxels is different in the different conditions. The null hypothesis asserts similarity between conditions, and the statistical test is aimed at rejecting it (Friston and others 1998).

In a pivotal article, Haxby and others (2001) introduced a new method for analyzing BOLD signals. Their main thrust was to increase analysis sensitivity so it would enable detecting subtle differences. They suggested adopting a multivariate approach instead of focusing on individual voxels. With this approach, the dataset is divided to a training set and a testing set. Machine-learning algorithms use the training set to find a common multivariate neuronal pattern of activation that corresponds to different cognitive states. The efficiency of the algorithm is then tested as it is applied to classify the trials on the testing set. Apart from the dramatic increase in sensitivity, multivariate pattern

analysis (MVPA) could be utilized to test for similarities. Training the classifying algorithm on one set of data and testing it on another could supply information regarding their similarity (Hanson and others 2004). In the case of mirror neurons, training the classifier on the brain activity associated with an actual subject's movements and testing it on neural recordings associated with subjects watching these movements and vice versa might reveal the similarities and dissimilarities in encoding.

In summary, mirror neurons are an intriguing phenomenon, offering us an elegant framework for explaining a vast array of cognitive functions. However, applying this framework should address theoretical and methodological issues. The case of MTS allows us to stress more general, scientific rules of thumb, which scientists should adopt when studying the involvement of mirror neurons in higher functions. Namely, these attempts should address the hallmarks of the mirror neurons, as observed in monkeys, to create a common theoretical ground.

Declaration of Conflicting Interests

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