

# Immediate Interpersonal and Intermanual Referral of Sensations Following Anesthetic Block of One Arm

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**Objectives:** To explore whether interpersonal and intermanual sensory referral occurs following anesthetic block of a limb and to test theories of disinhibition of mirror neuron activity and transcallosal referral.

**Design:** Case series.

**Setting:** Outpatient surgery at the University of California San Diego Medical Center.

**Patients:** Six patients who underwent orthopedic surgery.

**Main Outcome Measures:** Patient verbal ratings.

**Results:** Patients with brachial plexus blocks experienced touch sensations in the anesthetized arm when watching another person's arm being touched or when the contralateral intact hand was touched.

**Conclusions:** To our knowledge, this is the first demonstration of rapid reorganization of functional connectivity in the adult human brain, most likely in S2 neurons. This finding suggests that conscious perception of touch results from fluctuating mosaics of cortical excitation and inhibition between different regions within the patient's own S2 neurons and, more remarkably, from viewing others' sensations.

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**N**EURONS IN THE VENTRAL premotor area of primates ordinarily fire when the primate performs a specific action such as reaching for an object, putting it in his or her mouth, or pushing it. These "motor command neurons" orchestrate the sequence of muscle twitches required for the action.<sup>1</sup> A subset of these neurons—"mirror neurons"—fire even when the primate watches someone else move his or her hand, as if the neuron was simulating the other primate's movements and intentions.<sup>2</sup> There are also mirror neurons for touch; neurons in S2 fire when you are touched and also when you watch someone else being touched.<sup>3,4</sup>

If sensory mirror neurons fire when you observe touch, why do you not actually feel touch "quale" when another person is touched? You may empathize with the sensation but will not actually feel touch quale on your skin (although this does happen in a rare form of congenital synesthesia called *mirror-touch synesthesia*<sup>5</sup>). One possibility is that the absence of tactile receptor activity in your skin sends a null signal to your somatosensory cortex indicating that you are not being touched and preventing the mirror neuron system (MNS) activation from reaching the threshold of conscious sensation.

What if you are deprived of sensory information about a limb and observe the same

limb of another person being touched? In the absence of inhibition by the sensory signal, will MNS activity reach the threshold for conscious perception, leading you to feel touch quale on your limb? To explore this possibility our laboratory had previously examined 3 patients with phantom limbs.<sup>6</sup> Because these patients lacked tactile input from the phantom limb, we predicted that they would experience tactile quale in their phantom limb while observing touch to another person, and this is indeed what we found. This finding suggests that one's own skin is the only barrier to experiencing someone else's touch sensation. We call this clinical sign *hyperempathy*.

In that study, patients with phantom limbs were seen several months after amputation, allowing time for long-term cortical reorganization.<sup>6</sup> Stronger support for the MNS disinhibition hypothesis would be obtained if hyperempathy occurred rapidly after deafferentation, such as under anesthesia.

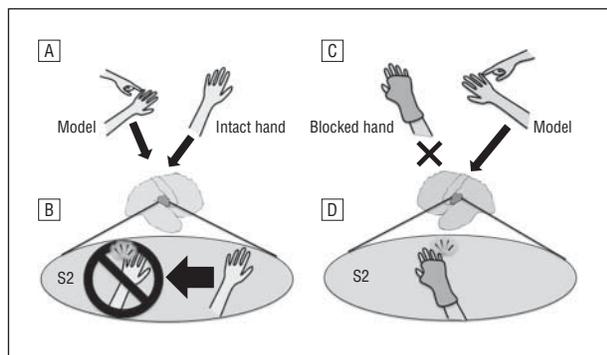
Another prediction about sensory referral under anesthesia can be made based on transcallosal connections between bilateral somatosensory cortices. Bilateral hand representation is found in the macaque somatosensory cortex,<sup>7</sup> and in humans the same arm muscles used in executing an action are activated while observing it in both the ipsilateral and contralateral forearms<sup>8</sup> of the observer. We therefore predicted intermanual referral of sensation from the in-

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**Table. Patient Characteristics and Observations<sup>a</sup>**

Characteristic	A	B	C	D	E	F
Sex/Age, y	M/21	F/25	M/70	M/29	M/44	F/57
Handedness	R	R	R	R	R	R
Blocked side	R	R	L	R	L	R
Referral to blocked arm	Yes	Yes	Yes	No	No	Yes
Referral to intact arm	Yes; less	No	Yes; less	No	No	No
Intermanual referral	Yes	Yes	Yes	No	No	Yes

<sup>a</sup>Patients are identified herein as A through F.



**Figure.** Interpersonal sensory referral. A, Patient observes touch to model's hand proximate to own intact hand. Patient's own hand is not touched. B, Right somatosensory cortex receives null signal indicating lack of touch to intact hand. Mirror neurons fire, representing observed touch to intact hand. Null signal inhibits mirror neurons. C, Patient's blocked hand is not touched. Patient observes touch to model's hand proximate to blocked hand. D, Left somatosensory cortex receives no signal from the blocked hand. Mirror neurons fire, representing observed touch to blocked hand.

tact hand to the anesthetized hand due to commissural input from the intact hand and lack of inhibition from the anesthetized hand. Indeed, our laboratory has previously shown that touching the intact hand of a patient whose arm had been amputated (with the patient's eyes closed during the touch) resulted in sensations perceived simultaneously in the phantom arm in a systematic, topographically organized manner (although there were minor deviations from topography presumably due to "noise" during reorganization).<sup>9,10</sup> Intermanual referral was also subsequently reported in a patient with deafferentation caused by stroke.<sup>11</sup>

## METHODS

We tested 6 randomly selected patients undergoing brachial plexus blocks in preparation for orthopedic surgery to determine whether interpersonal referral (hyperempathy) and intermanual referral would occur immediately following deafferentation (**Table**). Three additional patients were enrolled in the study and then withdrawn because they no longer wished to participate after surgery was completed ( $n=1$ ) or because of clear sensation in the anesthetized arm due to the diminishing effect of the anesthetic ( $n=2$ ). Clinical examination that was conducted before surgery revealed no neurologic abnormalities or preexisting sensory impairment recorded on the patients' medical charts. The patients were tested in the postoperative recovery room within 30 minutes after their surgical procedure; patients were awake and able to understand and respond to our questions, but the blocked arm remained anesthetized.

We first tested sensation in the blocked arm to ensure that the block remained complete. One patient (patient C) showed

very subtle sensitivity in a small part of the fourth and fifth digits of the anesthetized arm but was included in the analysis because all other parts of his arm lacked sensation.

Next, a volunteer's arm was positioned close to the intact arm or blocked arm (2 trials on each side in alternating order), and the patient was asked to watch while the volunteer was stroked on the surface of the arm, dorsum of the hand, fingers, thumb, and palmar surface by the experimenter for approximately 20 seconds in each location. The patient was asked to report any sensations felt in either arm. Patient F was tested using a double-blind procedure by a research assistant who was unaware of the purpose of the experiment. The patient was asked by the assistant to report sensation anywhere in the body. Sometimes when the patients indicated that they felt their blocked arm to be positioned in a different location from where it really was, the model's hand was placed near the felt location of the arm so that it was clearly visible. For example, patient F spontaneously reported that her anesthetized arm felt like it was lying across her chest, even though she knew it was lying at her side. She referred to this perceived limb as her "third arm."

During the blocked arm trials, 4 of the 6 patients reported that they could feel, in their anesthetized arm, the touch administered to the volunteer. Sensory referral tended to emerge quickly but not immediately. Patients expressed a variety of reactions including amusement, surprise, and disbelief. Patient A and C also reported feeling some referred sensation in the intact arm during the intact arm trials. This sensation was less pronounced than the sensation during the blocked arm trials (patients A and C estimated 50% and 5% more sensation, respectively, on the blocked side). Patient B reported no referral to the intact arm, and patient F reported 1 or 2 instances of referral to the blocked arm; this referral was negligible (infrequent and very weak) compared with the referral from the blocked side to the blocked arm.

We also asked 2 patients (C and F) to observe an ice cube placed on the volunteer's hand. Patient C felt cold on the blocked side but not the intact side. Patient F felt heaviness and numbness in response to ice on the blocked side but not on the intact side. This implies that there might be "mirror neurons" for cold; such neurons might have been constructed through Hebbian links formed between observing ice visually and touching it for a lifetime.

Why did any sensory referral to the intact side occur? We believe this referral can be explained by transcallosal connections. In a healthy individual, sensory input from the right arm is sent not only to the contralateral (left) hemisphere but also to the ipsilateral (right) hemisphere via commissural transcallosal fibers. This may contribute to partial tonic inhibition of MNS activity. When input from the right arm is blocked, its transcallosal contribution is also removed (**Figure**). This would lower the threshold for MNS activity on the right hemisphere (left arm) due to lower overall sensory input. This argument is supported by elegant work in monkeys and flying foxes showing an immediate expansion of receptive fields when transcallosal input is blocked, suggesting that callosal input provides

tonic inhibition and shaping of receptive fields.<sup>12</sup> Removing this inhibitory callosal input might allow MNS activity to compete more effectively for conscious representation.

Finally, we tested intermanual referral by touching the patient's intact hand and asking the patient to report any sensation perceived in the other arm. Four of the 6 patients showed systematic intermanual referral from the nonanesthetized hand to the anesthetized one. We also placed ice on the intact hand (not performed on patient F); referral of cold sensation occurred only for patient B. Intermanual referral did not occur for nonanesthetized regions proximal to the zone of anesthesia. Somatotopic organization was imprecise at times; in 1 patient, for example, touching the intact thumb referred sensation to both the blocked thumb and forefinger. We had predicted that the imprecise nature of deafferentation might lead to some imprecision of sensory referral.

Ipsilateral activation does not normally lead to conscious sensations in the left hand when the right hand is touched. This must be because, under normal conditions, transcallosal ipsilateral activation is inhibited and prevented from reaching consciousness by the "regular" contralateral input. If the arm is anesthetized, this tonic inhibition is removed and stimulation of the intact hand is referred to the anesthetized arm. To our knowledge, these findings provide the first evidence of functional reorganization of pathways connecting the somatosensory regions of both hemispheres, resulting in altered qualia.

## COMMENT

Taken collectively, these findings have some radical implications. They imply that the MNS can bridge the "qualia barrier" between one person's sensation and another's immediately following simple deafferentation. The referral of qualia soon after temporary anesthetization supports our conjecture that there is ordinarily tonic inhibition by the null signal from tactile receptors. We conclude that the final emergence and localization of touch sensations result from the coactivation and mutual inhibition of 4 systems: (1) afferents from the region touched; (2) tonic inhibition from null signals emerging from the untouched hand; (3) activation of the MNS while watching others; and (4) inhibition of MNS output, preventing it from reaching the threshold for conscious experience.

Confabulation is an unlikely explanation for these results for several reasons: (1) the findings were reliably repeatable across trials and participants; (2) tapping and ice were largely ineffective, while stroking was highly effective, and there would be no basis for such "selective" confabulation; (3) patients were surprised by the effect; (4) there was a latency period before the effect emerged and one might expect confabulation to be immediate; (5) in several patients sensation was referred to a different part of the hand from where the touch was—a strange thing to confabulate; and (6) referral occurred in patient F even though she was tested using a double-blind procedure.

The conventional model in neurology assumes that the adult brain contains immutable hardwired modules that interact very little. Our results point to a more dynamic picture of the brain in which different modules—or even different regions within a given sensory map—are in a constant state of dynamic equilibrium with

each other (and indeed with other brains). Neural dysfunction may often result from temporary shifts in equilibrium that could be shifted back to normal using the right procedures. We are presently conducting brain-imaging studies to explore these effects further, given the widespread belief among our colleagues that sophisticated brain imaging is an intrinsically meritorious activity whose results are more reliable than those of the simple tests used in classical neurology and psychophysics.

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**Author Contributions:** Ms Case and Dr Ramachandran had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Case and Ramachandran. *Acquisition of data:* Case, Abrams, and Ramachandran. *Analysis and interpretation of data:* Case and Ramachandran. *Drafting of the manuscript:* Case and Ramachandran. *Critical revision of the manuscript for important intellectual content:* Case, Abrams, and Ramachandran. *Statistical analysis:* Case. *Administrative, technical, and material support:* Case and Ramachandran. *Study supervision:* Abrams and Ramachandran.

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## REFERENCES

1. Mountcastle VB, Lynch JC, Georgopoulos A, Sakata H, Acuna C. Posterior parietal association cortex of the monkey: command functions for operations within extrapersonal space. *J Neurophysiol.* 1975;38(4):871-908.
2. Rizzolatti G, Fogassi L, Gallese V. Neurophysiological mechanisms underlying the understanding and imitation of action. *Nat Rev Neurosci.* 2001;2(9):661-670.
3. Keyserers C, Wicker B, Gazzola V, Anton JL, Fogassi L, Gallese V. A touching sight: SII/PV activation during the observation and experience of touch. *Neuron.* 2004;42(2):335-346.
4. Blakemore SJ, Bristow D, Bird G, Frith C, Ward J. Somatosensory activations during the observation of touch and a case of vision-touch synaesthesia. *Brain.* 2005;128(7):1571-1583.
5. Banissy MJ, Cohen Kadosh R, Maus GW, Walsh V, Ward J. Prevalence, characteristics and a neurocognitive model of mirror-touch synaesthesia. *Exp Brain Res.* 2009;198(2-3):261-272.
6. Ramachandran VS, Brang D. Sensations evoked in patients with amputation from watching an individual whose corresponding intact limb is being touched. *Arch Neurol.* 2009;66(10):1281-1284.
7. Iwamura Y, Iriki A, Tanaka M. Bilateral hand representation in the postcentral somatosensory cortex. *Nature.* 1994;369(6481):554-556.
8. Borroni P, Baldissera F. Activation of motor pathways during observation and execution of hand movements. *Soc Neurosci.* 2008;3(3-4):276-288.
9. Ramachandran VS, Rogers-Ramachandran D, Cobb S. Touching the phantom limb. *Nature.* 1995;377(6549):489-490.
10. Ramachandran VS, Hirstein W. The perception of phantom limbs [the D. O. Hebb lecture]. *Brain.* 1998;121(pt 9):1603-1630.
11. Sathian K. Intermanual referral of sensation to anesthetic hands. *Neurology.* 2000;54(9):1866-1868.
12. Clarey JC, Tweedale R, Calford MB. Interhemispheric modulation of somatosensory receptive fields: evidence for plasticity in primary somatosensory cortex. *Cereb Cortex.* 1996;6(2):196-206.