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

Laura K. Case, MA; Reid A. Abrams, MD; Vilayanur S. Ramachandran, MD, PhD

**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.

Arch Neurol. 2010;67(12):1521-1523

**NEURONS 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.**

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. There are also mirror neurons for touch; neurons in S2 fire when you are touched and also when you watch someone else being touched.

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 limb? To explore this possibility our laboratory had previously examined 3 patients with phantom limbs. 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. 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, and in humans the same arm muscles used in executing an action are activated while observing it in both the ipsilateral and contralateral forearms of the observer. We therefore predicted intermanual referral of sensation from the in-

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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 min-
utes 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 losal input is blocked, suggesting that callosal input provides an immediate expansion of receptive fields when transcal-
losal fibers. This may contribute to partial tonic inhibition of MNS activity. When input from the right arm is blocked, its 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 pa-
tient 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 numb-
ness in response to ice on the blocked side but not on the in-
tact side. This implies that there might be “mirror neurons” for cold; such neurons might have been constructed through Heb-
bian links formed between observing ice visually and touch-
input from the intact hand and lack of inhibition from the an-
esthesized 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 topog-
raphy presumably due to “noise” during reorganization).9,10

Intermanual referral was also subsequently reported in a patient with deafferen tation caused by stroke.11

The table provides patient characteristics and observations:

**Table**. Patient Characteristics and Observations

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex/Age, y</td>
<td>Male/21</td>
<td>Female/25</td>
<td>Male/70</td>
<td>Male/29</td>
<td>Male/44</td>
<td>Female/57</td>
</tr>
<tr>
<td>Handedness</td>
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<td>Right</td>
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<td>Right</td>
<td>Right</td>
<td>Right</td>
</tr>
<tr>
<td>Blocked side</td>
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<td>Right</td>
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<td>Left</td>
<td>Right</td>
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<tr>
<td>Referral to blocked arm</td>
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<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Referral to intact arm</td>
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<td>No</td>
<td>Yes; less</td>
<td>No</td>
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<td>No</td>
</tr>
<tr>
<td>Intermanual referral</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Patients are identified herein as A through F.
tonic inhibition and shaping of receptive fields.\textsuperscript{12} 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.

**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.

**Accepted for Publication:** March 18, 2010.

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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.

**Financial Disclosure:** None reported.

**Additional Contributions:** We thank David Brang, MA, for help and stimulating discussions and Abe Pollin, Richard Geckler, and Charlie Robbins for funding this research.

**REFERENCES**