Corrections

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Correction for "Restoring the sense of touch with a prosthetic hand through a brain interface," by Gregg A. Tabot, John F. Dammann, Joshua A. Berg, Francesco V. Tenore, Jessica L. Boback, R. Jacob Vogelstein, and Sliman J. Bensmaia, which appeared in issue 45, November 5, 2013, of *Proc Natl Acad Sci USA* (110:18279–18284; first published October 14, 2013; 10.1073/pnas.1221113110).

The authors note, "For the 'hybrid' location discrimination task, we report data obtained from 27 electrodes, 16 of which were in area 1; the 11 electrodes in area 3b were divided evenly across the two animals (6 and 5). We had previously tested all of the electrodes, including those in area 3b, in the detection and discrimination tasks (as shown in Fig. 3) and found them all to yield approximately equivalent performance (see Fig 3*A*). We noticed in the hybrid location discrimination task, however, that one of the animals performed much more poorly based on stimulation of area 3b than it did based on stimulation of area 1 (while the other animal performed better based on stimulation of area 1). Having no reason to question any of the arrays, we attributed this discrepancy to differences across animals and arrived at the conclusion, based on pooled data from both animals, that stimulation of the two areas yields equivalent performance in the 'hybrid location discrimination' task. The overall conclusion, then, was that stimulation of neurons in area 3b and 1 evokes percepts that are equally localized on the skin.

"Shortly after publication of the paper, we repeated detection experiments across the arrays and found that the animal could no longer detect stimulation through the array in area 3b that had yielded poor performance in the hybrid location discrimination task. It is therefore likely that this array had failed between the time we conducted the initial detection and discrimination experiments and the time we conducted the hybrid location discrimination task (which required 2–3 months of retraining). If this is the case, and we eliminate data from that bad array, then the median performance on hybrid trials is 83% (up from the 80% that was originally reported), which is still statistically poorer than that on the location-matched mechanical trials [median difference between performance on mechanical and hybrid trials was 3.3% rather than 5.6%, $t_{(119)} = 6.1$, $P < 0.001$] (see the corrected Fig. 2). Thus, we probably underestimated overall performance on hybrid trials, and thus the degree to which artificial percepts are localized, in the original publication. Importantly, however, performance on hybrid trials based on stimulation of area 3b was significantly better than performance based on stimulation of area 1 [median $\Delta p = 0.028$ and 0.054 for areas 3b and 1, respectively; t test: $t_{(76)} = 2.8$, $P < 0.01$]. Thus, based on the data obtained from only one animal, it seems as though stimulation of area 3b elicits more localized percepts than does stimulation of area 1, as might be expected given that neurons in area 3b tend to have smaller receptive fields than their counterparts in area 1 (1, 2)."

As a result of this error, Fig. 2 and its legend appeared incorrectly. The corrected figure and its corresponding legend appear below.
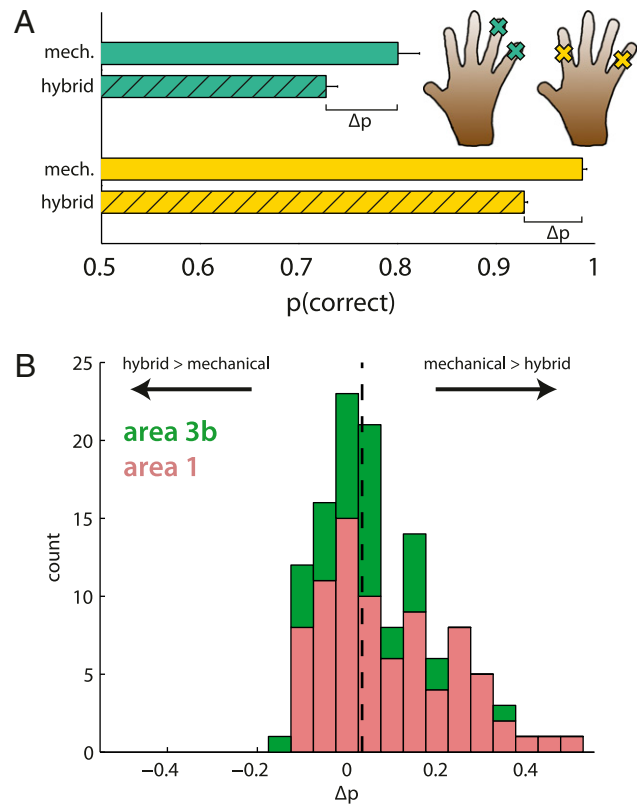

Fig. 2. Localization performance was similar with mechanical touch and ICMS. (*A*) On both mechanical and hybrid trials, the relative locations of stimuli applied to widely spaced digits were more accurately discriminated than were the relative locations of stimuli applied to adjacent digits. Measured from one animal, mechanical performance was based on 1,160 and 1,031 trials, respectively (green and gold); hybrid performance on 246 and 196 trials, respectively. To compare performance on hybrid trials and performance on mechanical trials matched for hand location, we computed the difference between the two: $\Delta p = p_{mech}(correct) - p_{hybrid}(correct)$. (*B*) Performance on mechanical and hybrid trials was nearly equivalent. Shown is the distribution of Δp for the two animals tested on this task (88 stimulus pairs, 21 different electrodes, 16 of which are UEAs). Across electrodes, performance was significantly above chance, demonstrating that ICMS yields spatially localized percepts. Performance on hybrid trials was somewhat lower than on mechanical location discrimination trials (median $\Delta p = 0.033$), suggesting that the elicited percepts may be somewhat more diffuse than natural ones. There was no significant difference in performance based on stimulation of areas 3b or 1, so data from these two areas are pooled.

1. Sur M, Garraghty PE, Bruce CJ (1985) Somatosensory cortex in macaque monkeys: laminar differences in receptive field size in areas 3b and 1. *Brain Res* 342(2): 391–395.

2. Sripati AP, Yoshioka T, Denchev P, Hsiao SS, Johnson KO (2006) Spatiotemporal receptive fields of peripheral afferents and cortical area 3b and 1 neurons in the primate somatosensory system. *J Neurosci* 26(7):2101–2114.

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Restoring the sense of touch with a prosthetic hand through a brain interface

Gregg A. Tabot[a,1], John F. Dammann[b,1], Joshua A. Berg[b], Francesco V. Tenore[c], Jessica L. Boback[b], R. Jacob Vogelstein[c], and Sliman J. Bensmaia[a,b,2]

[a]Committee on Computational Neuroscience and [b]Department of Organismal Biology and Anatomy, University of Chicago, Chicago, IL 60637; and [c]Research and Exploratory Development Department, The Johns Hopkins University Applied Physics Laboratory, Laurel, MD 20723

Our ability to manipulate objects dexterously relies fundamentally on sensory signals originating from the hand. To restore motor function with upper-limb neuroprostheses requires that somatosensory feedback be provided to the tetraplegic patient or amputee. Given the complexity of state-of-the-art prosthetic limbs and, thus, the huge state space they can traverse, it is desirable to minimize the need for the patient to learn associations between events impinging on the limb and arbitrary sensations. Accordingly, we have developed approaches to intuitively convey sensory information that is critical for object manipulation—information about contact location, pressure, and timing—through intracortical microstimulation of primary somatosensory cortex. In experiments with nonhuman primates, we show that we can elicit percepts that are projected to a localized patch of skin and that track the pressure exerted on the skin. In a real-time application, we demonstrate that animals can perform a tactile discrimination task equally well whether mechanical stimuli are delivered to their native fingers or to a prosthetic one. Finally, we propose that the timing of contact events can be signaled through phasic intracortical microstimulation at the onset and offset of object contact that mimics the ubiquitous on and off responses observed in primary somatosensory cortex to complement slowly varying pressure-related feedback. We anticipate that the proposed biomimetic feedback will considerably increase the dexterity and embodiment of upper-limb neuroprostheses and will constitute an important step in restoring touch to individuals who have lost it.

brain-machine interface | brain-computer interface | macaque

Although it has been shown that percepts can be elicited with intracortical microstimulation (ICMS) of primary somatosensory cortex (S1) (1–7), a major challenge in developing approaches to convey sensory feedback using ICMS in animal models is to assay the evoked sensations (8). One way to circumvent this obstacle is to train animals to discriminate sensory stimuli along a dimension of interest, and then to assess whether the animals can perform the task when physical stimuli are replaced with ICMS (2, 3). In this approach, ICMS regimes are designed to mimic the patterns of neuronal activation that encode the relevant sensory dimension. In the context of upper-limb neuroprostheses, contact location, pressure, and timing are three of the most basic cutaneous signals that mediate object grasping and manipulation (9). In somatosensory cortex of intact primates, the neural coding of stimulus location (i.e., which parts of the hand are contacting the object) presumably relies on somatotopic organization: The population of activated neurons within the body representations in S1 (one each in areas 3a, 3b, 1, and 2) determines where on the body the sensation is projected (10). We can attempt to convey information about contact location by targeting ICMS on populations of neurons with specific receptive field (RF) locations. The neural coding of contact pressure might rely on two mechanisms: (*i*) as the pressure exerted on the skin increases, the neuronal population with RFs under the stimulus becomes more active, and (*ii*) neurons with adjacent RFs will become activated so the size of the activated population will increase (11). We might thus convey information about pressure by increasing the amplitude of ICMS—thereby increasing both the strength of activation of neurons near the electrodes and the size of the activated population (12). The neural coding of contact timing—which signals when contact with an object is initiated and terminated—is thought to rely on the on and off responses produced in S1 neurons at the onset and offset of contact and lasting on the order of 50–100 ms (13). These temporally precise responses are relatively insensitive to object properties (14) and critical in guiding the dexterous manipulation of objects (9). We might convey information about contact timing by delivering phasic ICMS at the onset and offset of object contact. Our experimental approach consists in mimicking natural patterns in the brain and assessing whether the animal spontaneously interprets these induced patterns correctly.

Results

We began by training Rhesus macaques to perform perceptual tasks probing the perceived location and magnitude of skin indentions (Fig. 1 *A* and *B*). Once trained on the mechanical tasks, animals were implanted with arrays in the hand representations in area 3b [floating microelectrode arrays (FMAs); Microprobes for Life Science] and area 1 (Utah microelectrode arrays; Blackrock Microsystems) (Fig. 1*C*). We then mapped the receptive field of each electrode by identifying which areas of skin evoked multiunit activity (monitored through speakers)

Significance

Our ability to manipulate objects relies fundamentally on sensory signals originating from the hand. To restore motor function with upper-limb neuroprostheses requires that somatosensory feedback be provided to the tetraplegic patient or amputee. Accordingly, we have developed approaches to convey sensory information critical for object manipulation—information about contact location, pressure, and timing—through intracortical microstimulation of somatosensory cortex. In experiments with nonhuman primates, we show that we can elicit percepts that are projected to a localized patch of skin, that track the pressure exerted on the skin, and that signal the timing of contact events. We anticipate that the proposed biomimetic feedback will constitute an important step in restoring touch to individuals who have lost it.
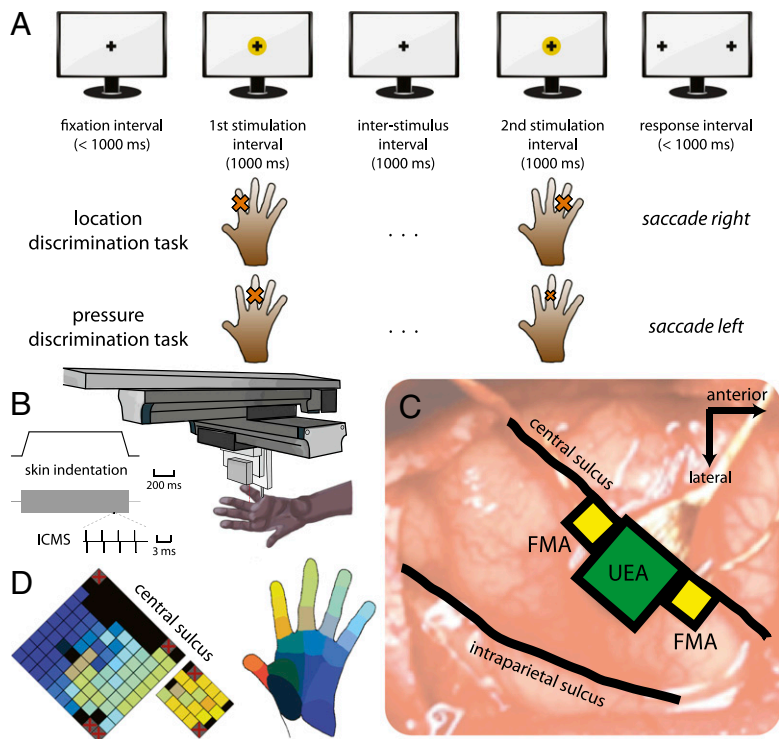
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Fig. 1. Experimental design. (*A, Upper*) Trial structure for all of the behavioral tasks: The cross is a fixation target or a response target, and the yellow circles indicate the two stimulus intervals. (*A, Lower*) One example trial each for the location discrimination and the pressure discrimination task. The size of the cross is proportional to the depth of indentation. (*B*) Depiction of the triaxial indenting stimulator. (*Upper Inset*) Trajectory of the tactile stimuli, which consisted of 1-s-long trapezoidal indentations into the skin. (*Lower Inset*) Structure of ICMS, which consisted of 300-Hz trains of symmetric biphasic pulses (phase duration = 200 μs, interphase duration = 53 μs) (38) lasting 1 s unless otherwise specified. (*C*) Chronic electrode implants in one of the three animals, showing the UEA, impinging on area 1, flanked by two FMAs, impinging on area 3b. We used FMAs to target area 3b, because the digit representation of area 3b is located deep in the posterior bank of the central sulcus and cannot be accessed with the 1.5-mm-long UEA electrodes. The UEA and the lateral-anterior FMA impinged on the hand representation; the medial-posterior FMA impinged on the arm representation in all three animals and so it was not used in the experiments. (*D*) RF map of the UEA and the lateral-anterior FMA. The UEA in this animal had RFs on the palm and digits 3–5; the FMA had RFs primarily on digit 2 (index). A red X denotes a reference electrode.

(Fig. 1*D*). RF mapping was repeated periodically throughout the study to verify that maps were consistent.

We assessed the extent to which the animals could perform these same tasks based on targeted stimulation of neuronal populations in S1. Importantly, ICMS trials were interleaved with mechanical trials, and individual experimental blocks comprised many different stimulus pairings (hand locations, stimulus amplitudes, etc.), which changed from block to block, so animals never had an opportunity to learn arbitrary stimulus-response contingencies on ICMS trials.

Signaling Contact Location. First, we sought to determine whether we could elicit percepts that are localized to a predetermined patch of skin (see refs. 15 and 16 for visual analogs). To this end, we sequentially delivered indentations to two different skin locations and had animals judge whether the second stimulus was medial or lateral to the first in a two-alternative forced-choice task (Figs. 1*A* and 2*A*). Once performance on the task leveled off, we replaced, on a subset of trials, one of the two mechanical stimuli with an ICMS train (Fig. 1*D, Inset*) delivered to a neuronal population whose RFs coincided with that of the replaced stimulus. We assessed whether the animal behaved as if an indentation had been delivered to that location. For example, if the index finger was indented in the first stimulus interval and neurons whose RFs are located on the small finger were stimulated in the second, the correct response was medial (and the animal saccaded to the right). These hybrid trials, in which a mechanical stimulus was paired with ICMS, were interleaved

with mechanical trials and multiple hand locations and electrodes were used in each experimental block. We found that performance on hybrid trials was significantly above chance [median performance 80% correct; *t* test: $t_{(131)} = 9.4$, $P < 0.001$], but generally poorer than on the location-matched mechanical trials [median difference between performance on mechanical and hybrid trials was 5.6%, paired *t* test: $t_{(131)} = 7.4$, $P < 0.001$] (Fig. 2*B*). Thus, the projection fields of the artificial percepts seem to be somewhat more diffuse than are the sensations evoked by punctate indentations, at least for a subset of electrodes. Performance on hybrid trials based on stimulation of area 3b was not significantly different from that based on stimulation of area 1 [*t* test: $t_{(130)} = 0.28$. $P > 0.5$]. Importantly, performance on the hybrid trials was high and significantly above chance even on the very first block [81% and 72% correct performance on 150 trials, χ^2 test: $\chi^2 (1) = 56.4$ and 29.0, $P < 0.001$], further bolstering the argument that the animal did not perform this task based on learned (and arbitrary) stimulus-response contingencies. We conclude that stimulation of a spatially restricted neuronal population elicits a percept that is spatially localized, with a projection field around its RF.

Signaling Contact Pressure. Next, we sought to develop approaches to convey information about the pressure applied on the prosthetic limb. We wished to elicit percepts whose magnitude spanned the range of natural tactile experience, ranging from just detectable to moderately intense. To this end, we first characterized sensitivity to both mechanical and electrical stimulation.
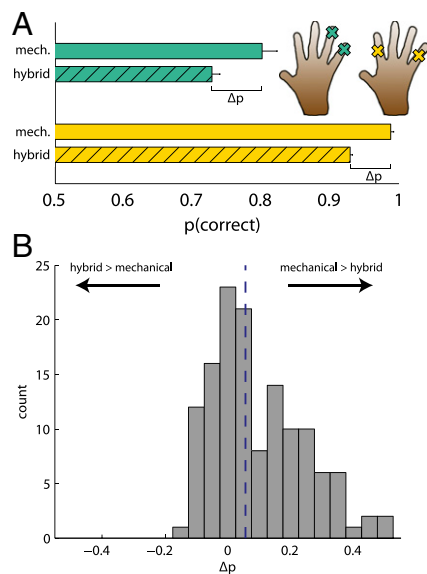
Fig. 2. Localization performance was similar with mechanical touch and ICMS. (*A*) On both mechanical and hybrid trials, the relative locations of stimuli applied to widely spaced digits were more accurately discriminated than were the relative locations of stimuli applied to adjacent digits. Measured from one animal, mechanical performance was based on 1,160 and 1,031 trials, respectively (green and gold); hybrid performance on 246 and 196 trials, respectively. To compare performance on hybrid trials and performance on mechanical trials matched for hand location, we computed the difference between the two: $\Delta P = p_{mech}(\text{correct}) - p_{hybrid}(\text{correct})$. (*B*) Performance on mechanical and hybrid trials was nearly equivalent. Shown is the distribution of Δp for the two animals tested on this task (132 stimulus pairs, 27 different electrodes, 16 of which are UEAs). Across electrodes, performance was significantly above chance, demonstrating that ICMS yields spatially localized percepts. Performance on hybrid trials was somewhat lower than on mechanical location discrimination trials (median $\Delta P = 0.056$), suggesting that the elicited percepts may be somewhat more diffuse than natural ones. There was no significant difference in performance based on stimulation of areas 3b or 1, so data from these two areas are pooled.

Specifically, animals performed a two-alternative forced-choice detection task, in which a skin indentation was delivered in one of two consecutive stimulus intervals. The animal indicated whether the stimulus was present in the first or second interval by saccading to the left or right, respectively. Once trained, the animals performed the detection task with ICMS pulse trains rather than with mechanical indentations; ICMS blocks were interleaved with mechanical blocks (Fig. 3*A*). We found most thresholds (defined as 75% correct performance on the detection task) ranged from 20 to 40 μA, with no differences across areas [two-way ANOVA: $F_{(1,55)} = 0.45$, $P = 0.5$] or animals [$F_{(2,55)} = 1.89$, $P = 0.16$]. From psychometric functions obtained in the mechanical and electrical conditions, we developed psychometric equivalence functions (PEFs), which relate electrical and mechanical stimuli of equal detectability (Fig. 3*B*) (*SI Experimental Procedures*). PEFs adopted a canonical form that was well approximated by a power function with exponents ranging from 0.3 to 0.5 ($R^2 = 0.995 \pm 0.006$, mean ± SEM).

To achieve a dynamic range of pressure-related sensations requires that regimes of ICMS extend beyond the periliminal range. Accordingly, we measured and compared the discriminability of supraliminal mechanical stimuli to that of electrical stimuli. Specifically, we had animals perform a two-alternative forced-choice pressure discrimination task in which they were sequentially presented with two indentations at different pressures and judged which of the two was stronger (Fig. 1*A*). To

ensure the animal had to attend to both stimulus intervals, two different standard stimuli (150 and 2,000 μm) were each paired, in every experimental block, with five comparison stimuli, ranging in amplitude from 150 to 2,000 μm. Once trained, the animals performed the same task but judged which of two ICMS pulse trains was more intense. To assess whether PEFs extrapolate to higher intensities, we used them to convert discrimination thresholds computed from ICMS trials to equivalent mechanical thresholds. We found that PEFs derived from (mechanical and electrical) detection data tended to overestimate the discrimination thresholds and adjusted the PEF parameters accordingly (*SI Experimental Procedures*, Fig. S1). To confirm that the adjusted PEFs provide an accurate mapping between mechanical and electrical stimuli across the range of stimulus intensities tested, we recomputed the mechanical equivalents of ICMS detection and discrimination thresholds (Fig. S2) and found that they were not significantly different from their actual mechanical counterparts (Fig. S3) [paired *t* tests: $t_{(30)} = 1.3, 0.7,$ and 0.5 for detection thresholds and discrimination thresholds with the two standards, respectively, $P > 0.2$]. These adjusted PEFs thus constitute an accurate mapping between mechanical and electrical stimuli of equivalent sensory magnitude.

Next, we wished to test the PEFs in the context of a real-time somatosensory neuroprosthesis. In these experiments, we had animals perform the detection and discrimination tasks based on mechanical stimulation of a prosthetic finger (from the Modular Prosthetic Limb, The Johns Hopkins Applied Physics Laboratory, Laurel, MD). Specifically, we delivered to the prosthetic finger the same stimuli used in the mechanical detection and discrimination experiments with the native finger. On each trial, the time-varying output of the pressure sensor on the prosthesis was converted into ICMS pulse trains by using the PEFs (see ref. 17 for a description of the hardware implementation). We found the animals' performance on experimental blocks with the prosthetic finger to be equivalent to that on experimental blocks with their native finger, which validates the PEFs (Fig. S4 and Fig. 3*C*). Finally, we verified that the animals were making analogous judgments in the mechanical and electrical stimulation conditions by showing that they could judge the relative intensity of paired electrical and mechanical stimuli (Fig. 4*A*). Thus, although we cannot make any claims as to the quality of the sensations evoked, we can make specific predictions as to the range of discriminable sensations that can be evoked through ICMS.

Signaling Contact Timing. The pressure signal produced during normal object manipulation evolves too slowly to provide temporally precise information about initiation or termination of object contact (18). Because contact with an object signals the end of the reach phase in natural reach and grasp (9), information about the timing of contact events must be precise. Thus, the slowly varying pressure-related feedback described above can be complemented by phasic ICMS pulse trains at the onset and offset of contact to signal the timing of contact events, thereby mimicking the natural on and off responses of S1 neurons (13). To be efficacious, however, these contact signals must also be clearly perceptible. Accordingly, we measured the effect of varying stimulus duration on the detectability of ICMS by having animals perform a detection task with pulse trains that varied in amplitude and duration. We found that detection functions were largely equivalent for durations of 100 ms or longer (Fig. 4*B*). Thus, an 80-μA, 100-ms pulse train (chosen because it is reliably supraliminal), which corresponds approximately to the duration of on and off responses in somatosensory cortex—can be used to signal contact events, whereas the pressure exerted on the object is signaled through an ICMS

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Fig. 3. Information about contact pressure was conveyed by varying ICMS amplitude. (*A*) Detection of ICMS in areas 3b and 1 followed a sigmoidal relationship to amplitude, shown here for one animal (area 3b: 19,184 trials, 7 electrodes; area 1: 29,498 trials, 27 electrodes). The horizontal dashed line indicates the threshold criterion. (*Inset*) Distribution of detection thresholds (75% detection) for all three animals (area 3b: 19 electrodes; area 1: 35 electrodes). There were no significant differences in sensitivity to ICMS across animals or anatomical areas. (*B*) ICMS amplitude was a power function of mechanical amplitude matched in perceived magnitude. Shown are PEFs derived from all of the electrodes for which there were both detection and discrimination data. Mechanical data from the electrode's RF was used to generate the function. The two colors correspond to two different monkeys with 4 and 12 electrodes (the third did not perform the discrimination task so did not yield PEFs). The darker traces show the pooled PEFs for each monkey. The equations are for the power functions fit to the pooled PEFs for the two monkeys are shown. (*C*) Discriminability of stimulus amplitude is equivalent when mechanical indentations are applied to the animal's own finger (blue) or to a prosthetic finger and converted to ICMS (red) (two animals with 240 and 360 trials with the prosthetic finger and 1,120 trials with the native finger). The mapping between time-varying pressure and time-varying ICMS amplitude was achieved by using the PEF. See Fig. S4 for analogous results in a detection task.

signal that is modulated according to the pressure exerted on the object throughout contact.

Discussion

Somatosensory feedback plays a critical role in the dexterous manipulation of objects (9). Indeed, signals from mechanoreceptive afferents in the skin convey information about the location of contact (19, 20) and about the forces exerted on the skin when an object is grasped (21–25). Cutaneous afferents also signal when our grip on an object is slipping (26). This critical information is unavailable visually and, when available, is generally inadequate to guide motor behavior. Without somatosensory input, then, we would routinely crush or drop grasped

objects. In addition, the sense of touch confers to our limbs embodiment, making them feel a part of us (27–29). Finally, touch plays an important role in communicating emotions and is a fundamental component of sexual behavior and experience. Given the importance of somatosensation, upper-limb neuroprostheses will not be clinically relevant until they provide for somatosensory inputs. Although the need for a highly invasive surgery sets the bar high for efficacy and reliability (30), ICMS has the potential to achieve sufficient sensory restoration to justify the risk, particularly in spinal cord injury patients, for whom many less-invasive options are not available.

The present findings provide a blueprint to convert the output of sensors on a prosthetic limb into patterns of ICMS that elicit

Fig. 4. (*A*) Animals are able to compare mechanical indentations to ICMS pulse trains scaled by using PEFs. The monkey compared a standard mechanical stimulus of fixed amplitude to a comparison electrical stimulus of variable amplitude (ranging from 20 to 80 μA) (performance pooled over 4 electrodes, 2 UEAs, and 2 FMAs for a total of 4,114 trials). The amplitude of the standard was matched in subjective magnitude with an electrical stimulus of amplitude 50 μA based on the PEF of each electrode tested (mean amplitude = 440 μm, range 200–750 μm). The animal judged which of the two stimuli was stronger, demonstrating that it could compare mechanical and electrical stimuli along a single perceptual dimension (magnitude). Error bars denote the SEM. (*B*) Sensitivity to ICMS increases with duration up to ~100 ms. Thresholds decrease as duration increases from 50 to 100 ms then level off. Thus, a 100-ms pulse at 80 μA will be clearly perceptible and can be used to signal the onset and offset of contact, mimicking the onset and offset responses observed in the somatosensory cortex of intact individuals. Error bars denote the SEM. These functions show the mean performance across four electrodes in area 3b in one animal.

somatosensory percepts that can then be used to guide the manipulation of objects.

Our approach consists of exploiting existing neural representations in somatosensory cortex to convey tactile information important for object grasping and manipulation. First, we show that ICMS elicits spatially localized percepts, a phenomenon that relies on the somatotopic organization of S1 and can be used to convey information about contact location. Although the degree to which the artificial percepts are localized remains to be elucidated, our results suggest that the projections fields may be more diffuse than are sensations elicited by a punctate indentation, at least for some electrodes. The diffuseness of the sensations is not surprising given that ICMS has been shown to evoke sparse, spatially distributed neuronal activity (31). Second, we show that the magnitude of the artificial percepts is graded according to the ICMS amplitude, a phenomenon that can be used to convey information about contact pressure. To ensure that artificial percepts operate over the same dynamic range as natural ones, we create mapping between the sensory magnitude of artificial and natural percepts (PEFs). The question remains whether the quality of the percept changes as ICMS amplitude increases, a question that can be addressed only in experiments with human subjects (32, 33). Third, we measure the effect of pulse train duration on detectability to identify the shortest detectable ICMS pulse train. We propose that a phasic pulse train can be used to mimic the cortical signature of contact events, namely a phasic burst mediated at the periphery by rapidly adapting mechanoreceptive afferents (13). This phasic pulse train can then be used to precisely signal the timing of the onset and offset of contact with objects.

To instrument a tetraplegic or amputated patient with a neuroprosthesis, the somatotopic organization of the array can be mapped by delivering ICMS pulses through each electrode and having the patient report the projected location of the sensation on the hand or phantom hand (34). Then, the pattern of stimulation delivered through each electrode can be determined in real time based on the output of sensors on the corresponding location of the prosthesis. Contact with an object would be signaled by a phasic ICMS pulse train of fixed amplitude followed by a tonic pulse train, the time-varying amplitude of which tracks the time-varying pressure exerted on the sensor according to a PEF (calibrated based on the sensitivity of that electrode to electrical stimulation). Somatosensory feedback can be delivered with a delay matching that associated with signal transmission from periphery to cortex with an intact limb so that feedback signals can be naturally integrated with ongoing motor planning and execution. The extent to which the proposed approaches will need to be modified for patients whose somatosensory cortex has been deafferented (through amputation or spinal cord injury) remains to be tested. However, we anticipate that the proposed biomimetic feedback will considerably increase the dexterity and embodiment of upper-limb neuroprostheses (such as that described in ref. 35) without extensive training on the patient's part and will constitute an important step in restoring touch to individuals who have lost it.

Experimental Procedures

Animal care and handling conformed to the procedures approved by the University of Chicago Animal Care and Use Committee.

Animals. Three Rhesus macaques (two males, one female) were used in this study; all three were 6 y of age and ranged in weight from 6.5 to 12 kg.

Implants. Each of three animals was implanted with one Utah electrode array (UEA; Blackrock Microsystems) in the hand representation of area 1 in the right hemisphere. The UEA consists of 96 1.5-mm-long electrodes, spaced 400 μm apart, and spanning a 4 × 4-mm area. Two FMAs (Microprobes for Life Science) were implanted flanking the UEA and impinged on area 3b. Each FMA consists of 16 3-mm-long electrodes spanning a 2.5 × 1.95-mm area.

Only the FMA that impinged on the hand representation was used in the stimulation experiments (the other, more medial and posterior one, impinged on the arm representation in all three animals). In experiments with electrode drives, it has been shown that the distal digit representations in area 1 are at the surface, whereas the distal digit representations in area 3b are ~3 mm deep (36). We had specified electrode lengths of 3 mm based on our previous experience that the distal digit representation in area 3b lies at that depth. That our receptive fields on the FMAs were exclusively cutaneous and located at or near the tip of the finger indicates that these electrodes were impinging on area 3b.

RF Mapping. We mapped the receptive field of the neuronal populations surrounding each electrode (in awake animals) by identifying which areas of skin evoked multiunit activity (monitored through speakers). RF mapping was repeated periodically throughout the study to verify that maps were consistent. All three animals yielded maps consistent with previous studies, with a progression from D5 (small finger) to D1 (thumb) proceeding laterally and anteriorly along the central sulcus (37).

Stimulation. The monkey's arms were placed in padded arm holders and loosely secured in place by Velcro straps. The hand to be stimulated was placed palmar side up onto an acrylic mold of that animal's hand. A drop of ethyl cyanoacrylate (Loctite 401; Henkel) was placed on each aluminum finger cup fixed within the mold. Each fingernail was then pressed into its respective finger cup and held for ~10 s until the fingers were fixed in place. Animals were trained to hold their hand in position with the palm facing up; the glue was used to assist the animal in keeping its hand in position and was not strong enough to prevent it from freeing its finger(s). The experimenter carefully monitored the animal's hand throughout each experimental block to ensure that the hand remained in position and that the tactile stimulator indented the skin as intended. The animal's view of its hand and of the stimulating apparatus was obstructed.

Mechanical stimuli consisted of trapezoidal indentations delivered by using a custom-designed and built triaxial indenting stimulator (TIS). The TIS consists of a high-precision low-profile Z-stage (MX80L; Parker Hannifin) mounted on an XY stage (PRO115; Aerotech). The stage allowed us to position the Z stage anywhere on the hand with micometer precision, whereas the linear motor allowed us to indent the skin with a punctate probe with a diameter of 1 mm. In the location discrimination task, the 3D structure of the hand was first mapped by using a high-precision rangefinder (Accurange 200–25; Acuity Lasers), mounted on the XY stage, so that the depth of indentation could be controlled, with ~10-μm precision, relative to the height of the skin surface at each stimulated location. On each trial, the TIS indented one location, then the next, with a short interstimulus interval. In the detection and pressure discrimination tasks, the stimulator was preindented into the skin by 500 μm. Any auditory cues from the TIS were masked by presenting white noise through speakers.

ICMS trains, lasting 1 s unless otherwise specified, consisted of symmetric biphasic pulses delivered at 300 Hz using a CereStim 96 (BlackRock Microsystems). The phase duration was 200 μs, the interphase duration was 53 μs, and amplitudes ranged from 10 to 100 μA (2–20 nC per phase). We verified that ICMS did not trigger short latency muscle activation (*SI Experimental Procedures*, Fig. S5).

Psychophysical Tasks. All of the tasks were two alternative forced choice tasks whose sequence and timing are shown in Fig. 1A. The design was counterbalanced so that correct responses were as often "left" as they were "right" to eliminate any possible confounding effect of response bias. Correct responses were rewarded with juice or water. Performance was computed as the proportion correct in each stimulation condition. Because the motivation of the animals fluctuates somewhat from day to day, we eliminated blocks in which the animal performed poorly (did not reach 85% correct on the easiest condition, on which the animals typically reached near perfect performance). Importantly, we applied the same exclusion criterion to the mechanical and electrical trials. Performance as a function of comparison amplitude was then fit by using a standard sigmoid.

Signaling contact location. Two mechanical stimuli (duration = 1 s) were presented on each trial, one in each stimulus interval (separated by a 1.5-s interstimulus interval), at two locations that were displaced from one another along the mediolateral axis. For example, one stimulus might be presented to the index fingertip, and the second might be presented to the small fingertip (both on the same hand). The animal's task was to indicate whether the second stimulus was medial or lateral to the first by saccading to the appropriate target (in this example, to the right). The amplitude of the stimulus varied pseudorandomly from trial to trial, and ranged from

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1,000 to 2,000 μm, so the animal could not use any intensive cues to perform the task. On hybrid trials, one of the two mechanical stimuli was replaced with an electrical stimulus delivered through an electrode whose RF location matched the location of the replaced mechanical stimulus. In these experiments, the intensity of the electrical stimulus was 80 μA to ensure it was suprathreshold. The animal was rewarded if it responded (that is, produced a saccade) as if a mechanical stimulus had been delivered to that RF location. Hybrid trials were always interleaved with mechanical trials (with two indentations). Furthermore, multiple hand locations, spanning the palmar surface of the hand, and corresponding electrodes were interleaved to preclude the animal from learning stimulus-response contingencies (11.2 ± 6.0 stimulus pairs per block, mean ± SD). In a subset of measurements, the amplitude of the ICMS pulses was varied on hybrid trials, yielding identical results. We report stimulus conditions with at least 20 responses (76 ± 28 and 56 ± 26 mean ± SD for mechanical and hybrid trials, respectively).

Signaling contact pressure. Detection. One of the two stimulus intervals contained a mechanical or electrical stimulus and the other was empty. The animal's task was to indicate whether the stimulus was presented in the first or the second interval by saccading to the left or right target, respectively. Mechanical indentations varied in amplitude from 50 to 1,000 μm; ICMS amplitude varied from 10 to 50 μA. In detection and discrimination experiments, the animal had to perform at least 100 trials on any given experimental block for the data to be reported.

Pressure/intensity discrimination. Two mechanical or two ICMS pulse trains were presented: One of the two stimuli was a standard stimulus at one of two amplitudes and the other was a comparison stimulus, whose amplitude varied over a range. The animal's task was to indicate whether the second stimulus was smaller or larger in amplitude than the first by saccading to the left or right target, respectively. In the pressure discrimination task, the amplitude of the standard stimulus was 150 or 2,000 μm, and was paired with a comparison stimulus, whose amplitude ranged from 150 to 2,000 μm (excluding the amplitude of the standard). In the electrical stimulation condition, the standard amplitude was 30 or 100 μA, and comparisons ranged from 30 to 100 μA. The two standard stimuli were (approximately) matched in sensory magnitude with their mechanical counterparts (based on PEFs derived from detection performance). Standard stimuli were interleaved from trial to trial to ensure that the animals attended to both stimulus intervals. Furthermore, mechanical blocks were interleaved with electrical blocks to minimize the animal's ability to learn arbitrary stimulus-response pairings on ICMS blocks.

Detection and discrimination task based on stimulation of the prosthetic finger. The details of the implementation are described (17). The time varying output of the sensor was converted into an equivalent indentation depth (based on an empirically established relationship), which was then converted into an electrical pulse train by using the PEF.

Signaling contact timing. The objective of this experiment was to determine the minimum ICMS duration that elicits a detectable percept to be triggered at the onset and offset of contact. One of the two stimulus intervals contained a mechanical or electrical stimulus and the other was empty. The animal's task was to indicate whether the stimulus was presented in the first or the second interval by saccading to the left or right target, respectively. ICMS amplitude varied from 10 to 50 μA and duration varied from 50 to 500 ms.

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