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What Neuromodulation and Lesion studies tell us about the function of the mirror neuron system and embodied cognition

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Abstract

We review neuromodulation and lesion studies that address how activations in the mirror neuron system contribute to our perception of observed actions. Past reviews showed disruptions of this parieto-premotor network impair imitation and goal and kinematic processing. Recent studies bring five new themes. First, focal perturbations of a node of that circuit lead to changes across all nodes. Second, primary somatosensory cortex is an integral part of this network suggesting embodied representations are somatosensory-motor. Third, disturbing this network impairs the ability to predict the actions of others in the close (~300ms) future. Forth, disruptions impair our ability to coordinate our actions with others. Fifth, disrupting this network, the insula or cingulate also impairs emotion recognition.

Introduction

Over the past two decades, the discovery of mirror neurons has been amongst the most influential neuroscience discoveries [1–4]. It triggered such wide interest because it spoke to a long-standing debate about how the brain processes the social world. Some had argued that we process what goes on in the mind of others using embodied cognition, i.e. using representations that are specific to our body and that would look different if our bodies were different [5]. Adam Smith [6] for instance suggested we care about what a man being whipped feels because our mind makes us feel that whip on our own skin. This suggests representations of our own bodily pain, i.e. embodied representations, play a role in understanding what others feel. That mirror neurons were found in the motor system and are part of controlling the specific body of the monkey, shows that they are embodied. That they also respond when seeing other people's actions shows that the brain indeed recruits some embodied representations while witnessing what others do. Initially, much effort was directed at questioning and establishing whether humans had a similar mirror system. Over

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the last two decades behavioral, neuroimaging, TMS and even single cell studies in humans provided clear evidence that humans do indeed have a similar system [2,7,8] (Figure 1).

Hence, humans also recruit embodied motor representations while witnessing the actions of others but what, if anything, do these embodied representations contribute to our perception of the actions of others? Answering this question requires a different, causal approach, in which brain activity in regions associated with the mirror neuron system are perturbed, either non-invasively using TMS or tDCS, or as a result of stable lesions following for instance a stroke, and changes in social cognition are measured. In 2014, Urgesi and collaborators [9] elegantly reviewed these causal efforts, including an excellent historical review of case studies, a detailed analysis of neuromodulation studies and a quantitative analysis of voxel-based lesion symptom mapping studies. They conclude that perturbing the mirror neuron system leads to measurable impairments in how well participants analyze the kinematics of observed actions (e.g. recognizing actions from point light displays) and deduce the goal of actions (e.g. what object would have been used in a pantomime). This was true for both the nodes where mirror neurons were recorded in the monkey [3,4,10]: the premotor cortex (PM, including BA6 and the inferior frontal gyrus) and the inferior parietal lobe (IPL). Since, a number of additional neuromodulation and lesion studies have confirmed this conclusion [11–16]. Here, we will not systematically review this literature. Rather, we will focus on a number of themes that have more recently emerged and that refine our understanding of the contributions of embodied neural representations to how we perceive and react to the actions of others.

Networks not brain regions

It is often assumed that if applying neuromodulation (for instance TMS) on a particular region X impairs performance in a particular task, then region X must directly contribute to that task. However, recent studies shed doubt on that localist interpretation. When neuromodulation is integrated with neuroimaging techniques (such as fMRI or EEG) stimulation-dependent effects can be observed in remote regions that have a functional connectivity with the targeted region [17–22]. A recent study applied TMS over the hand representation of the primary somatosensory cortex (SI) while participants observed hand actions in an fMRI scanner [23]. The local perturbation on SI was found to cause altered activity in all the nodes typically recruited during action observation, including PM and IPL and even high level visual cortices. This shows that somatosensory (SI) and motor (IPL and PM) regions form an integrated somatosensory-motor network – so that altering activity in one node alters activity in the others during action observation. Embodied cognition thus also recruits representations of what it would feel like to move in the observed ways (see ‘Somatosensation in Action Perception’). This spread of activation across the network helps understand how mirror activity could reach consciousness: electrical stimulation of premotor cortex triggers movements but little conscious experiences[24], while electrostimulation in IPL and SI triggers rich conscious intensions and sensations that could provide a gate for the network activity to enter consciousness.

Another powerful approach evidencing the distal effects of TMS is the application of TMS at two sites (dual-coil approach) [25], showing that M1 excitability is altered after

stimulation of several premotor and parietal regions [26–28]. Together these results emphasize that we must interpret findings of neuromodulation and lesion studies in terms of perturbations of entire networks. Ideally, we should use neuroimaging methods in combination with neuromodulation to interpret brain-behavior associations accurately.

Somatosensation in Action Perception

Classically, action observation was associated with the recruitment of *motor* embodied representations. That the posterior most part of SI, specifically Broadman areas BA1 and 2, were also systematically activated while viewing the actions of others led to increased interest in somatosensory embodied representations during action observation [8,29,30]. Over the past 3 years, studies show that disturbing activity in SI impairs action perception. Given that perturbing SI perturbs activity in PM and IPL and even in the visual cortex, these studies should not be interpreted to suggest that SI, by itself, contributes to the perception of actions, but rather, that it is a formally neglected causal player in a somatosensory-motor network that supports action perception [23]. Two studies targeted SI using TMS. Valchev et al found this to impair how accurately viewers can judge the weight of a little box from subtle differences in the observed kinematics of a person lifting that box with the hand [31]. Jacquet and Avenanti [16] found this to perturb how participants process whether an action is aimed at lifting or turning an object. Two studies found that facilitating neural activity in SI increases how much participants experience touch on their own body while witnessing touch in others [32,33]. Voxel-based lesion symptom association studies complement these findings. Lesions in a parietal cluster including SI were found to impair action imitation even with the good, ipsilesional hand [34,35]. De Wit and Buxbaum showed participants movies of actions, occluded a segment and asked the participants if the action continued as it should, or was time shifted [36]. Lesions in SI were associated with impairments in detecting such discontinuities. Finally, mild deficits in the ability to process the meaning of observed actions were also found following lesions encompassing SI [35].

Predictions and Somatosensory-motor embodied representations

Because our somatosensory-motor system coordinates and controls the timing of our own action chains, it is intuitively appealing to believe that activating a specific part of an action chain in this somatosensory-motor control loop would activate those actions that would normally follow the observed action in our own motor system, thereby performing a prediction of what would come next. Specifically, while we observe our own actions Hebbian learning in the synapses that connect visual with the somatosensory-motor system should wire up our brain to connect the sight of an action with the somatosensory-motor representation of the upcoming action [37] that would then inhibit the likely-to-come actions in the visual system in a predictive coding architecture [37,38]. These connections would then allow us to activate predicted actions when observing those of others. Indeed, single cell recordings in monkeys and single pulse TMS provide evidence that our motor system indeed activates representations of up-coming actions [10,39,40]. Studies now start to show interfering with somatosensory-motor embodied representations impairs the ability to predict how observed actions will continue. Football players become less able to predict where a ball will go from seeing the kicking motion under the influence of TMS on PM [41] and a study leveraging that tDCS can facilitate (anodal) and inhibit (cathodal) neural activity

found that facilitating PM representations (via the inferior frontal cortex) improves - and inhibiting PM impairs - people's ability to predict which of two objects will be grasped from witnessing the initial phase of the reaching movement [42]. Participants ability to judge whether an action continues as expected after being temporarily occluded was found to be impaired in patients with lesions in PM, SI and IPL [36]. In all of these tasks, the predictions to be performed are in the order of a few hundreds of milliseconds, a time scale that is very important for our motor system. It is likely that long term predictions (e.g. what will my son do when he comes of age in 5 years) rely on very different mechanisms.

Social Interactions

Without the ability to predict, acting in synchrony with others would be impossible: to for instance clap together, I would need to hear your clap (which takes ~100ms), then program and execute my own clap (~200ms), and my clap would come much after yours (~300ms delay). From the study of music we know people can synchronize their actions down to less than 50ms -- too short to simply react to the actions of other musicians. Instead, the brain must be predicting the actions of the other by some hundreds of milliseconds to have the time to plan and execute its own actions in good time. Using one's somatosensory-motor system to perform such predictions would be elegant: the predicted information would already have the somatosensory-motor format necessary to plan appropriate motor responses. While this field is very young, one elegant study shows that disrupting the PM impaired the accuracy with which one pianist could pick up the melody played by another in a musical turn-taking task [43]. Efforts to understand how disrupting embodied representations impacts on our ability to coordinate our actions with others is likely to become an exciting and rewarding enterprise. In this domain, animal studies can also provide important contributions.

Animal Studies

In animal models, optogenetics now provides ways to inhibit and excite populations of neurons with high temporal resolution. Song birds have premotor mirror neurons active when singing and listening to others. Juvenile birds learn to sing by silently listening to adult tutors and later trying to imitate their song. Triggering premotor optogenetic inhibition during listening while leaving activity unaltered during imitation phases severely impaired this learning[44]. This establishes the necessity of premotor activity in the social acquisition of vocal skills. Given the emergence of optogenetics in marmosets and macaques, species with mirror neurons for hand actions[4,39,45], similar experiments on the social transmission of manual skills become feasible. This emergent ability to disrupt mirror neuron activity with fine temporal control in animal models paves the way to tease apart the contribution of mirror neurons to social cognition at different stages of development. Would for instance interfering with mirror neuron activity early in life derail social development more than in adulthood? These questions have clinical relevance given that transient dysfunctions in mirror neuron activity during childhood and adolescence have been speculated to derail normal social development in disorders such as autism[46].

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Emotions

Causal neuroscientific evidence also provides evidence that embodied cognition contributes to how we perceive and react to the emotions of others [47]. Interfering with the PM-SI-IPL network disrupts our ability to recognize the bodily and facial emotional expressions of others [48–55]. We also recruit regions involved in our own emotions, in particular the insula and cingulate, while we witness the emotions of others[56,57]. These regions are too deep to target with TMS, but lesion studies show disrupting the insula in particular impairs emotion recognition and sharing [58–63]. The recent development of rodent models of emotional contagion is starting to unleash the power of modern opto- and chemogenetic methods to test whether altering brain activity in the insula and cingulate invasively alters emotion sharing [64,65].

Conclusions

After two decades of work establishing the existence of a mirror neuron system, evidence accumulates that PM, SI and IPL form a strongly integrated somatosensory-motor functional network during action observation that contributes in several ways to our social cognition and behavior. While the focus had been on benefits in imitation and perceiving the goal and kinematics of observed actions, recent studies have added new themes to this research. First, studies that not only perturb brain activity but also measure where the perturbation alters brain activity have emphasized that focal methods perturb entire networks. Second, SI, with its somatosensory representation, is an important player in network recruited during action observation suggesting that embodied representations of observed actions are somatosensory-motor in nature. Third, disturbing embodied representations disrupts our ability to predict the actions of others in the close (~300ms) future. Forth, the field is starting to examine how such disruptions impair our ability to coordinate the timing of our own actions with those of others without the delays that would result from our sensorimotor latencies. Fifth, animal models pave the way to investigating how transient deactivations can impact social development. Finally, this network is also necessary to recognize emotions from social displays together with the insula and cingulate.

Within neuroscience, these studies and trends are exciting in that they unravel the neural mechanisms that causally contribute to perception and social actions. Outside of the neurosciences, however, these studies contribute to a much broader discussion about whether and how embodied cognition can contribute to cognition and behavior. That disrupting motor and somatosensory cortices disrupts how we predict and react to the behavior of others shows that embodied representations are not an epiphenomenon but an important mechanism. This help us interpret why we are better at reading and predicting the inner states of people that have embodiments that resemble our own [66,67], and poses interesting challenges for human-machine interactions in which embodiments are fundamentally different [68].

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Highlights and Graphical Abstract

- Disturbing premotor, SI or inferior parietal corteces impairs action prediction
- Disturbing one of the nodes disturbs activity in the other nodes
- Disturbing that circuitry interferes with interpersonal coordination
- Perturbing that circuitry, insula or cingulate disturbs emotion recognition
- Embodied representations are essential for processing and interacting with others.

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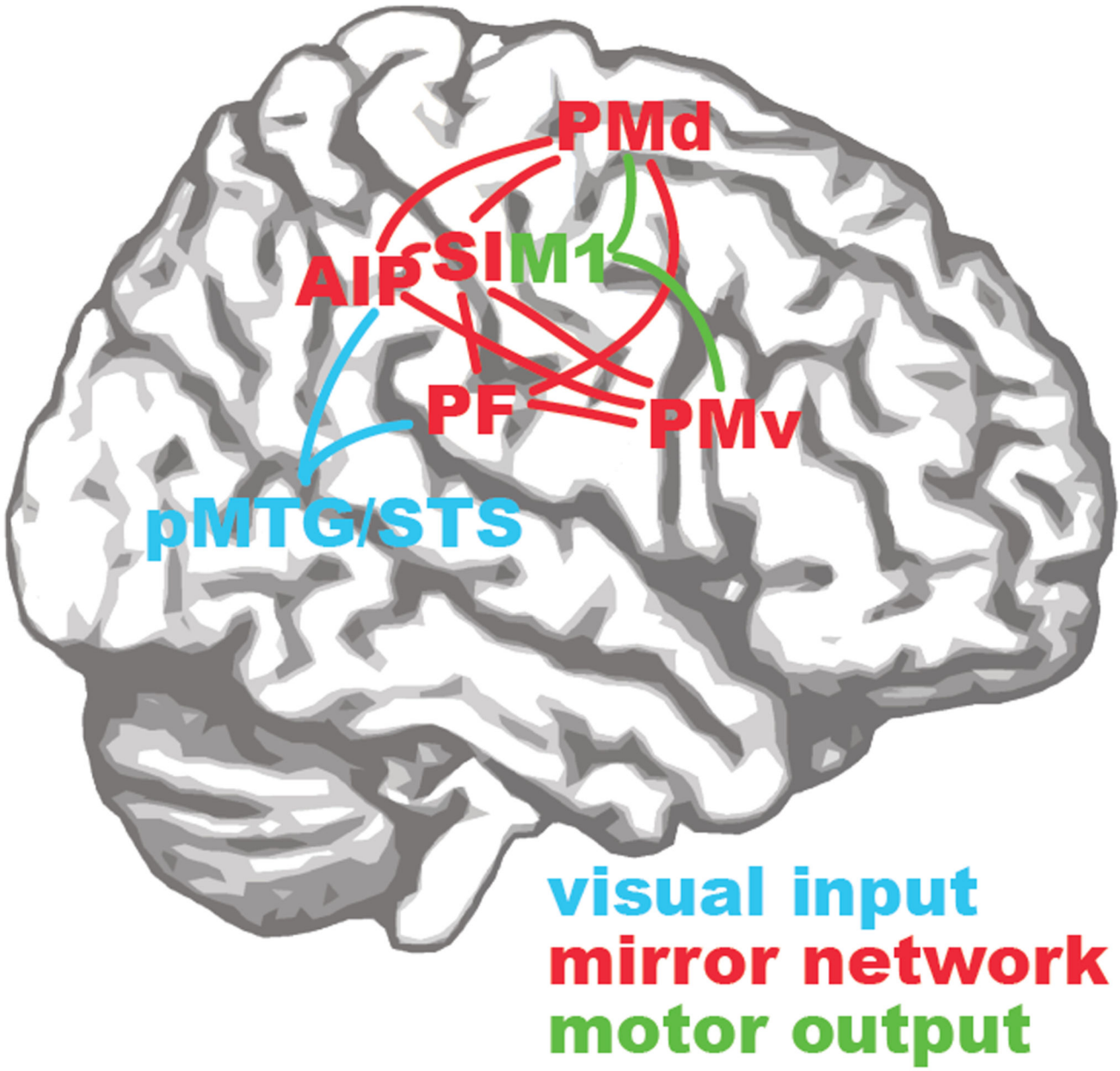

Figure 1.

Location of the main regions associated with the mirror neuron system in humans together with their anatomical interconnections (red). Visual input to this system mainly originates from the posterior mid temporal gyrus and superior temporal sulcus (blue). Motor output is sent to the primary motor cortex (M1, green). Abbreviations: AIP= Anterior IntraParietal; PF= area F of the Parietal lobe according to von Bonin & Bailey (1947); PMv and PMd = ventral and dorsal premotor cortex; pMTG=posterior Mid Temporal Gyrus; STS=superior temporal sulcus, SI=primary somatosensory cortices, including areas 3a, 3b, 1 and 2; M1=primary motor cortex; IPL in the text=AIP+PF