HEALTH PSYCHOLOGY

I Feel Your Pain: Mirror Neurons and Empathy

Lindsey MacGillivray, BSc

ABSTRACT

The old adage "I feel your pain" may be closer to reality than you think. Empathizing with another person's pain activates areas in our own brain that typically get turned on while we ourselves experience pain. And remarkably, this mirror-like reflection of the feelings and experiences of others is not limited to watching another in pain. Whether it be hearing a child cry out in pain or watching a soccer player kick a ball, mirror mechanisms in our brain allow us to directly map an external sensory perception onto our own neural action areas. Hence, we have firsthand recognition of the actions, thoughts and feeling of others because a sensory perception of another elicits a similar state in oneself. The most likely cellular mediator of this mapping between self and other are the so-called mirror neurons, neurons originally discovered in the monkey that respond both to observation of an action and to completion of the action itself. The mirror neuron circuit in humans is thought to be mediate imitation and may subserve higher functions such as empathy and intention understanding. Given that mirror neurons are a putative neural substrate of empathy, it follows that dysfunctional mirror neuron systems might underlie disorders characterized by empathy deficits, such as autism.

INTRODUCTION

The old adage "I feel your pain" may be closer to reality than you think. Most of us grimace if we see or hear a person receive a physical blow and our muscles may even twitch, almost as if we were actually experiencing that pain. Well, as it turns out, that may indeed be the case. Empathizing with another person's pain activates areas in our own brain that typically get turned on while we ourselves experience pain. Remarkably, this mirror-like reflection of the feelings and experiences of others is not limited to watching another in pain. Whether it be hearing a child cry out in pain or watching a soccer player kick a ball, mirror mechanisms in our brain allow us to directly map an external sensory perception onto our own neural action areas. Hence, we have firsthand recognition of the actions, thoughts and feeling of others because a sensory perception of another elicits a similar state in oneself.

This automatic mapping between self and other is a core feature of empathy and relies on integration of sensory information. There is little doubt that our ability to hear, see and touch others contributes to the ease with which we can understand and empathize with others. Only recently, however, has science provided us with any clues about the neu-

ral mechanisms that facilitate this multisensory integration and underlie our capacity to empathize.

I FEEL YOUR PAIN

Although pain is an inherently personal phenomenon, the ability to understand the pain of others is innate to most humans and is important for social relations. The expression "I feel your pain" is common, and justifiably so – tears well up in our eyes when we see another cry, we shudder at the sight of a needle penetrating the skin and, most males at least, nearly double over when they see an unfortunate athlete mistakenly kneed in the groin area.

Capacity to empathize with a person in pain is practically universal. Researchers at McGill University recently discovered that mice become sensitized to pain while watching one of their cagemates being subjected to that same insult. During each trial, two mice were injected with a weak acetic acid solution in order to elicit a writhing response. These mice were placed together in a plexiglass box and observed. Mice displayed significantly greater pain behaviour when in the presence of another mouse in pain, but interestingly, only if that other mouse was a familiar cagemate.[1] Whether or not such a demonstration constitutes true empathy is debat-

able, but at the very least it appears that mice can communicate their pain to others, and that others can react in kind, not unlike a young baby that starts to cry when it hears another baby crying.

Key Points

- Empathy may be facilitated through a process of automatic mapping between self and other. Perception of the actions and emotions of others activates areas in our own brain that typically respond when we experience those same actions and emotions. Empathy for another person's pain, for example, activates areas in our own brain that typically get turned on while we ourselves experience pain.

- Multisensory cues give us information about other persons' internal mental states, their intentions, and enable us to predict how they might react in a given situation.

- Mirror neurons respond both when perceiving an action and while executing an action. They provide a direct internal experience of another person's actions or emotions and may be the neurological basis of empathy.

- The multimodal nature of mirror neurons reflects the multisensory environment that we live in. Visuomotor mirror neurons, audiovisual mirror neurons and somatosensory mirror neurons permit us to make use of all available sensory information to understand and empathize with the actions, intentions and emotions of others.

- Dysfunctional mirror neuron systems might underlie disorders characterized by empathy deficits, such as autism.

Most would agree that the human capacity to empathize is greater that of other animals. Nevertheless, empathy encompasses an ability to accurately perceive the internal mental states of others and, in that respect, we have much in common with our animal friends. Empathy for another requires perception of their condition and that perception requires activation of sensory pathways. We see a man grimace with pain and we immediately understand his condition. Not only does sensory information allow us to perceive events, but our assessment and interpretation of such events is coloured by sensory detail. To illustrate, consider the contributions of sensory information to our own experience of pain.

The contributions of vision to our personal experience of pain are perhaps obvious – the sight of blood makes a cut seem all the more painful, or the patient arriving at the emergency room screaming in agony and pointing to a large nail lodged in their foot, only to subsequently realize that the nail had penetrated the boot only. The contributions of other sensory modalities to the tactile experience of pain, albeit more subtle, are present also and give significance to the physical insult. An individual's perceived pain might be enhanced if an injury is accompanied by the sharp sound of a bone breaking or by the subtle smell of blood. Given that perception of our own pain relies on a compilation of multisensory information, it only makes sense that our understanding of,

and empathy for, the pain of others would rely on a host of sensory information as well. Clearly, vision is the most obvious contributor. Seeing another person in pain facilitates an automatic representation of that state in our own minds.[2]

An interesting study on the somatosensory perception of pain in romantically involved couples highlights the mirror nature of empathy for pain. Seeing a loved one receive a painful shock activates brain areas associated with our own experience of pain.[2] Researchers made the reasonable assumption that couples in love will feel empathy for the other, especially if the other person is subjected to an unpleasant or painful experience. During the experiment, the female partner was placed in a functional magnetic resonance imaging (fMRI) scanner. Her male counterpart sat just outside the scanner with his hand positioned on a board such that it was visible to his partner. Signals that indicated which pain condition was coming (no pain or painful shock) and to whom it would be applied (herself or her male partner) were presented to the female in a random order. This enabled researchers to study the brain activity of the female while she was either experiencing pain or watching her partner receive a shock with the knowledge that he was feeling that same pain. Many of the same brain regions that were activated in the female during the painful shock (well-recognized pain areas such as the insula, anterior cingulate cortex, thalamus and somatosensory cortices, for example) were also activated during the observation of her partner in pain.

Taken together with a host of neuroimaging data that demonstrates shared representation for perception of pain in self and other,[3,4] these lines of evidence suggest that the mere observation of another person in pain can cause a pain-related neural response. Multisensory neurons in the brain that are specific for pain information may facilitate this process. During single neuron recordings in patients undergoing brain surgery, some neurons in the anterior cingulate cortex (a brain region associated with the emotional facet of pain) appear to respond both to a painful mechanical stimulus and to the anticipation or observation of a painful stimulus applied to an experimenter.[5] These mirror mechanisms in our brain allow us to directly map an external sensory perception onto our own neural action areas. Hence, we have firsthand recognition of the thoughts and feeling of others because a sensory perception of another elicits a similar state in oneself. The most likely cellular mediator of this mapping between self and other are the so-called mirror neurons, neurons originally discovered in the monkey that respond both to observation of an action and to completion of the action itself.

MONKEY SEE, MONKEY DO

The discovery of mirror neurons was made by an Italian research group studying the neural activity associated with hand and mouth movements in monkeys. Single neuron recordings in the premotor cortex (specifically in a region

known as area F5) gave a surprising result: instead of firing only when the monkey made a movement, a select population of neurons in the premotor cortex fired when the monkey observed that same action taking place. For example, motor neurons that fired when a monkey grasped a piece of fruit also fired when the monkey saw someone else grasp a piece of fruit.[6] Broadly speaking, this special class of motor neurons fires when the animal executes a goal-directed action and when he observes the same action as it is performed by others.[6-8] In addition to those identified in the premotor area of the frontal cortex, mirror neurons were later discovered in the inferior parietal lobe. These two brain areas communicate with one another, and the current hypothesis is that together these frontal and parietal regions form an integrated mirror neuron system.

Mirror neurons, appropriately named for their ability to record actions executed by another in the observer's brain, do more than just visually register an observed action – they facilitate an understanding of that action. This was perhaps best demonstrated by a large subgroup of mirror neurons in the monkey that fired while watching an experimenter reach for an object hidden behind a screen. The monkey did not necessarily need to see the object; prior knowledge of the object's presence enabled the monkey to gauge the intention of the experimenter. The grasping motion alone was not sufficient to activate mirror neurons. If monkeys first saw that no object was behind the screen, mirror neurons did not discharge on observation of a grasping motion.[9] This differential activation of mirror neurons suggests that actions are understood within a particular context.

Mirror neurons in the macaque inferior parietal lobe have a remarkable ability to discern intention, even between similar motor acts. Although a mirror neuron is initially activated by either carrying out of a motor act or perception of that act, the neuron differentially discharges, depending on the final goal. For instance, monkey mirror neurons know the difference between grasping food with the intention to eat, and grasping food with the intention to put it in a container. Populations of mirror neurons in the monkey parietal cortex are specific for particular contexts: some groups of neurons, for example, fire more intensely when grasping to eat rather than grasping to place while other neuronal populations display the opposite.[10]

Mirror neurons reflect the happenings of the outside world. Given the speed and ease with which humans can understand the actions and intentions of others, it seemed plausible that an analogous mirror neuron system to that of the monkey would be present in humans. A variety of neuroimaging and neurophysiological evidence points to the existence of a human mirror neuron system. Observation of a motor act, in the absence of any motor execution, activates the motor cortex in humans.[11,12] Indirect evidence was first provided by Gastaut and colleagues when they noted that movement and observation of movement both induced

desynchronization of an electroencephalogram (EEG) rhythm.[13] Later action observation studies employing transcranial magnetic stimulation (TMS)[14] or positron emission tomography (PET)[15] techniques provided additional support for a human mirror neuron system.

The inferior frontal gyrus and the adjacent ventral premotor cortex comprise the anterior portion of the putative human mirror neuron circuit. The inferior parietal lobe forms the posterior portion of the circuit. These regions, which correspond to area F5 of the macaque inferior frontal cortex and area PF/PFG of the monkey inferior parietal cortex, respectively, are activated during observation of motor events. The superior temporal sulcus is also included in the core circuit, as it represents the main visual input to the mirror neuron system and serves as a feedback centre that permits matching between sensory predictions of motor action and the visual stimuli gained from the observed action.[16] Together, the inferior frontal gyrus, adjacent inferior parietal cortex and superior temporal gyrus mediate the mapping of sensory input onto motor programs.[17] This circuitry likely mediates imitation in both monkeys[18] and humans[19] and may subserve higher functions such as empathy and intention understanding. Individuals often imitate each other during social interaction[20] and in addition, individuals that engage in frequent imitation are apt to be more empathic.[21]

Critics of the mirror neuron theory point out that there is presently no direct evidence for mirror neurons in humans and warn against premature acceptance of a mirror neuron substrate for higher cognitive functions. Dinstein and colleagues used fMRI to compare the spatial distribution of cortical responses within the intraparietal sulcus (IPS) to observed and performed movements.[22] Although single neuron recordings have localized mirror neurons in the IPS of monkeys and researchers have postulated that an analogous group of mirror neurons exist in humans, Dinstein's group noted that the spatial patterns of response to the observed and executed movements did not overlap, suggesting that there are relatively few mirror neurons in the area. To date, the scientific literature has been broadly supportive of the mirror neuron theory and a distillation of those findings is the primary focus of this paper. Nevertheless, the function and clinical relevance of mirror neurons is not universally agreed upon and the anomalous finding by Dinstein highlights the need for further research. The reader is referred to a recent review by Hickok for a more in-depth assessment of the potential problems associated with the mirror neuron theory of action understanding.[23]

Although the mirror neuron system was initially thought to be visuomotor only, audiovisual[24-26] and somatosensory[27-29] mirror neurons have recently been discovered. Select population of mirror neurons of macaque monkeys respond to the sound of an action, even in the absence of visual input.[24,25] In area F5 of the monkey premotor cortex,

for example, certain neurons respond not only when the monkey breaks a peanut or when he sees a researcher breaking a peanut, but also when the he hears a peanut breaking in the absence of visual input.[24] Some of these neurons display remarkable specificity: in one neuron that was selectively activated by action-related sounds, the neuron responded vigorously when the monkey both saw and heard a peanut breaking, showed a lesser but still significant response when the monkey only heard the peanut breaking, but did not respond at all to merely seeing the peanut break. For other mirror neurons, the intensity of the neuron response was approximately the same, regardless of whether the monkey only saw an action, only heard an action, or both saw and heard an action. In a small population of neurons, the intensity of the response to sound alone was strongest.[24] This variation in neuronal discharge properties reflects the multiple ways in which sensory inputs combine to inform us about the external world. That a large population of neurons requires both visual and auditory information for activation underscores the importance of multisensory integration for action understanding. Indeed, for most everyday events, each source of sensory information available to us enriches our understanding of that event; the multimodal properties of mirror neurons may reflect learned associations among actions and their sensory characteristics.

An analogous auditory mirror neuron system to that demonstrated in the monkey may exist in humans. The sound of a salient motor action activates in the human the same brain areas responsible for executing that action. Researchers used fMRI analysis to show that performing a hand action (such a ripping a piece of paper) and listening to the sound of that action both activate a temporo-parietal-premotor brain circuit.[26] Much of this auditory mirror neuron circuitry overlaps with the previously described visual mirror neuron system, again highlighting the multisensory nature of the mirror neuron system.

An auditory mirror neuron system may ultimately enhance our ability to understand others. If we hear an individual gasping in pain, whooping with joy or yelling in anger, most of us can reliably assess their emotional condition. Interestingly, those individuals that are good at imagining the perspective of another, a measure of empathy, tend to have a more easily activated auditory mirror neuron system[26] supporting the putative link between mirror neurons and empathy.

BROKEN MIRRORS

Given that mirror neurons are a putative neural substrate of empathy, it follows that dysfunctional mirror neuron systems might underlie disorders characterized by empathy deficits, such as autism. Autism sufferers perform poorly on imitation tasks and are unable to adequately assess the meaning of another person's actions.[30,31] Because mirror neurons mediate a connection between self and others and

are thought to be involved in imitation, empathy and perception of others' intentions,[19,32,33] it has been proposed that a mirror neuron system dysfunction might be at the root of autism symptoms.[34] The argument for a mirror neuron dysfunction in autism is compelling. Empathy requires that one has the capacity to understand the mental state of another, yet many autism sufferers seem oblivious to the suffering of distressed individuals.[35] Moreover, language impairments and an inability to imitate the actions of others are hallmark features of autism. As mirror neurons are theorized to serve as a functional neural basis for all of these attributes, mirror neuron dysfunction in autism sufferers is plausible.[30] Concrete evidence is scant thus far, but preliminary EEG[36] and fMRI[37] activation pattern studies suggest that mirror neuron dysfunction does indeed contribute to the core deficits of autism. The strongest evidence for the mirror neuron theory of autism stems from studies on brain rhythms. As briefly mentioned earlier, the mu brain wave is suppressed during voluntary muscle movements and while watching as another individual performs that same motor action,[13,36] a pattern notably similar to mirror neuron activation. These waves are derived from sensorimotor cortex and can be detected with non-invasive EEG devices. As such, it was thought that mu wave suppression might be an effective means for monitoring mirror neuron activity.

At rest, sensorimotor neurons have a large amplitude oscillation a frequency of 8 to13 Hz (the mu rhythm). Motor action (a hand movement, for example) disrupts the rhythm and suppresses the EEG oscillations.[38] In fact, voluntary movement, imagined movement and observed movement all induce mu wave suppression,[12,39,40] strengthening the likelihood that mu-wave properties are reflective of mirror-neuron activity. High functioning autistic individuals show mu wave suppression during voluntary movement, just like typically developing controls. During observation of that same action, however, mu wave suppression was absent in the autistic subjects but not the control subjects. The lack of mu wave suppression in autistic subjects during observation but not action suggests that although the subject's motor command system was intact, the mirror neuron system was dysfunctional.[36]

These results are corroborated by similar studies employing magnetoencephalography,[41] fMRI[37] and TMS techniques.[42] For instance, TMS-induced hand movements are typically enhanced when subjects watch video footage of the same movements; this enhancement is much reduced in autistic individuals.[42] The perception-action theory of empathy applies to any sensory modality. Sensory perception of others, whether by visual, auditory, tactile or even olfactory information, activates the brain areas necessary to facilitate understanding of that action. Moreover, the mirror neurons that facilitate this firsthand experience of our sensory perceptions are by necessity multisensory. Visuomotor,

audiovisual, somatosensory and perhaps other mirror neuron subtypes not yet discovered mediate the matching of actions of others onto our own sensorimotor representations. A holistic perception of another individual's mental state is more readily achievable if all available sensory information is taken into account. Given the putative mirror neuron dysfunction and the sensory integration deficits inherent in autism,[43],[44] an impairment in multisensory processing is likely associated with the notable absence of empathy in autism sufferers.

REFERENCES

1. Langford DJ, Crager SE, Shehzad Z, et al. Social modulation of pain as evidence for empathy in mice. Science 2006; 312: 1967-70.
2. Singer T, Seymour B, O'Doherty J, et al. Empathy for pain involves the affective but not sensory components of pain. Science 2004; 303: 1157-62.
3. Botvinick M, Jha AP, Bylsma LM, et al. Viewing facial expressions of pain engages cortical areas involved in the direct expression of pain. Neuroimage 2005; 25: 312-19.
4. Jackson PL, Meltzoff AN, Decety J. How do we perceive the pain of others? A window into the neural processes involved in empathy. Neuroimage 2005; 24: 771-79.
5. Hutchison WD, Davis KD, Lazano AM, et al. Pain-related neurons in the human cingulate cortex. Nat Neurosci 1999; 2: 403-05.
6. Gallese V, Fadiga L, Fogassi L, et al. Action recognition in the premotor cortex. Brain 1996; 119: 593-609.
7. di Pellegrino G, Fadiga L, Fogassi L, et al. Understanding motor events: A neurophysiological study. Exp Brain Res 1992; 91: 176-80.
8. Rizzolatti G, Fadiga L, Gallese V, et al. Premotor cortex and the recognition of motor actions. Brain Res Cogn Brain Res 1996; 3: 131-41.
9. Umilta MA, Kohler E, Gallese V, et al. I know what you are doing: A neurophysiological study. Neuron 2001; 31: 155-65.
10. Fogassi L, Ferrari PF, Gesierich B, et al. Parietal lobe: From action organization to intention understanding. Science 2005; 308: 662-67.
11. Hari R, Forss N, Avikainen S, et al. Activation of human primary motor cortex during action observation: A neuromagnetic study. Proc Natl Acad Sci USA 1998; 95: 15061-65.
12. Cochin S, Barthelemy C, Roux S, et al. Observation and execution of movement: Similarities demonstrated by quantified electroencephalography. Eur J Neurosci 1999; 11: 1839-42.
13. Gastaut HJ & Bert J. EEG changes during cinematographic presentation; moving picture activation of the EEG. Electroencephalogr Clin Neurophysiol Suppl 1954; 6: 433-44.
14. Fadiga L, Fogassi L, Pavesi G, et al. Motor facilitation during action observation: A magnetic stimulation study. J Neurophysiol 1995; 73: 2608-11.
15. Rizzolatti G, Fadiga L, Metelli M, et al. Localization of grasp representation in humans by PET: 1. Observation versus execution. Exp Brain Res 1996; 111: 246-52.
16. Iacoboni M, Koski LM, Brass M, et al. Reafferent copies of imitated actions in the right superior temporal cortex. Proc Natl Acad Sci USA 2001; 98: 12995-13999.
17. Iacoboni M & Dapretto M. The mirror neuron system and the consequences of its dysfunction. Nat Rev Neurosci 2006; 7: 942-51.
18. Ferrari PF, Visalberghi E, Paukner A, et al. Neonatal imitation in rhesus macaques. PLoS Biol 2006; 4: e302.
19. Iacoboni M, Woods RP, Brass M, et al. Cortical mechanisms of human imitation. Science 1999; 286: 2526-28.
20. Iacoboni M. Neural mechanisms of imitation. Curr Opin Neurobiol 2005; 15: 632-37.
21. Chartrand TL & Bargh JA. The chameleon effect: the perception-behavior link and social interaction. J Pers Soc Psychol 1999; 76: 893-910.
22. Dinstein I, Gardner JL, Jazayeri M, et al. Executed and observed movements have different distributed representations in human aIPS. J Neurosci 2008; 28: 11231–39.
23. Hickok, G. Eight problems for the mirror neuron theory of action understanding in monkeys and humans. J Cogn Neurosci 2009: 1-15 (Epub ahead of print).
24. Kohler E, Keysers, C, Umilta, MA, et al. Hearing sounds, understanding actions: Action representation in mirror neurons. Science 2002; 297: 846-48.
25. Keysers C, Kohler E, Umilta MA, et al. Audiovisual mirror neurons and action recognition. Exp Brain Res 2003; 253: 628-36.
26. Gazzola V, Aziz-Zadeh L & Keysers C. Empathy and the somatotopic auditory mirror system in humans. Curr Biol 2006; 16: 1824-29.
27. Keysers C, Wicker B, Gazzola V, et al. A touching sight: SII/PV activation during the observation and experience of touch. Neuron 2004; 42: 335-46.
28. Avenanti A, Bueti D, Galati G, et al. Transcranial magnetic stimulation highlights the sensorimotor side of empathy for pain. Nat Neurosci 2005; 8: 955-60.
29. Bufalari I, Aprile T, Avenanti A, et al. Empathy for pain and touch in the human somatosensory cortex. Cereb Cortex 2007; 17:2553-61.
30. Williams JH, Whiten A, Suddendorf T, et al. Imitation, mirror neurons and autism. Neurosci Biobehav Rev 2001; 25: 287-95.
31. Williams JH, Whiten A & Singh T. A systematic review of action imitation in autistic spectrum disorder. J Autism Dev Disord 2004; 34: 285-99.
32. Johnson-Frey SH, Maloof FR, Newman-Norlund R, et al. Actions or hand-object interactions? Human inferior frontal cortex and action observation. Neuron 2003; 39: 1053-58.
33. Iacoboni M, Molnar-Szakacs I, Gallese V, et al. Grasping the intentions of others with one's own mirror neuron system. PLoS Biol 2005; 3: e79.
34. Ramachandran, VS & Oberman LM. Broken mirrors: a theory of autism. Sci Am 2006; 5: 62-69.
35. Bacon AL, Fein D, Morris R, et al. The responses of autistic children to the distress of others, J Autism Dev Disord 1998; 2: 129-42.
36. Oberman LM, Hubbard, EM, McCleery JP, et al. EEG evidence for mirror neuron dysfunction in autism spectrum disorders. Brain Res Cogn Brain Res 2005; 24: 190-98.
37. Dapretto M, Davies MS, Pfeifer JH, et al. Understanding emotions in others: mirror neuron dysfunction in children with autism spectrum disorders. Nat Neurosci 2006; 9: 28-30.
38. Salmelin R & Hari R. Spatiotemporal characteristics of sensorimotor neuromagnetic rhythms related to thumb movement. Neuroscience 1994; 60: 537-50.
39. Pineda JA, Allison BZ, Vankov A. The effects of self-movement, observation and imagination on mu rhythms and readiness potentials: toward a brain-computer interface. IEEE Trans Rehabil Eng 2000; 8: 219-22.
40. Muthukumaraswarmy SD, Johnson BW, McNair NA. Mu rhythm modulation of an object-directed grasp. Brain Res Cogn Brain Res 2004; 19: 195-201.
41. Nishitani N, Avikainen S, Hari, R. Abnormal imitation-related cortical activation sequences in Asperger's syndrome. Ann Neurol 2004; 55: 558-62.
42. Theoret H, Halligan E, Kobayashi M, et al. Impaired motor facilitation during action observation in individuals with autism spectrum disorder. Curr Biol 2005; 15: R84-85.
43. Iarocci G & McDonald J. Sensory integration and the perceptual experience of persons with autism. J Autism Dev Disord 2006; 36: 77-90.
44. Kern JK, Trivedi MH, Garver CR, et al. The pattern of sensory processing abnormalities in autism. Autism 2006; 10: 480-94.

Author Biography

Lindsey MacGillivray is a second year MD/PhD student in Medical Sciences at the Michael G. DeGroote School of Medicine at McMaster University. She previously completed her Honours BSc Biology degree at St. Francis Xavier University in 2005.