MODULATION OF CUTANEOUS RESPONSES IN THE CUNEATE NUCLEUS OF MACAQUES DURING ACTIVE MOVEMENT

Qinpu He[1], Christopher S. Versteeg[2], Aneesha K. Suresh[1], Joshua Rosenow[3], Lee E. Miller[2], and Sliman J. Bensmaia[1,4,5]

[1]Committee on Computational Neuroscience, University of Chicago, Chicago, IL
[2]Department of Biomedical Engineering, Northwestern University, Chicago, IL
[3]Department of Neurological Surgery and Neurology, Northwestern University, Chicago, IL
[4]Department of Organismal Biology and Anatomy, Chicago, IL
[5]Grossman Institute for Neuroscience, Chicago, IL

ABSTRACT

To achieve stable and precise movement execution, the sensorimotor system integrates exafferent sensory signals originating from interactions with the external world and reafferent signals caused by our own movements. This barrage of sensory information is regulated such that behaviorally relevant signals are boosted at the expense of irrelevant ones. For example, sensitivity to touch is reduced during movement – when cutaneous signals caused by skin stretch are expected and uninteresting – a phenomenon reflected in a decreased cutaneous responsiveness in thalamus and cortex. Some evidence suggests that movement gating of touch may originate from the cuneate nucleus (CN), the first recipient of signals from tactile nerve fibers along the dorsal columns medial lemniscal pathway. To test this possibility, we intermittently delivered mechanical pulses to the receptive fields (RFs) of identified cutaneous CN neurons as monkeys performed a reach-to-grasp task. As predicted, we found that the cutaneous responses of individual CN neurons were reduced during movement. However, this movement gating of cutaneous signals was observed for CN neurons with RFs on the arm but not those with RFs on the hand. We conclude that sensory gating occurs in the first processing stage along the somatosensory neuraxis and sculpts incoming signals according to their task relevance.

INTRODUCTION

Touch is typically engaged during goal-directed interactions with objects and conveys information about the objects and about our interactions with them (Goodman & Bensmaia, 2018; Johansson & Flanagan, 2009). However, touch signals are also triggered by the movement itself (Johansson, 1978). For example, as we reach for an object, nerve fibers that innervate the skin of the shoulder and elbow become activated by the skin stretch that accompanies the joint deflections (Costanzo & Gardner, 1981). To the extent that the cutaneous signals associated with movement convey information about limb posture, these signals are largely redundant with those from the muscles and tendons. Accordingly, it may make sense to suppress cutaneous signals triggered by movement-related skin stretch so that these do not interfere with signals arising from object interactions.

Consistent with this hypothesis, sensitivity to cutaneous stimulation has been shown to be reduced during reaching movements (Chapman et al., 1987). The neural correlates of this sensory gating have been observed in local field potentials (or the equivalent) measured in the spinal cord (Confais et al., 2017; Seki & Fetz, 2012), medial lemniscus, thalamus (Chapman et al., 1988), and somatosensory cortex of macaques (Seki & Fetz, 2012) and humans (Kurz et al., 2018). The cuneate nucleus (CN) is the first stage of processing of tactile signals along the dorsal column medial lemniscal pathway and receives abundant descending inputs from cortex (Conner et al., 2021; Loutit et al., 2020). Accordingly, this tiny structure in the brainstem is well positioned to play a role in task-dependent gain modulation. However, this suppression has not been characterized at the single level so it is unclear (1) whether all CN neurons are subject to gating or only a subpopulation is; (2) whether gating is deployed homogeneously over the entire body map or rather sculpted depending on the body location of incoming signals; and (3) whether this gating is binary or graded according to movement parameters.

To address these questions, we had rhesus macaques perform a reach-to-grasp task while we delivered tactile stimuli intermittently to the identified locations of the receptive fields (RFs) of cutaneous neurons in CN. As the animals performed the task, we measured neuronal responses, tracked limb movements, and measured the forces exerted by the monkey on the manipulandum. We found that cutaneous responses in CN were systematically suppressed during movement for neurons with RFs on the arm but were elevated for neurons with RFs on the palmar surface of the hand, where object contact was anticipated. In some cases, cutaneous responses of arm CN neurons were also suppressed during maintained grasp force. Finally, gating was observed for some units before movement initiation and was not observed when the arm was moved passively, demonstrating the top-down origins of the gating observed during reach and grasp. We conclude that CN plays a major role in the movement gating of tactile signals.

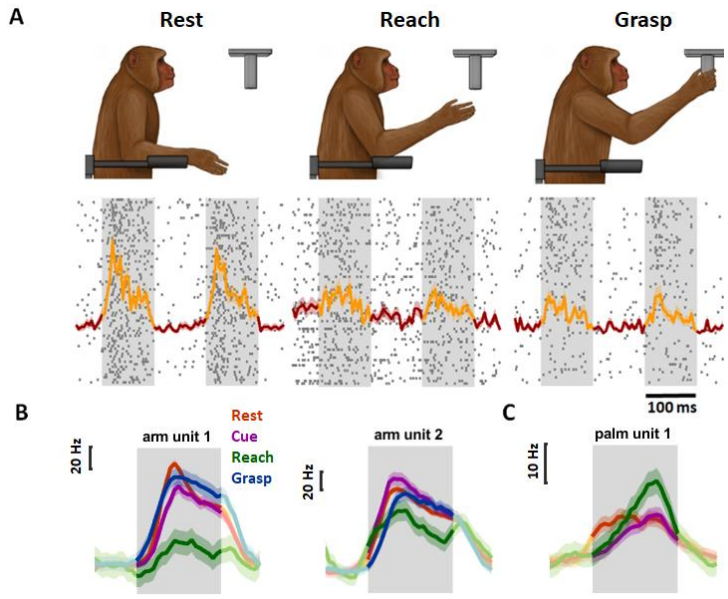


Figure 1. Behavioral task and neural data. A| Behavioral task. The monkey placed its free arm onto the arm rest for an interval of variable duration (rest epoch) before he initiated a trial cued by an LED. The animal then reached toward (reach epoch) and grasped the manipulandum, applied the cued force (force epoch), received a water reward, then returned its arm to the arm rest to wait for the start of the next trial. Tactors placed over identified receptive fields pulsed every 200 ms for 100 ms throughout the entire task. One exemplary arm tactile CN neuron's responses over 50 trials depicted below the behavioral diagram. The PSTHs are overlaid on top with orange segments of the PSTH denoting the stimulation-induced response and red segments the baseline. B| Demeaned average responses of two exemplary cutaneous CN arm neurons with RFs on the arm. Gray shading denotes the stimulation epoch. Orange, purple, green, and blue lines stand for the average responses during rest, cue, reach, and grasp epochs, respectively. The cue epoch is that between the onset of the LED and the start of the reach. C| Same as B but for one exemplary palm unit. Tactile responses during grasp epoch is not shown as vibration-elicited palm unit responses are contaminated by the grasp during this epoch.

RESULTS

We recorded the responses of 31 CN cutaneous neurons, which responded to light touch over a restricted patch of skin, from a total of five Rhesus Macaques. Of these, 18 neurons had RFs on the arm (including one on the dorsal surface of the hand) and 11 on the palmar surface of hand.

Animals were trained to perform a reach-and-grasp task. On each trial, an LED cued the animal to reach to and grasp a joystick-like manipulandum and apply a force the magnitude of which was also cued by the LED. The animal obtained a water reward if it held the specific force for the required duration (see Methods for details). After obtaining the reward, the animal returned its arm to the arm rest and the next trial was initiated 2 seconds later. Each trial was then split into different epochs: rest, cue, reach, and grasp. To assess whether CN responses are state dependent, we compared stimulus-evoked responses during rest to those evoked during the other three epochs (Figure 1A). To this end, we first aligned the response of each neuron to the onset of each stimulation pulse, computed the response to each stimulation pulse (bottom row of Figure 1A), then averaged these separately for each epoch (Figure 1B,C).

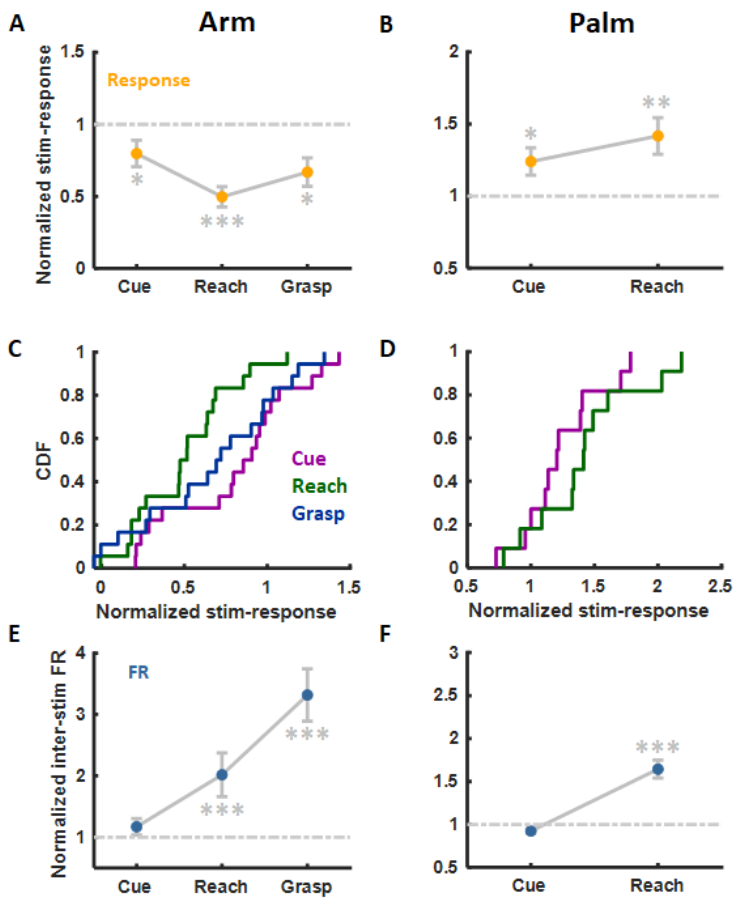


Figure 2. Stimulation-evoked and baseline responses of arm and palm cutaneous neurons. A| Mean normalized stimulation-evoked responses of all cutaneous neurons with RFs on the arm (n=18) to stimulation during the cue, reach, and grasp epochs normalized to the rest responses. Responses were significantly reduced during all three epochs. (*p<0.05, **p<0.01, ***p < 0.001, significant deviation from rest epoch, Wilcoxon signed-rank test). B| Mean stimulation-evoked responses of all cutaneous neurons with RFs on the palmar surface of the hand (n=11) during different epochs. Responses were significantly enhanced during the cue and reach epochs. C| Cumulative histograms of normalized stim-responses of all arm neurons during the three behavioral epochs. A total of 5, 12, and 7 out of 18 total arm cutaneous units showed significantly suppression during cue, reach, and grasp period, respectively (p<0.05, Wilcoxon rank sum test). D| Same as panel C but for all palm neurons. A total of 4 and 5 out of 11 palmar cutaneous units exhibited significantly elevated responses during the cue and reach periods, respectively. E| Mean baseline response to the same arm neurons as in A. Baseline firing rates were significantly elevated during reach and grasp compared to rest. F| Mean baseline responses of the same palm units as in B.

We also computed the mean firing rate (FR) during the inter-pulse intervals to assess how the baseline response varied across epochs (Figure 2E,F).

Behaviorally dependent modulation of cutaneous responses

To gauge the response modulation, we divided the mean stimulus-evoked response during each epoch by the mean stimulus-evoked response during rest. Accordingly, values greater than 1 indicated elevated responses with respect to rest whereas values less than 1 indicated suppression. To the extent that CN responses exhibit movement gating, the stimulation-evoked response of cutaneous neurons would be weaker during the reach epochs and perhaps during the grasp epochs compared to their rest counterparts. As predicted, the tactile responses of arm cutaneous units were significantly weaker during reach and grasp epochs (Figure 2), as evidenced by normalized stim-responses below 1 during movement. The attenuation of the responses occurred even before the start of movement, as shown by the decreased responses during the cue epoch. Note that the baseline response during the cue and rest epochs were equivalent, confirming that the monkey was still during the cue epoch. The presence of such gating during preparation phase implicates descending inputs. We found that the responses of 77% (14/18) of the cutaneous units with

RFs on the arm were significantly suppressed during at least one behavioral epoch: 11% throughout all three, 33% throughout two, and another 33% during only one.

Note, however, that the baseline responses – measured during the inter-pulse intervals – were elevated during the reach and grasp epochs (Figure 2E), opening up the possibility that the reduced activity during movement and force epochs reflected saturation of the responses when reafferent and exafferent signals co-occur. However, evidence ruled out the possibility that saturation caused the observed suppression. There was no relationship between the strength of the movement gating and the baseline (non-stimulus evoked) activity (Supplementary Figure 2). That is, neurons whose baseline response increased the most during movement or those whose baseline firing rate was highest did not systematically exhibit the strongest suppression of the stimulus-evoked during movement. Hence, movement induced gating is not a trivial consequence of response saturation.

Dependence of modulation on behavioral variables

The suppression of cutaneous sensitivity at the lemniscal, thalamic, and cortical levels has been shown to be dependent on the speed of movement (Chapman et al., 1988; Ghez & Pisa, 1972). With this in mind, we examined the degree to which the suppression was modulated by behavioral parameters, including movement speed as well as applied force. We found that, of the 18 cutaneous neurons with RFs on the arm, four were gated more strongly at higher speeds during the reach epoch (Supplementary Figure 1A). The influence of grasp force on modulation (during the grasp epoch) also varied: Four neurons showed significantly elevated responses and two showed significantly decreased responses at higher grasp forces (Supplementary Figure 1B). Thus, the dependence of the gain modulation on behavioral variables is heterogeneous: The gating is all-or-none for some neurons and graded with behavior for others.

Modulation of cutaneous neurons with RFs on the hand

All the analyses described above were performed on cutaneous neurons with RFs on the arm. A handful of recorded neurons had cutaneous RFs on the glabrous skin (palmar surface) of the hand. Unlike their counterparts with receptive fields on the arm, CN neurons with RFs on the glabrous skin exhibited systematically elevated stimulus-evoked responses during the reach epoch (Figure 2 B&D). Responses of hand neurons during grasping epochs were not included for analysis because contact with the manipulandum would contaminate stimulus-evoked responses. In total, the responses of 10% of palm units

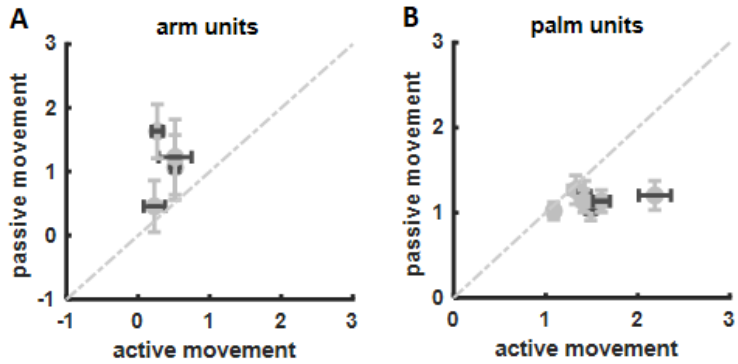


Figure 3. Stimulation-evoked responses of arm and palmar cutaneous neurons under active vs. passive movement. A| Mean stimulation-evoked responses of all cutaneous neurons with RFs on the arm (n=4) to stimulation during three event epochs normalized to the rest responses. A darker color error bar on the abscissa or ordinate denotes a significant movement-related modulation under active or passive conditions, respectively. None of the four units showed significantly reduced responses during passive manipulations. B| Mean stimulation-evoked responses of all cutaneous neurons with RFs on the palm (n=6). None of the six units showed significantly elevated responses during passive manipulations. (Wilcoxon rank sum test).

were consistently elevated throughout all three behavioral epochs, 27% throughout two epochs, and another 27% during only one.

The modulation of cutaneous sensitivity thus seems to depend on RF location, which may reflect the task relevance of signals from different body regions: Signals from the proximal limb are likely reafferent and not particularly informative, whereas signals from the hand carry information about contact with the manipulandum and are thus critical to task performance.

Modulation during imposed movement

To assess the degree to which the observed task-related modulation of cutaneous sensitivity was mediated by top-down signals, we compared the stimulus-evoked responses during active movements and to those during passively imposed movements. To the extent that gating was caused by top-down signals, we expected it to be absent in the passive condition. We found that, indeed, the stimulus-evoked responses of CN neurons with RFs on the arm during imposed arm movements were not significantly different from those at rest (Figure 3A; $p = 0.9578$, Wilcoxon rank sum test) and were significantly elevated compared to those measured during active reach ($p < 0.001$). Similarly, the responses of CN neurons with RFs on the glabrous skin were not significantly modulated during passively imposed movements ($p = 0.3194$) and were significantly lower than those measured during active reach (Figure 3B; $p < 0.001$). That movement gating of sensory signals is only observed during actively generated movements is consistent with the hypothesis that this gating originates centrally.

DISCUSSION

In summary, we show that the cutaneous sensitivity of CN neurons with RFs on the proximal limb is systematically suppressed during reaching movements. In contrast, the sensitivity of CN neurons with RFs on the hand is either unaffected or elevated. In some neurons (39%), cutaneous sensitivity is also modulated as the animal applies isometric forces on the manipulandum, in the absence of movement. The modulation of CN responses has a central origin as evidenced by the fact that it is observed even before movement (28% of arm and 36% of palm units) – i.e., before reafference is engaged – and only during active reaching movements. The strength of the modulation varies across neurons from 25 to 95% suppression for the arm and from 20% to 220% elevation for the hand. The dependence of modulation on behavioral parameters – including movement speed or exerted force – also varies widely across neurons: In most neurons the modulation is all-or-none whereas, in a subpopulation, the modulation is graded by the speed or exerted force. Our results are consistent with the view that top-down signals sculpt the sensory input to squelch behaviorally irrelevant and possibly distracting cutaneous signals and enhance behaviorally relevant ones.

Sculpting of cutaneous signals according to task relevance

We show that cutaneous sensitivity is not homogeneously gated over the entire body during a reaching movement. CN neurons with RFs on the arm are suppressed whereas neurons with RFs on the glabrous skin are sensitized. This spatial specificity of gating has also been observed in human psychophysical experiments: tactile thresholds near the moving segment increased most and less so further away (Post et al., 1994; Williams et al., 1998). The differential modulation of signals from different body regions may reflect their differential utility in accomplishing a task (Juravle et al., 2017). In a reach-to-grasp task, cutaneous signals from the palmar surface of the hand signal contact with the manipulandum and trigger

the end of the grasp (Johansson & Flanagan, 2009), whereas signals from the arm reflect reafference and are less behaviorally relevant. The observed modulation would then enhance the task-relevant hand signals and suppress the task-irrelevant arm signals. Consistent with this interpretation, detection thresholds at the forearm have been shown to increase during a reach-to-grasp while those of distal digits did not (Colino et al., 2014). The task-dependence of modulation has been observed in a variety of other contexts, not limited to upper limb behavior (Juravle et al., 2013; Staines et al., 2000, 2002).

Dependence of modulation on behavioral variables

We find that the magnitude of the modulation is largely independent of behavioral variables, such as movement speed and applied force. Indeed, only a few CN neurons exhibited cutaneous responses whose strength depended on the speed of the reach or the force applied on the manipulandum. For most neurons, the modulation was all-or-none. The mixture of behaviorally graded and all-or-none modulation at the single-cell level is consistent with the observation that lemniscal potentials measured in cats and primates are more suppressed at higher velocities (Chapman et al., 1988; Ghez & Pisa, 1972; Rushton et al., 1981). Indeed, field potentials reflect the mixed activity of neurons that exhibit speed-dependent and speed-independent suppression. Similarly, sensory thresholds measured in human observers have been shown to increase with movement speed (Angel & Malenka, 1982; Schmidt et al., 1990). In contrast, responses reflecting whisker contact in the trigeminal nucleus of rats seem to be suppressed during active whisking in all-or-none fashion, though the this phenomenon was not analyzed at the single-cell level, leaving open the possibility that a subpopulation with graded modulation exists (Chakrabarti & Schwarz, 2018).

Studies of the effect of force exertion on cutaneous sensitivity have yielded mixed results. Varying isometric force was found to have no effect on cutaneous signals measured in the somatosensory cortex of humans (Rushton et al., 1981) and on medial lemniscus potentials in cats (Ghez & Pisa, 1972). However, forces exerted by the lower limb did modulate cutaneous signals in cortex in a graded fashion (Cohen & Starr, 1985; Sakamoto et al., 2004; Wasaka et al., 2005). In line with the latter result, psychophysical experiments with human observers revealed an increase in detection thresholds during higher isometric force production (Post et al., 1994). This seeming heterogeneity across studies may reflect the fact that only a small subpopulation of CN neurons exhibits a force-dependent modulation so these effects may be subtle at the population level, depend on the specific ranges of forces applied, and vary depending on which muscles are activated and where the tactile stimulus is applied.

Central origins of modulation

The modulation of tactile sensitivity observed in the present study likely has a central origin. Indeed, cutaneous responses are suppressed or enhanced before movement onset and this modulation is not observed during passive movements. A putative circuit to mediate this centrally driven modulation has been identified in mice. The CN can be divided into two regions: a core that receives the bulk of the input from the periphery and an outer shell that comprises mostly inhibitory interneurons (Conner et al., 2021). Each region receives a distinct pattern of projections from cortex: The core receives excitatory inputs from somatosensory cortex whereas the shell receives both excitatory and inhibitory input from a variety of motor structures. Together, these top-down pathways can account for the observed modulation of cutaneous sensitivity. Excitatory projections from motor cortex to inhibitory neurons in the shell region could account for the suppression of cutaneous signals. Excitatory projections from somatosensory cortex to the core region or inhibitory projections from motor cortex to the shell region could mediate the

observed elevation of cutaneous sensitivity. While the relevant anatomy of rodents and primates differs, similar principles likely underlie the present findings. Indeed, primate CN also receives a mix of excitatory and inhibitory inputs from cortex (Biedenbach, 1972; Loutit et al., 2020).

METHODS

Experimental apparatus

A joystick was mounted to a high-sensitivity force sensor (ATI Six-Axis Force/Torque Transducer). Two arrays of LEDs were placed above the sensor, one to cue the level of grasp force the monkey needed to exert to obtain a reward and the other reflecting the actual force applied to the manipulandum in real time. Tactile stimulation was delivered using DC coreless vibration motors (7mm × 25mm, Speed: 8000-24000RPM), which were fixed to various locations on the monkeys' arms, each corresponding to the identified RF of a CN neuron. The onset of movement was signaled by photoresistors embedded in the arm rest of the monkey chair and arm and hand movements were tracked using a camera and two wireless motion trackers attached to the upper and lower arm (Xsens 3D Motion Tracking System, Enschede, Netherlands).

Behavioral paradigm

We trained five rhesus macaques (four males, one female, ages 5-10 yr) to perform a reach-and-grasp task (Figure 1A). Monkeys were seated upright at the experimental chair, with one arm restrained and the other free, facing LEDs and the joystick. The animal placed its free arm onto the arm rest for a random delay of 0.5-2s (rest epoch) to initiate a trial. A trial began when the first row of LEDs lit up, signaling the monkey to initiate a reach towards the manipulandum. The LED prescribed the amount of force, which varied across trials, that the monkey needed to apply to the manipulandum on that trial. Application of a load on the joystick activated the second row of LEDs, with the number of activated LEDs proportional to the applied force. If the amount of force exceeded the required force for a required interval (varying between 0.1-2.0s; hold), the monkey would receive a liquid reward. The animal then returned its arm to the arm rest for 2s, received a second water reward, the LEDs were turned off, and the animal waited for the initiation of the next trial. Recordings from the first reward onset to the end of every trial were not included in data analysis to minimize the influence of task-unrelated movement, as the animal fidgeted as it consumed its rewards.

Before the start of every recording session, we performed receptive field mapping to locate tactile CN units. We classified a unit as cutaneous if it responded to gentle stroking of the skin but not to lengthening and palpation of the muscle underneath the skin. During the recording sessions, 60-100Hz vibrations were applied to the RFs of identified CN units in regular intervals (100-ms on, 100-ms off). The vibrating tactors were firmly attached to the locations on the arm corresponding to the RFs of the neurons using glue then secured in place with three layers of vet wrap. The arm was shaved at each RF location before the experiments began. As the animal performed the task, arm movements were tracked using two accelerometers attached to the proximal and distal arms via velcro bands. Data recorded from days when the tactors or accelerometers were found to have moved at the end of recording sessions were excluded. A camera monitored the monkey's behavior throughout the recordings. A publicly available motion-tracking package was used to track the monkey's arm movements and to infer reaching speeds based on these (DeepLabCut, Mathis et al., 2018).

On some trials, we manually manipulated the monkey's hand to mimic reaching movements. Specifically, we followed the same procedure as in the active reaching task (Figure 1), except that the experimenter held the monkey's arm to reach toward the manipuladum and return to the arm-rest. The experimenter avoided contact with the tactors placed during these passive trials.

Neural Data Acquisition

We implanted 96-channel iridium-oxide Utah arrays (UEA) (Blackrock Microsystems, Inc., Salt Lake City, UT) in all five monkeys. We used customized 8x12 shank rectangular array with 1.5 mm electrode length and 9-cm wire bundle between array and pedestal. Neural data were acquired using a digital CerePlex E headstage and CerePlex Direct acquisition system (Blackrock Microsystems). We bandpass-filtered neural signals between 250 Hz and 5000 Hz and set the voltage threshold for every channel manually before the start of every recording session. We recorded the time of every threshold crossing on every channel and saved the neural waveforms over a 1.6-ms window for off-line spike sorting (Plexon, Dallas, TX).

We simultaneously recorded timestamps that indicated when stimulation and behavioral events occurred, along with the neural data while the monkey performed the task.

Surgical Procedures

All experimental protocols were reviewed and approved by the University of Chicago Animal Care and Use Committee and complied with the National Institutes of Health *Guide for the Care and Use of Laboratory Animals*. We anesthetized animal using ketamine HCl (3 mg/kg im) and dexmedetomidine (75 µg/kg) and fixed animal's head in a stereotaxic frame such that neck was flexed to be ~ 75 degree relative to the body to allow for maximum exposure of brainstem. We first made a midline incision from the occipital bone to approximately C1~C3 and removed posterior cervical muscles along midline using cautery. We secured the pedestal to the skull with bone screws such that the routing of the wire bundle lead between it and the array in the brainstem would be flexible enough to enable normal neck movements. We then exposed the foramen magnum and the occipitocervical dura using cautery and sharp dissection. We identified the location of Obex and used the stereotaxic frame to target 2-mm lateral to midline and 2-mm anterior to Obex to aim for maximum coverage of distal limb cutaneous regions of upper body (Darian-Smith & Ciferri, 2006; Loutit et al., 2020; Qi & Kaas, 2006; Suresh et al., 2017, 2021; Versteeg et al., 2021). The UEA was then implanted into the brainstem using a pneumatic inserter (BlackRock microsystem).

Data Analysis

Offline Redefinition of Task Epochs

To evaluate the epoch-dependent modulation of responses, we first defined each behavioral epoch by using the output the photoresistor, accelerometer, and force gauge. Reaching onset was defined as the first time when photoresistors on the arm rest were uncovered while reaching offset was defined based on when the force applied on manipulandum rose above the threshold. The start and end of reach were accompanied by (and confirmed via) changes in the acceleration of the arm.

After finding the onset and offset of the reach, we defined four movement-related epochs for analysis: (1) rest, from the start of the photoresistors coverage until the onset of the cue; (2) cue, from the onset of the cue to the onset of movement; (3) reach, from the onset of the photoresistor signal to the onset of force production on the manipulandum; (4) grasp, from onset of force production to start of triggering of the water reward (Figure 1A). Only trials during in which all behavioral events were properly recorded were analyzed. In addition, to minimize the possibility of movement during the rest and cue epochs, we only included stimulation snippets surrounded by baseline FRs that were within three standard deviations away from the mean FR during these two epochs.

Compiling Stimulation-Elicited Response and Firing Rates for Each Behavioral Epoch

First, we computed the firing rate of each neuron evoked during each 100-ms stimulus and the firing rate evoked in the 50-ms before and the 50-ms after the stimulus came on (the baseline). Then, we computed the mean difference between stimulus evoked and baseline for each epoch separately (Figure 1B&C). Next,

we compared the rest responses to those of the other three epochs (cue, reach, and grasp) using the Wilcoxon signed-rank test. Finally, we divided the mean stimulus-evoked response in each epoch by the mean response during rest to as an index of the modulation effect (Figure 2).

Dependence of Gating on Movement Speed

To investigate the influence of movement speed on modulation, we derived movement speed during each reach using DeepLabCut (Mathis et al., 2018). First, we manually labeled fifty randomly sampled videos from all monkeys to train the network. From these networks, we reconstructed the time varying arm postures and derived from these the time varying movement speed. Speeds were split into quartiles and the mean normalized stimulus evoked responses were then computed for each quartile (Supplementary Figure 1).

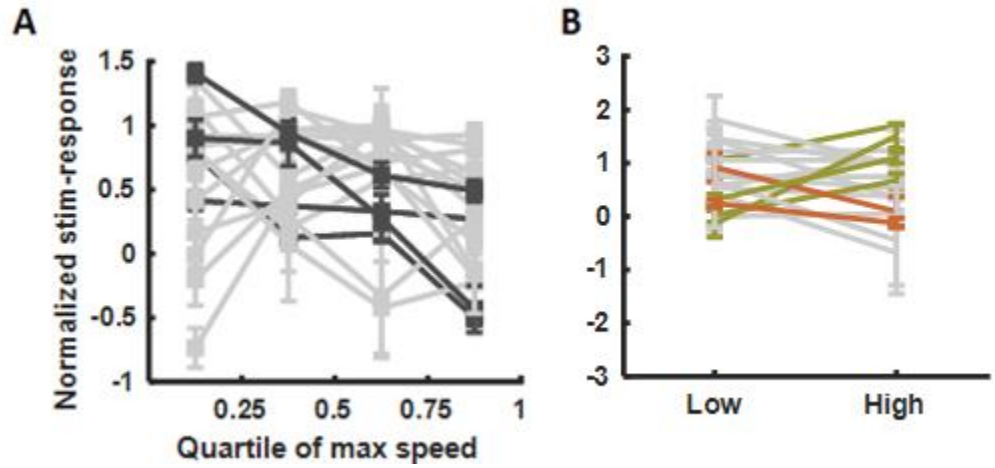
Dependence of Gating on Force parameters

To study the influence of load on modulation, we split the grasping forces into categories at the median. We then averaged the stimulus-evoked responses at the two grasping levels (Supplementary Figure 1).

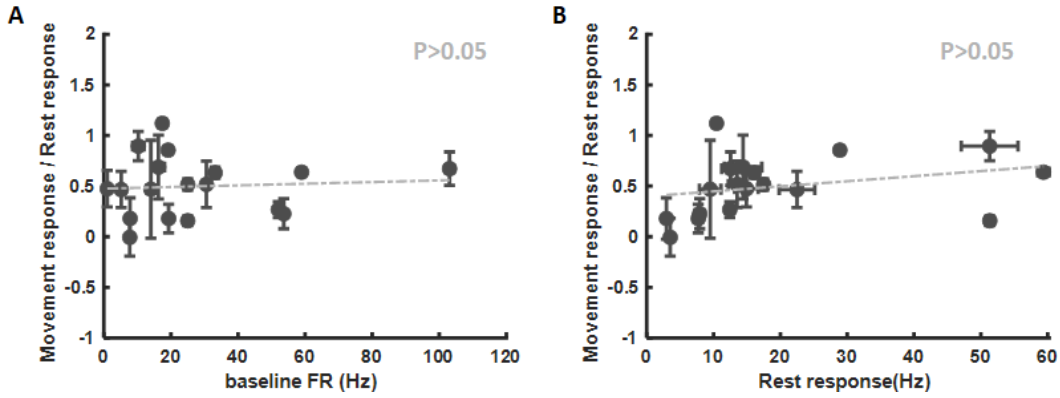
Influence of the Firing Rate Saturation Effects on Movement Gating

To verify that the apparent suppression of cutaneous responses during movement and force epochs was not simply due to response saturation, we calculated baseline firing rates (at rest or during movement) and examined whether the strength of the effect was related to baseline, computed either during rest or throughout the movement. If the suppression were due to response saturation, we expected that neurons with higher baseline firing rates or neurons whose firing rate increased the most during movement would exhibit the strongest modulation (Supplementary Figure 2).

SUPPLEMENTARY FIGURES

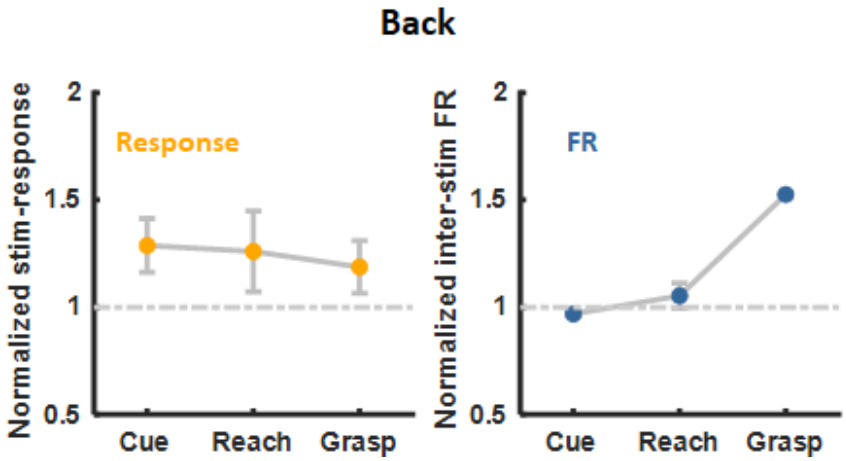


Supplementary Figure 1. Dependence of the modulation effect on movement parameters. A| Dependence of the modulation on speed. Every line shows the responses of one cutaneous arm neuron. Dark grey traces denote the neurons for which the modulation was significantly dependent on speed. B| Dependence of modulation on force. Green traces denote neurons whose sensitivity was significantly elevated during high force trials; red traces denote neurons whose sensitivity was significantly suppressed sensitivity during high-force trials; grey traces denote neurons whose sensitivity was not significantly different across force levels.



Supplementary Figure 2. Saturation effects analysis. A| The effects of baseline firing rates on the degree of normalized stim-evoked responses during movement.

Dotted line denote the fitted line, the slope of which is not significantly different from 0. B| The same thing as A but plotted against stim-elicited responses during rest. The data do not show a saturation effect.



Supplementary Figure 3. Stimulus-evoked response and firing rates modulation of back cutaneous neurons. A| The same stimulus-elicited response plot as fig. 2A but for all tactile neurons with RFs on the back (n=2). One of out of the two back cutaneous units showed significantly elevated responses during cue and grasp periods respectively ($p<0.05$, Wilcoxon rank sum test). B| The same inter-stimulus firing rate plot as fig. 2B but for back cutaneous units. No significant changes were observed during any event epoch for both stim-evoked response and firing rates.

References

Angel, R. W., & Malenka, R. C. (1982). Velocity-dependent suppression of cutaneous sensitivity during movement. *Experimental Neurology*, *77*(2), 266–274. https://doi.org/10.1016/0014-4886(82)90244-8

Biedenbach, M. A. (1972). Cell density and regional distribution of cell types in the cuneate nucleus of the Rhesus monkey. *Brain Research*, *45*(1), 1–14. https://doi.org/10.1016/0006-8993(72)90212-0

Chakrabarti, S., & Schwarz, C. (2018). Cortical modulation of sensory flow during active touch in the rat whisker system. *Nature Communications*, *9*(1), 3907. https://doi.org/10.1038/s41467-018-06200-6

Chapman, C. E., Bushnell, M. C., Miron, D., Duncan, G. H., & Lund, J. P. (1987). Sensory perception during movement in man. *Experimental Brain Research*, *68*(3), 516–524. https://doi.org/10.1007/BF00249795

Chapman, C. E., Jiang, W., & Lamarre, Y. (1988). Modulation of lemniscal input during conditioned arm movements in the monkey. *Experimental Brain Research*, *72*(2). https://doi.org/10.1007/BF00250254

Cohen, L. G., & Starr, A. (1985). Vibration and muscle contraction affect somatosensory evoked potentials. *Neurology*, *35*(5), 691–691. https://doi.org/10.1212/WNL.35.5.691

Colino, F. L., Buckingham, G., Cheng, D. T., van Donkelaar, P., & Binsted, G. (2014). Tactile gating in a reaching and grasping task. *Physiological Reports*, *2*(3), e00267. https://doi.org/10.1002/phy2.267

Confais, J., Kim, G., Tomatsu, S., Takei, T., & Seki, K. (2017). Nerve-Specific Input Modulation to Spinal Neurons during a Motor Task in the Monkey. *The Journal of Neuroscience*, *37*(10), 2612–2626. https://doi.org/10.1523/JNEUROSCI.2561-16.2017

Conner, J. M., Bohannon, A., Igarashi, M., Taniguchi, J., Baltar, N., & Azim, E. (2021). *Modulation of tactile feedback for the execution of dexterous movement* [Preprint]. Neuroscience. https://doi.org/10.1101/2021.03.04.433649

Costanzo, R. M., & Gardner, E. P. (1981). Multiple-joint neurons in somatosensory cortex of awake monkeys. *Brain Research*, *214*(2), 321–333. https://doi.org/10.1016/0006-8993(81)91197-5

Darian-Smith, C., & Ciferri, M. (2006). Cuneate nucleus reorganization following cervical dorsal rhizotomy in the macaque monkey: Its role in the recovery of manual dexterity. *The Journal of Comparative Neurology*, *498*(4), 552–565. https://doi.org/10.1002/cne.21088

Ghez, C., & Pisa, M. (1972). Inhibition of afferent transmission in cuneate nucleus during voluntary movement in the cat. In *Brain Research* (Vol. 40, Issue 1, pp. 145–151). https://doi.org/10.1016/0006-8993(72)90120-5

Goodman, J. M., & Bensmaia, S. J. (2018). The Neural Basis of Haptic Perception. In *Stevens' Handbook of Experimental Psychology and Cognitive Neuroscience* (pp. 1–39). American Cancer Society. https://doi.org/10.1002/9781119170174.epcn205

Johansson, R. S. (1978). Tactile sensibility in the human hand: Receptive field characteristics of mechanoreceptive units in the glabrous skin area. *The Journal of Physiology*, *281*(1), 101–125. https://doi.org/10.1113/jphysiol.1978.sp012411

Johansson, R. S., & Flanagan, J. R. (2009). Coding and use of tactile signals from the fingertips in object manipulation tasks. *Nature Reviews. Neuroscience*, *10*(5), 345–359. https://doi.org/10.1038/nrn2621

Juravle, G., Binsted, G., & Spence, C. (2017). Tactile suppression in goal-directed movement. *Psychonomic Bulletin & Review*, *24*(4), 1060–1076. https://doi.org/10.3758/s13423-016-1203-6

Juravle, G., McGlone, F., & Spence, C. (2013). Context-dependent changes in tactile perception during movement execution. *Frontiers in Psychology*, *4*. https://doi.org/10.3389/fpsyg.2013.00913

Kurz, M. J., Wiesman, A. I., Coolidge, N. M., & Wilson, T. W. (2018). Haptic exploration attenuates and alters somatosensory cortical oscillations. *Journal of Physiology*, *596*(20), 5051–5061. https://doi.org/10.1113/JP276263

Loutit, A. J., Vickery, R. M., & Potas, J. R. (2020). *Functional Organisation and Connectivity of the Dorsal Column Nuclei Complex Reveals a Sensorimotor Integration and Distribution Hub* [Preprint]. BIOLOGY. https://doi.org/10.20944/preprints201911.0084.v3

Mathis, A., Mamidanna, P., Cury, K. M., Abe, T., Murthy, V. N., Mathis, M. W., & Bethge, M. (2018). DeepLabCut: Markerless pose estimation of user-defined body parts with deep learning. *Nature Neuroscience*, *21*(9), 1281–1289. https://doi.org/10.1038/s41593-018-0209-y

Post, L. J., Zompa, I. C., & Chapman, C. E. (1994). Perception of vibrotactile stimuli during motor activity in human subjects. *Experimental Brain Research*, *100*(1). https://doi.org/10.1007/BF00227283

Qi, H.-X., & Kaas, J. H. (2006). Organization of primary afferent projections to the gracile nucleus of the dorsal column system of primates. *The Journal of Comparative Neurology*, *499*(2), 183–217. https://doi.org/10.1002/cne.21061

Rushton, D. N., Roghwell, J. C., & Craggs, M. D. (1981). GATING OF SOMATOSENSORY EVOKED POTENTIALS DURING DIFFERENT KINDS OF MOVEMENT IN MAN. *Brain*, *104*(3), 465–491. https://doi.org/10.1093/brain/104.3.465

Sakamoto, M., Nakajima, T., Wasaka, T., Kida, T., Nakata, H., Endoh, T., Nishihira, Y., & Komiyama, T. (2004). Load- and cadence-dependent modulation of somatosensory evoked potentials and Soleus H-reflexes during active leg pedaling in humans. *Brain Research*, *1029*(2), 272–285. https://doi.org/10.1016/j.brainres.2004.09.054

Schmidt, R. F., Schady, & Torebjork. (1990). *Gating of tactile input from the hand*. 6.

Seki, K., & Fetz, E. E. (2012). Gating of Sensory Input at Spinal and Cortical Levels during Preparation and Execution of Voluntary Movement. *Journal of Neuroscience*, *32*(3), 890–902. https://doi.org/10.1523/JNEUROSCI.4958-11.2012

Staines, W. R., Brooke, J. D., & McIlroy, W. E. (2000). Task-relevant selective modulation of somatosensory afferent paths from the lower limb: *NeuroReport*, *11*(8), 1713–1719. https://doi.org/10.1097/00001756-200006050-00024

Staines, W. R., Graham, S. J., Black, S. E., & McIlroy, W. E. (2002). Task-Relevant Modulation of Contralateral and Ipsilateral Primary Somatosensory Cortex and the Role of a Prefrontal-Cortical Sensory Gating System. *NeuroImage*, *15*(1), 190–199. https://doi.org/10.1006/nimg.2001.0953

Suresh, A. K., Greenspon, C. M., He, Q., Rosenow, J. M., Miller, L. E., & Bensmaia, S. J. (2021). *Sensory computations in the cuneate nucleus of macaques* [Preprint]. Neuroscience. https://doi.org/10.1101/2021.07.28.454185

Suresh, A. K., Winberry, J. E., Versteeg, C., Chowdhury, R., Tomlinson, T., Rosenow, J. M., Miller, L. E., & Bensmaia, S. J. (2017). Methodological considerations for a chronic neural interface with the cuneate nucleus of macaques. *Journal of Neurophysiology*, *118*(6), 3271–3281. https://doi.org/10.1152/jn.00436.2017

Versteeg, C., Rosenow, J. M., Bensmaia, S. J., & Miller, L. E. (2021). Encoding of limb state by single neurons in the cuneate nucleus of awake monkeys. *Journal of Neurophysiology*, *126*(2), 693–706. https://doi.org/10.1152/jn.00568.2020

Wasaka, T., Nakata, H., Kida, T., & Kakigi, R. (2005). Changes in the centrifugal gating effect on somatosensory evoked potentials depending on the level of contractile force. *Experimental Brain Research*, *166*(1), 118–125. https://doi.org/10.1007/s00221-005-2333-7

Williams, S. R., Shenasa, J., & Chapman, C. E. (1998). Time Course and Magnitude of Movement-Related Gating of Tactile Detection in Humans. I. Importance of Stimulus Location. *Journal of Neurophysiology*, *79*(2), 947–963. https://doi.org/10.1152/jn.1998.79.2.947