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Electrotactile Feedback Outweighs Natural Feedback in Sensory Integration during Control of Grasp Force

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Abstract

The nervous system subconsciously estimates the state of the body as a weighted average of the information from various sensory sources, where the weights reflect the perceived reliability of each source. Loss of motor functions can be partially compensated using assistive systems (e.g. prostheses), which may also restore somatosensory feedback through tactile stimulation. Whether such artificial feedback is integrated in the neural state estimation process is not known. In this study, able-bodied subjects performed a grasp force matching task with supplementary non-invasive electrotactile stimulation with a frequency proportional to grasp force magnitude. Before the task, a brief training session taught the subjects to associate the sensation of electrotactile stimulation with the generated grasp force. In some trials, the force-frequency mapping was biased to introduce an unnoticeable mismatch between natural and electrotactile force feedback, thereby provoking the subject to subconsciously estimate the force as a compromise between the two sources of information. The outcome of this compromise revealed the weights assigned to each feedback type. The grasp forces were significantly affected by the biased mappings, as indicated by the average estimated relative weights (electrotactile: 0.69 ± 0.29; natural: 0.31±0.29). Across subjects, this weight was correlated ($r^2 = 0.75$) with the improvement in force matching precision when adding the unbiased electrotactile feedback to the natural force feedback, as predicted by maximum likelihood estimation. This shows that even after minimal training the nervous system adopts electrotactile stimulation as a highly reliable source of information that can improve the precision in the estimation of the grip force. This result has important implications for the restoration of sensory feedback in upper limb prostheses as it indicates that even non-invasive stimulation can be integrated naturally (i.e., subconsciously and effectively) in the motor control loop.

Keywords: Motor control, electrotactile stimulation, sensory feedback, sensory integration, sensory substitution, human-machine interface.

Introduction

Somatosensory feedback is an integral part of human neural control of movement and this is particularly evident from the impact on motor performance when the feedback is absent [1,2]. Humans integrate information from various sources to generate a state estimate from which future movements can be planned [3]. For this reason, interacting with an artificial system (e.g., assistive robot) through a human-machine interface is challenging if the interface does not provide rich (multimodal) sensory feedback about the machine actions to the user. One example of this problem is the use of upper-limb myoelectric prostheses, where poor controllability and lack of feedback are amongst the features which lead to the low acceptance rate by myoelectric forearm prostheses users [4–6].

Several different approaches have been proposed to restore sensory feedback from the amputated limb. In targeted sensory reinnervation, the sensory nerves from the amputated limb are redirected to skin areas e.g. on the chest, which implies that touch on these areas can be intuitively associated with touch on the prosthesis [7,8]. This has been further exploited to evoke an illusion of limb movement by applying vibration on the reinnervated areas [9]. Alternatively, invasive electrical stimulation of nerve branches at the periphery [10–13] or at the cortex [14–16] can to some degree generate sensations that are perceived as emanating from the amputated limb. These methods elicit somatotopic sensations, which are experienced as coming from the missing limb. Importantly, it has been shown that the somatosensory information conveyed by this stimulation can be integrated in the sensory integrationprocess similarly to natural sensory feedback. For natural feedback, this integration occurs optimally as redundant sources of information (e.g. from proprioception, tactile sense, and vision) are weighted according to their perceived reliability in accordance with maximum likelihood estimation (MLE) [17–20]. Feedback from cortical stimulation in monkeys has been shown to be integrated according to this principle [21] and a recent study in one human prosthesis user indicated that this was also the case for invasive peripheral nerve stimulation [22]. In this study, Risso and colleagues recreated the experimental setup from the seminal study by Ernst & Banks [17] by asking the amputee subject to estimate the size of a hand-held object based on proprioception arising from the nerve stimulation and from vision. It was found that the weights assigned to visual input and nerve stimulation, respectively, when estimating object size were predicted by the accuracy of each of these signals as quantified by the Just Noticeable Difference (JND).

Although the invasive methods can restore somatosensory feedback in a way that is compatible with the motor control processes of the central nervous system, they involve complicated hardware and specialized surgical procedures. This might be an obstacle to their wider clinical application. For instance, even in the case of prostheses, many amputees are reluctant to undergo additional surgery [23]. A simpler and more practical solution is sensory substitution feedback, where the sensory modality is typically conveyed to the subject by non-invasive electrotactile or vibrotactile stimulation and the somatosensory information can be encoded by modulating stimulation parameters (e.g., the intensity of the stimulation [24,25]). Such feedback can improve control performance in some conditions [26–29], although this approach requires the subject to re-interpret the perceived sensation (e.g. tingling on the forearm) as another sensory modality (e.g. prosthesis grasp force) [30]. Due to this additional layer of processing, it is normally assumed that such feedback is exclusively processed on a conscious level as opposed to natural feedback which is largely processed subconsciously [25].

In this study, we investigated the integration of non-invasive electrotactile stimulation by the nervous system during closed-loop control of grasping force. Specifically, able-bodied subjects performed a grasp force-matching task with natural force feedback (combination of proprioception and cutaneous sensation) as well as electrotactile feedback representing the generated force. In a subset of the repetitions of this task, an unnoticeable bias was introduced in the electrotactile feedback, provoking the subject to subconsciously generate a weighted average of the two sources of information when estimating the state of the task (i.e. estimating grasp force to enable adjustments to the appropriate level). In this way, a non-zero weight of the electrotactile feedback would indicate that the nervous system adopts the information from this feedback and integrates it naturally (i.e. in accordance with MLE).

Methods

Participants

Fourteen healthy subjects (8 males and 6 females, 29.1 ± 3.9 yrs.) were recruited for the main study, and four subjects (2 males and 2 females, 27.4 ± 4.2 yrs.) were recruited for the pilot study. The experiment was conducted in accordance with the declaration of Helsinki, approved by the local ethics committee, and the subjects signed an informed consent form before commencing with the experiment**.**

Experimental setup

The experimental setup consisted of the closed-loop system depicted in figure 1.A. The system included a grip force dynamometer (G200, Biometrics Ltd, USA; sensitivity: 1.5 V/mV), a standard PC, an electrical stimulator (DS8R Biphasic Constant Current Stimulator, Digitimer, USA) connected to a pair of stimulation electrodes (Dura-Stick Self-Adhesive Premium Stimulating Electrodes, round, Ø: 3.2 cm), and a data acquisition card to sample the force and also generate analog input (command signal) to the stimulator. The test bench model was implemented in Matlab 2019a (MathWorks, USA), Simulink, using a toolbox for human manual control [31] and Simulink 3D Animation. The force signal was sampled and processed on a PC, where it was encoded in real time in the train of pulses generated by the stimulator. The recorded force signal was mapped linearly to the frequency of the stimulation pulses. In addition, the system included a visual representation of the generated force on the computer screen, where a vertical bar illustrated the instantaneous force. In this way, the generated grasp force was fed back to the user by up to three different channels: natural feedback (hand grasping the gripper), the sensation of the electrotactile stimulation, and visual feedback on the screen. The control loop ran at 1 kHz, where each cycle included sampling of the force signal and updating the command input into the stimulator.

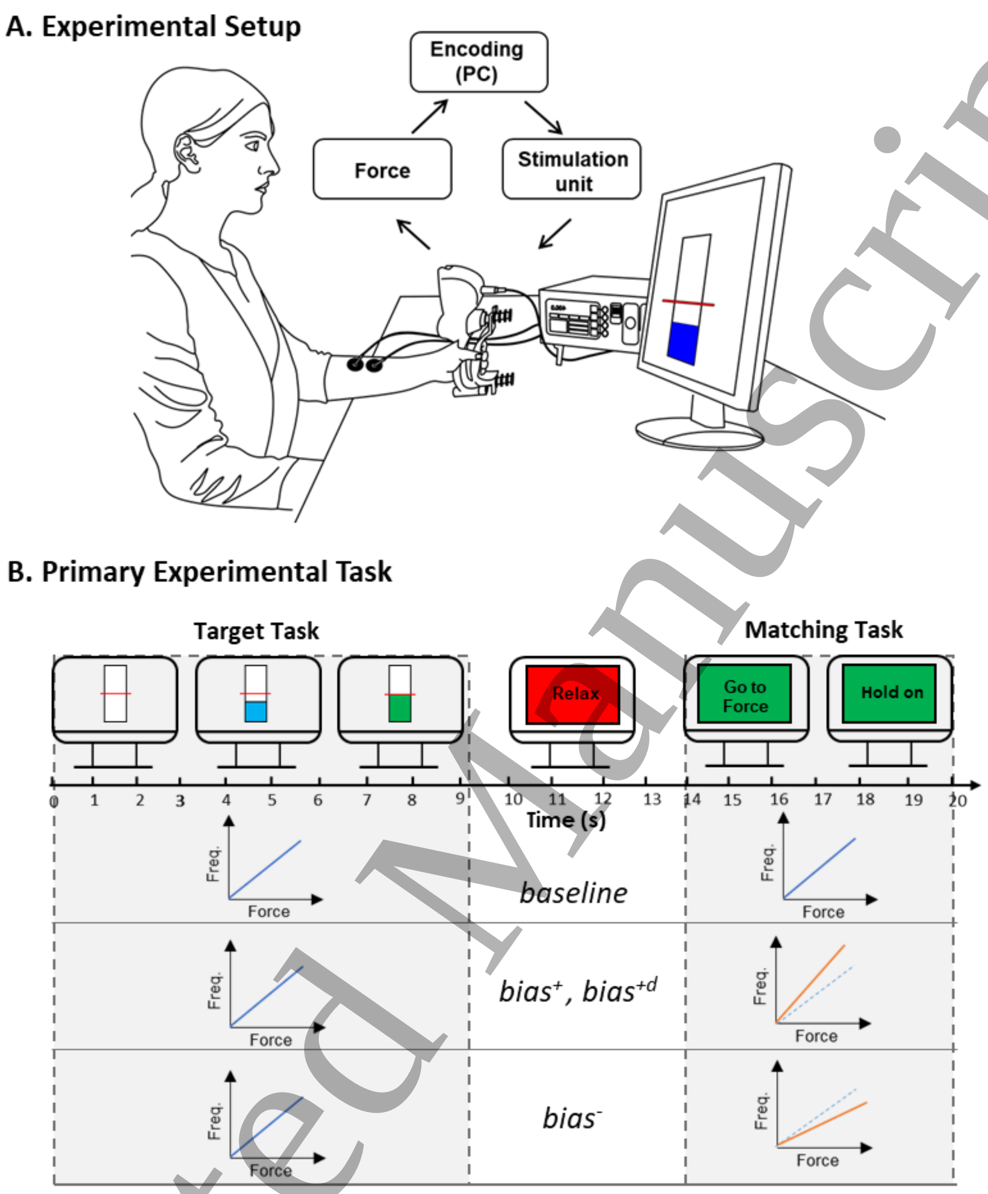

Figure 1. The closed-loop system (A) records the force signal generated by the subject through the handgrip dynamometer and encodes it into a stimulation pattern delivered by electrical stimulation. In the primary experimental task (B), each trial was started by a target task where the subject was asked to produce a specific force based on visual feedback and hold this force as accurately as possible over a period of 5 s (target task). After relaxing for 5 s, the subject was asked to generate the same force without visual feedback and to hold it for 3 s (matching task). In a subset of trials, the stimulation frequency encoding the force was either increased during the matching task (*bias*$^+$ and *bias*$^{+d}$; Eq. 2&3) or decreased (during *bias*$^-$; Eq. 2&4) by 80% of *JND* with respect to the *baseline* mapping (Eq. 1). In the target task, the *baseline* mapping (Eq.1) was always used. In addition to the conditions illustrated in this figure, the tasks were also completed without electrotactile feedback (*natural feedback only* condition).

Experimental procedure

Throughout the main experiment, the subject was seated comfortably in front of a desk with the force transducer and a computer screen positioned approx. 50 cm away from the subject (figure. 1.A). The subject placed the dominant arm on the surface of the table. First, the maximum voluntary contraction (MVC) force was measured by asking the subject to grasp the hand dynamometer with maximum strength for 5 seconds. The mean force during the force plateau was extracted. The average plateau force across the three repetitions separated by >1 min was adopted as the MVC. In the following phases of the experiment, the generated force was normalized to the MVC so that all force signals were expressed in the range from 0 to 100%.

Next, the participants underwent two training sessions lasting approximately 5 minutes in total to generate an intuitive understanding of the relation between natural feedback (proprioception, cutaneous and visual input) and the generated force. First, the subject was asked to generate a specific force level (randomly selected from the range 15-30 %MVC) indicated by a horizontal line on the screen. The resolution of the bar indicating instantaneous force was 5 % MVC/cm. In 12 consecutive trials, the subject had 6 s to match the target force and 4 s to relax before the start of the next trial. The second training task was similar to the first, but the visual feedback of the instantaneous force was absent for the first three seconds, leaving the subject to rely only on natural feedback to produce the desired force. The bar reappeared during the last three seconds of the trial, so that the subject was able to see the generated force and correct it if necessary.

After this training procedure, the subjects performed two blocks of trials with the primary experimental task illustrated by figure 1.B. Each trial consisted of two contractions. First, the subject was asked to generate a specific force based on visual feedback by reaching and holding this force as accurately as possible over a period of 5 s, hereafter denoted as the *target task*. As long as the applied force *was in* the *range* of ± 5% of the target force the floating bar turned green as an indicator of success. After relaxing for at least 5 s, the subject was asked to generate the same force without visual feedback and hold it for 3 s, hereafter denoted as the *matching task*. In each trial the target force was set to a random value in the range 15-30 %MVC. Each of the two blocks contained 15 trials and the blocks were separated by 2 minutes. We refer to these trials as the *natural feedback only* condition.

Next, electrotactile feedback was introduced. First, this feedback was calibrated by measuring the subject's detection threshold, pain threshold and Just Noticeable Difference (JND). The JND was defined as the smallest change in stimulation frequency that could be detected by the subject (see *Calibration* section for details). Following the psychometric tests, the subject repeated the two training sessions, but this time frequency-modulated electrotactile feedback (Eq. 1) was also provided in order for the subject to learn to associate the generated force with the sensation evoked by the stimulation. The amplitude of the stimulation was set to the average of detection and pain threshold to produce a clear non-painful sensation (pulse width: 500 μs). In the training, the instantaneous frequency of the electrotactile stimulation (*F*) was determined based on the normalized force (*f*) as:

$$F_{baseline}(t) = 60f(t) + 5 \quad (1)$$

In this way, the complete range of force evoked stimulation frequencies in the range 5-65 Hz. This range was adopted from a previous study with frequency-modulated electrotactile feedback [32] and is compatible with the typical range of discharge rates for cutaneous receptors [33]. This mapping will be referred to as the *baseline* condition (figure 1.C). After the training, the subjects performed eight blocks (total of 120 trials) of the primary experimental task with electrotactile feedback. Each block was separated by breaks of 2 minutes to minimize mental and muscle fatigue. In the matching task of a subset of these trials, the mapping indicated by Eq. 1 was altered (biased mapping, Eq. 2) so a given force would now generate a different stimulation frequency (figure 1.C). In this way, if the subject perfectly repeated the target force in the matching task, the stimulation frequency would be different, and vice versa for the force if the frequencies were matched across the two tasks. The magnitude of this mismatch in the stimulation frequency was always equal to 80% of JND, which implied that in principle all mappings should be consciously perceived as identical by the subject. Importantly, while the subjects were informed about the experimental task and the number of blocks, they were not informed that the mapping would be biased in some trials. Any implicit or explicit indication that the subject noticed the bias in some trials were noted by the experimenter, and after the experiment the subject was asked if he/she had noticed any variations in the force-frequency mapping across trials.

Specifically, the biased mappings were characterized by Eq. 2:

$$F_{bias}(t) = B \times F_{baseline}(t) \quad (2)$$

, where B determines the magnitude of the bias. In the *bias*$^+$ condition *B* was calculated as

$$B = (1 + \frac{0.8 \cdot JND^+}{100}) \quad (3)$$

and as

$$B = (1 - \frac{0.8 \cdot JND^-}{100}) \quad (4)$$

in the *bias*$^-$ condition, where JND^- and JND^+ correspond to the JND measured by approaching the baseline from below and above, respectively (see *Calibration* section). According to Eqs. 3 and 4 the stimulation frequency encoding the force was either increased or decreased by 80% of *JND* with respect to the baseline mapping (Eq. 1). This implies that during the matching task in the *bias*$^+$ condition, the subject received electrotactile stimulation with higher pulse train frequency when generating a lower force than in the target task. Similarly, in the *bias*$^-$ condition, the stimulation frequency at a given force was lower compared to the baseline mapping. Finally, in the *bias*$^{d+}$ condition (Eq. 4), the mapping was the same as in the *bias*$^+$ condition, but a delay of 125 ms was imposed between the measured force and the corresponding frequency. This delay was selected to simulate a realistic time lag between activation and movement of a prosthesis [35].

The fact that the bias was implemented as a gain (determined by JND) is compatible with Weber's law stating that the smallest difference in the intensity of a stimulus that can be perceived is proportional to the magnitude of the stimulus [36]. In this way, the JND values estimated at a baseline frequency of 15 Hz (see *Calibration*) could be extrapolated to the full range of frequencies. To compensate for potential minor deviations from the perfect proportional relation predicted by Weber's law (i.e. the subject may be more sensitive to relative change at other frequencies than 15 Hz), and to mitigate potential learning effects of long-term exposure to stimulation [37], the gain was set to 80% of JND. This ensured a safety margin so that the biased mappings were unnoticed by the subjects at all times.

The order of the trials for the four conditions was randomized, so that each block of 15 trials contained different mappings (Eq. 1-4).

Experimental procedure, pilot experiment

The aim of the pilot test was to investigate whether the presence of electrotactile stimulation impaired the reliability of natural force sensation. The task was similar to experimental task of the main study but included two conditions (each 30 trials): *natural feedback only* in which the subject did not receive the electrical stimulation and *constant feedback* in which the subject was stimulated with a constant frequency of 30 Hz during both target and matching tasks. In the latter condition, the electrotactile feedback did not convey any task-relevant information. The subject performed 6 blocks of 5 trials of each of the two tasks in randomized order.

Calibration

To calibrate the electrotactile feedback the stimulation electrodes were placed on subject's skin at one third of the length of the radial side of the forearm measured from the wrist. This location is potentially relevant in practical applications for electrotactile feedback, including prosthesis users with transradial amputation. First, the detection and pain thresholds were determined using the method of limits [38]. Specifically, a number of 1-s trains of stimulation pulses were delivered, separated by 0.5 s pause. The stimulation amplitude was increased in steps of 0.1 mA while the stimulation frequency and the stimulus pulse width were kept constant at 50 Hz and 500 µs, respectively. The detection threshold was set to the lowest current amplitude producing detectable sensation, while the pain threshold was the lowest current at which the subject perceived the stimulation as painful. Both thresholds were measured three times and the average values were adopted as the final thresholds. The electrical stimulation in the present study was used to generate superficial current flow that activates skin afferents, thereby eliciting "pure" tactile sensations located below the electrodes. Accordingly, if the stimulation at any point during this procedure evoked radiating sensations or motor responses (muscle twitching), the electrodes were repositioned to ensure that only local sensations below the electrode were evoked. In one subject, the electrode placement was adjusted by approximately 1 cm with respect to the initial position due to muscle twitching.

To determine the JND (main experiment only), the adaptive weighted staircase procedure was used [39]. Specifically, two 1-s trains of stimulation pulses with different, constant frequencies were delivered, separated by a pause of 0.5 s. For both pulse trains, the pulse amplitude was set halfway between the detection and pain thresholds (pulse width: 500 µs) to produce a clear and comfortable sensation. The frequency in one of the pulse trains was constant across all trials (baseline frequency: 15 Hz), while the frequency of the other train (test frequency) was modulated across trials. After receiving the two trains of pulses in randomized order, the subject was asked to indicate if the first or the second pulse train had the higher frequency. If the subject selected the correct pulse train, the test frequency for the next trial was adjusted to be closer to the baseline frequency and vice versa when indicating the wrong train. This procedure was repeated until the subject guessed incorrectly seven times. The JND was computed by averaging the test frequencies in the trials with wrong answers (i.e. "reversal" of the staircase). The test frequency was adjusted by 1 Hz in the case of a correct answer and 3 Hz following a wrong answer. This procedure implied that the estimated JND corresponded to the difference in frequency that the subject was able to recognize with a success rate of 75% [40]. The *JND was measured* three times *for* initial test stimulus set to 5 Hz (below the baseline, JND^-; test stimulus frequency increased for correct answers) and 25 Hz (above the baseline, JND^+; test stimulus frequency decreased for correct answers), respectively. JND- and JND+ were determined as the average values across the three repetitions and were expressed in percent of the baseline frequency.

Data analysis

The main outcome measure was the plateau force in the matching task (f_{mt}) expressed as a percentage of the plateau force in the target task (f_{tt}), hence 100% indicates that a subject has perfectly reproduced the target force. f_{mt} was extracted from the matching force by computing the average of the recorded signal between 17 to 20 s (when the hold on message appeared on the screen; figure 1.B). Additionally, the parameter $f_{electro}$ was defined as the force that the subject would need to generate to obtain the same frequency of electrotactile stimulation that he experienced when producing the target force in the target task (Figure 2). This parameter was also expressed as a percentage of f_{tt}. Specifically, in the bias conditions, $f_{electro}\{bias^*\}$ where * stands for (+, -, +d), is the force that fulfills

$$F_{bias} = F_{baseline} \quad (5)$$

,which cf. Eq. 1 and 2 is equivalent to

$$B(60f_{electro} + 5) = 60f_{tt} + 5 \quad (6)$$

and this implies that

$$f_{electro} = \frac{1}{B}\left(f_{tt} + \frac{1}{12}\right) - \frac{1}{12} \quad (7)$$

Prior to analysis, the erroneous trials were removed from the dataset. For example, in a subset of trials, it was clear that the subject momentarily lost focus. This was evident from trials with a large difference between the forces during the two tasks, or highly variable force during the matching task. Specifically, trials with matching task plateau force >10% MVC from the target force or trials with coefficient of variation (standard deviation/mean of matching task plateau force) > 20 were excluded.

The average f_{mt} for all included trials for each of the five conditions (*natural feedback only*, *baseline*, *bias*+, *bias*-, and *bias*+d) as well as the variance of f_{mt} across trials were calculated. In addition, the force at the first force turn in the matching task (i.e. force amplitude where the force had its first negative slope after the initiation of that task) normalized to f_{tt} and the time to the first turn was calculated for all included trials.

The average f_{mt} and force at the first force turn were compared across *bias*$^-$, *baseline*, *bias*$^+$, and *bias*$^{+d}$ conditions using one-way repeated measure analysis of variance test and Bonferroni post-hoc test for pairwise comparison across the conditions.

The weight assigned to the electrotactile feedback ($W_{electro}$) by the CNS in the sensory integration process relative to the weight of the natural feedback ($W_{natural}$) was estimated from the *bias*$^-$, *bias*$^+$, and *bias*$^{+d}$ conditions using Eq. 8:

$$W_{electro} = \frac{f_{mt}\{bias^*\} - 100}{f_{electro}\{bias^*\} - 100} \qquad (8)$$

, where $f_{mt}\{bias^*\}$ is the average matching task plateau force expressed as the percentage of the target force in each trial, $f_{electro}\{bias^*\}$ refers to the force that should be generated in the matching task in order to produce the target frequency (i.e. the frequency experienced at the target force in the target task) also expressed as a percentage of the target force, and * indicates the condition (+, -, +d). The numerator in this equation therefore represented the average displacement of the matching task plateau force from the target force (100%, since f_{mt} was normalized to the target force; Figure. 2). This difference was then normalized (denominator) to the force difference expected in the bias conditions if the subject aimed at perfectly replicating the stimulation frequency. Therefore, $W_{electro} \sim 1$ would indicate that the subject strongly reacted to the bias in the electrotactile feedback which in turn implies that when reproducing the target force he/she focused mostly on the electrotactile stimulation rather than natural feedback input.

It was observed that in some subjects f_{mt} in the *baseline* condition ($f_{mt}\{baseline\}$) was consistently above or below the target force. As Eq. 8 assumed that subjects could, on average, generate the appropriate target force in the *baseline* condition, this equation was adjusted to compensate for such systematic deviations from the reproduction of the target force in the *baseline* trials:

$$W_{electro} = \frac{(f_{mt}\{bias^*\} - (f_{mt}\{baseline\} - 100)) - 100}{f_{electro}\{bias^*\} - 100} = \frac{f_{mt}\{bias^*\} - f_{mt}\{baseline\}}{f_{electro}\{bias^*\} - 100} \qquad (9)$$

$W_{electro}$ for each subject was determined as the average value across the values obtained in the three bias conditions.

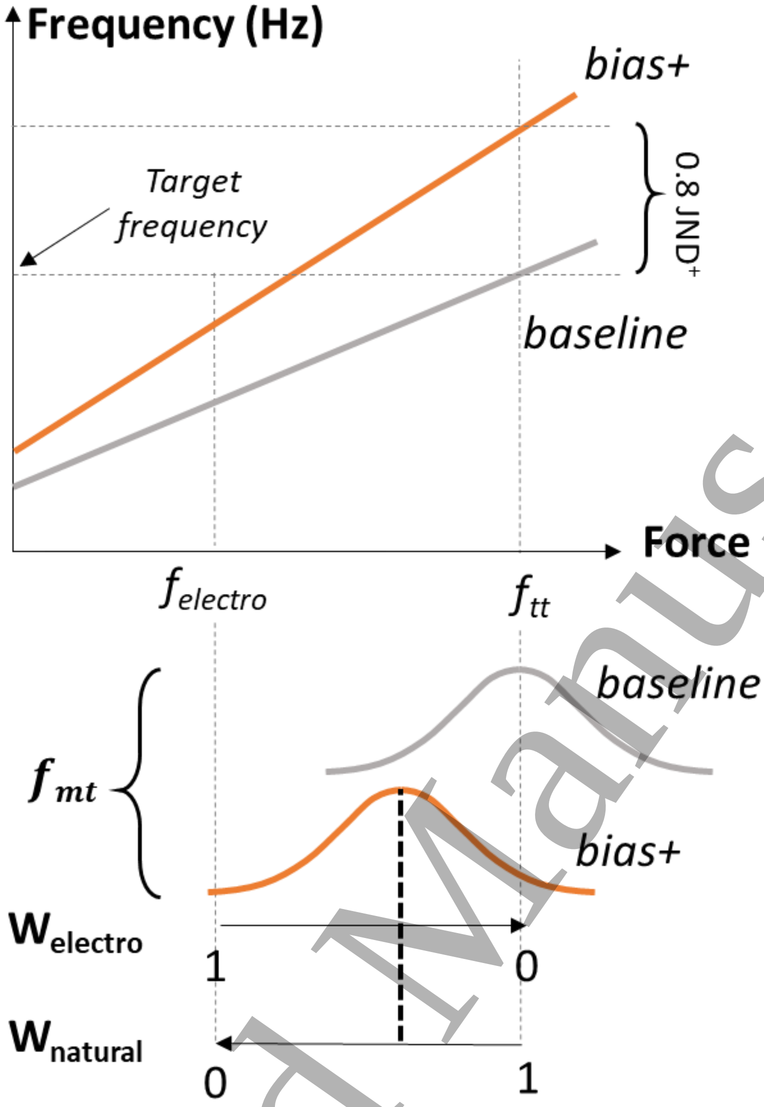

Figure 2: The instantaneous force determined the stimulation frequency in different ways across conditions. In the target task, the *baseline* mapping (blue line; top panel) was always used. In the matching tasks in some trials, different mappings were used to introduce an unnoticeable bias. The orange line (top panel) illustrates the mapping used in the *bias*$^+$ condition. The difference in frequency evoked by the force in this mapping versus the baseline was determined by the normalized *JND*$^+$. In this way, the change in frequency due to the biased mapping was not noticeable to the subject. From 30 repetitions of the task in each condition, the distribution of matching task plateau force (f_{mt}) was derived. Across repetitions of the *baseline* condition, it was expected that the distribution of normalized f_{mt}would be centered around f_{tt} (blue curve). In the matching task in the *bias*$^+$ condition, however, it was no longer possible for the subject to reproduce the same natural sense of force magnitude as well as the same electrotactile stimulation frequency (due to the biased mapping). Here, $f_{electro}$ refers to the force that must be generated by the subject in order to evoke the same stimulation frequency as in the target task (*baseline* mapping). In this case, the center of the distribution of f_{mt} (orange curve) would indicate the relative weight assigned to the two feedback sources in the neural integration process ($W_{electro}$ and $W_{natural}$, respectively). The larger the displacement of this distribution center with respect to the *baseline* condition, the higher the weight of the electrotactile feedback.

MLE predicts that precision of the state estimate based on the available feedback sources can be predicted from the variance of these feedback sources [17]. Accordingly, if $W_{electro}$ is high it can be expected that the precision of the state estimate improves when electrotactile feedback is provided since the variance of the information provided by the stimulation is presumably low (and vice versa for low $W_{electro}$). We tested this hypothesis by comparing the change in variance of f_{mt} in the conditions with and without electrotactile feedback (i.e. *baseline* vs. *natural feedback only* condition) depending on the estimated $W_{electro}$ using linear regression analysis. Specifically, the change in precision was estimated as the ratio between the variance of all matching task average f_{mt} in the *baseline* condition and the *natural feedback only* condition. In this way, a low value implied a large improvement in precision, where the values at or higher than 1.0 indicate the same or lower precision with the addition of the electrotactile feedback.

In addition, the paired t-test was used to investigate the difference between JND^+ and JND^- and linear regression was used to investigate the relation between $W_{electro}$ and the following parameters: magnitude of MVC, average magnitude of JND, variance of f_{mt} in *natural feedback only* condition and the range between sensation and discomfort thresholds. Adjustment for pairwise comparisons was performed using Bonferroni correction.

To investigate whether learning occurred across the 30 trials in each condition, the rectified normalized error ($|F_{mt}$-$F_{tt}|$) was calculated per trial, per subject split by five conditions. The average error for each subject in the first and in last 10 trials was calculated for each condition and was compared using t-test.

The distributions of normalized plateau forces from the pilot experiment were analyzed statistically using a two sampled t test and bootstrap resampling to compare the tested conditions (natural feedback only and constant stimulation) for each subject.

Prior to all tests, the normality of the data was checked using one-sample Shapiro-Wilk tests. In all above analysis, a significance level was set at $p < 0.05$.

Results

The average JND was 18.91 ± 5.91% and 17.47 ± 5.62 % of the baseline stimulation frequency for ascending (JND^+) and descending (JND^-) tests, respectively ($p = .002$). These values implied that in the matching task, the subject should produce forces that deviated, on average, by 15% and 14% of the target force (conditions *bias*$^+$ or *bias*$^-$, respectively) in order to receive electrotactile stimulation at the frequency experienced as in the target task (Eq. 3&4). None of the subjects indicated that they noticed that the bias was introduced in the force-frequency relation in some trials: neither spontaneously during the experiment nor when asked explicitly after the experiment. On average, 5.6 ± 7.7 % (maximum number: 8/30) of the trials were excluded for each of the five conditions due to indications that the subject was not attentive to the task in the trial (see *Data analysis*). Specifically, this occurred in 10.9 ± 12.0 % of the trials in the *natural feedback only* condition, in 3.1 ± 4.0 % of the trials in the *baseline* condition, in 5.4 ± 7.4 % of the trials in the *bias*$^+$ condition, in 4.0 ± 5.4 % of the trials in the *bias*$^-$ condition, and in 3.5 ± 3.5 % of the trials in $bias^{+d}$. Across all conditions, 6.4 ± 5.1 % of all trials with low target forces (<22.5% MVC) were excluded, while 4.4 ± 3.2 % of the trials with high target forces (≥22.5% MVC) were excluded.

In the pilot test, the variance of f_{mt} was 185 ± 64 (*natural feedback only*) and 192 ± 83 (*constant stimulation*). The similarity between these two numbers indicated that the presence of electrotactile stimulation did not impair the ability of subjects to estimate the grasp force via natural feedback. No statistically significant difference was observed across the distributions of normalized plateau force for any of the subjects (p-values in the four subjects ranging from 0.34-0.89). Figure 3.A shows representative force traces generated by one subject in three trials with similar target force (approximately 20% MVC) with and without bias (*baseline*, *bias*$^-$ and *bias*$^+$ conditions, respectively), while Figure 3.B depicts the corresponding profiles of instantaneous frequency of the electrotactile feedback delivered to the subject. In the target task (contraction during approx. the first 7 s), the generated force accurately matched the target for all conditions. Across the three conditions, a force close to the target was reached rapidly (at the first force turn) after which slower adjustments in the force occurred. The nature of these adjustments, however, depended on the condition. In the matching task of the *baseline* condition, the target force was accurately reproduced, whereas the plateau forces were markedly shifted in the two conditions with the bias. Figure 3.B, illustrating the instantaneous stimulation frequency, demonstrates that in these conditions the subject subconsciously generated the force by making a compromise between matching the perceived force (natural feedback) versus replicating the perceived stimulation frequency that were experienced in the target task. Here, a compromise was needed since the bias implied that both sensations could not be reproduced as in the *baseline* condition. Specifically, in this example, the plateau force in the matching task of the *bias*$^+$ condition was approximately 2% MVC below the force produced in the target task while the stimulation frequency was approximately 2 Hz higher than during the target task. The opposite behavior was observed for the *bias*⁻ condition.

Figure 4 displays the deviations in f_{mt} produced across all trials and conditions for two subjects.

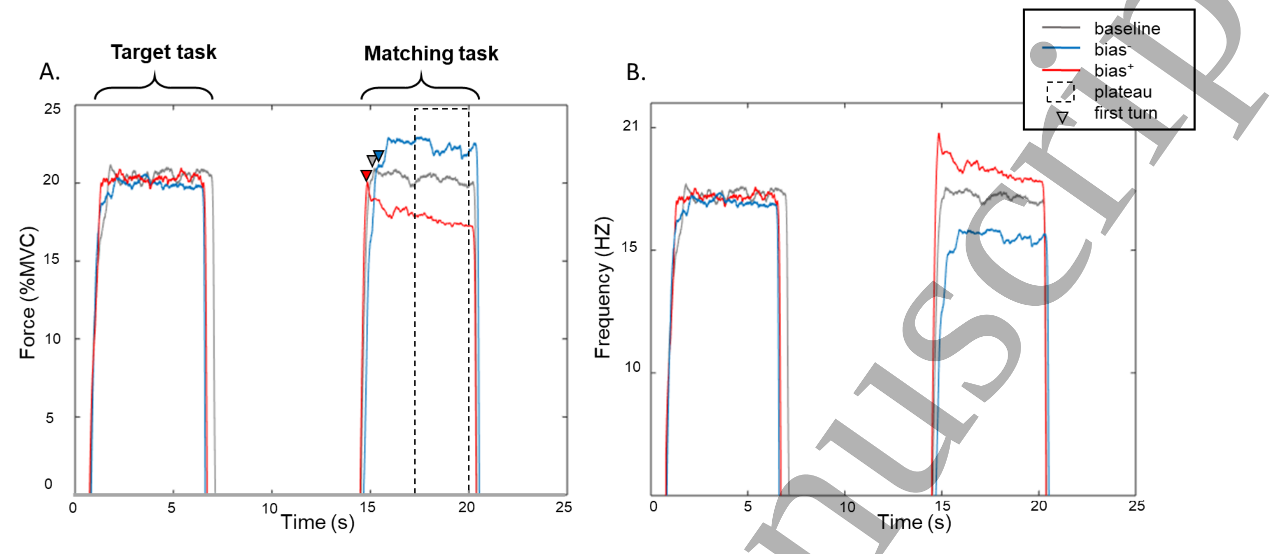

Figure 3. Force traces (A) and instantaneous stimulation frequency (B) from three trials in *baseline*, $bias^-$ and $bias^+$ conditions, respectively, from one subject. Triangles indicate the force at the first turn in the matching task for each condition. The dashed black box in the matching task in panel A represents the period from which the plateau force was extracted. In some cases, including the target task of the baseline condition in this example, the subject terminated the contraction with some delay (in this case approximately 1 s) with respect to the instruction. We suspect this reflects that the subject briefly directed the attention away from the instructions on the screen.

These two subjects responded to the bias in highly different ways. The first subject (No.6; left-hand side of figure 4) exhibited a substantial increase in the precision of the plateau force produced in the matching task (i.e. variance decreased to <50% of the variance in *natural feedback only* condition). This suggests that the information carried by the electrotactile feedback was exploited by the CNS to generate a more reliable, and thus more reproducible, estimate of the target force. Furthermore, the magnitude of the matching task plateau force varied systematically with the bias, indicating that electrotactile feedback dominated the compromise between the two sensory modalities. Here, the dominance implies that the sensation of the electrotactile feedback from the target task was closer to being accurately reproduced than the sensation of natural force feedback during the matching task. This dominance was not influenced by the delay ($bias^{+d}$). On the other hand, the electrotactile feedback and the bias conditions had little impact on the behavior of subject No.11 (right-hand side of figure. 2). Specifically, the electrotactile feedback implied a minor decrease in the matching task precision and the mean value of normalized plateau force appeared to be largely unaffected by the bias. Within all conditions, the error in f_{mt} with respect to the target force did not exhibit learning effects across the 30 trials, (first 10 trials: 17.80 ± 4.36; Last 10 trials 17.34 ± 3.58; p=0.96).

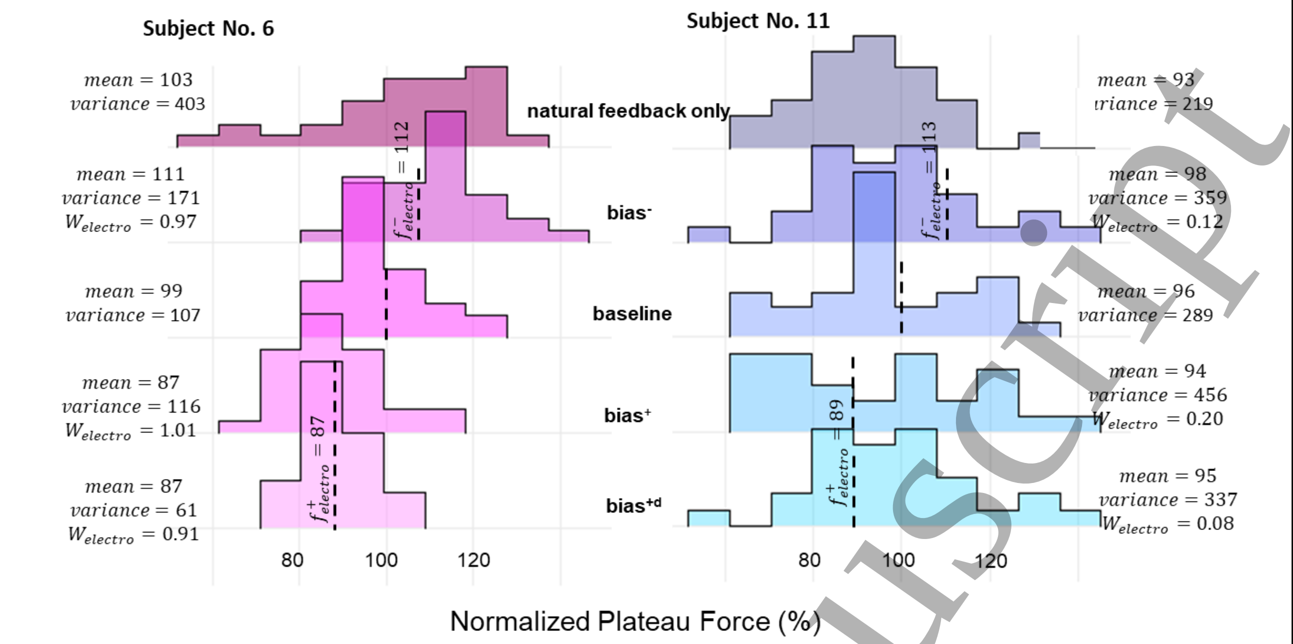

Figure 4. Distribution of matching task plateau forces normalized to the respective target forces across all conditions for two subjects. The dashed, vertical lines in the conditions with the bias in the encoding between force and stimulation frequency indicate the $f_{electro}$ in each condition. The $f_{electro}$ in both directions are indicated by dashed lines.

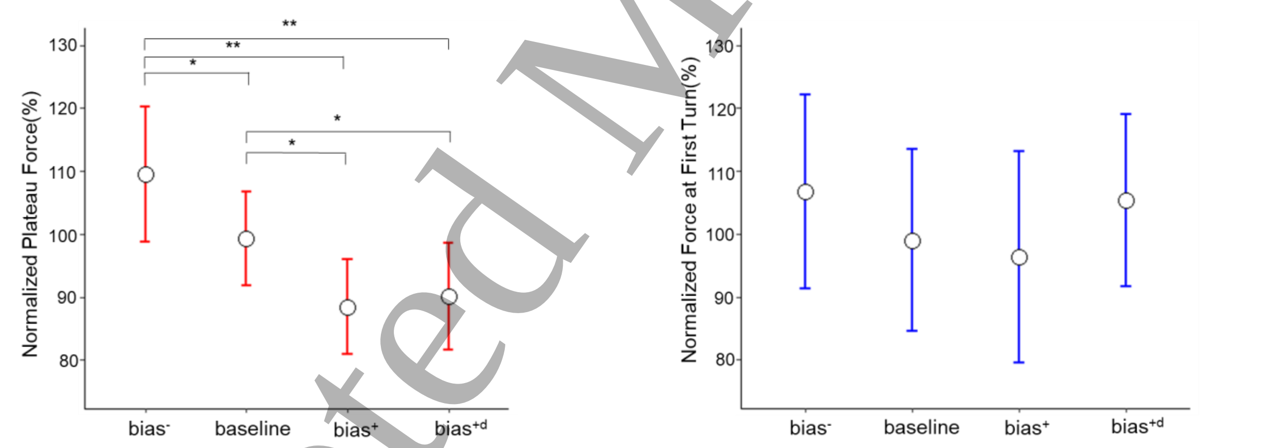

Figure 5. Mean ± standard deviation of normalized plateau force (a) and normalized force at the first turn (b) during different conditions across all subjects. The horizontal bars indicate statistically significant differences (ANOVA followed by the pairwise multiple-comparison test with Bonferroni correction). **, $p \leq 0.001$; *, $p \leq 0.05$.

Across all subjects, however, the bias did significantly affect the matching task plateau force ($p < 0.001$) (Fig. 5). While the target force was accurately reproduced in the *baseline* condition (average f_{mt}: 99.3 ± 7.5 %), f_{mt} was 109.8 ± 11.6 % in the *bias*$^-$ condition and 88.6 ± 7.4% in the *bias*$^+$

condition. The post-hoc test indicated that there was a highly significant difference ($p < 0.001$) between *bias*$^-$ versus *bias*$^+$ and *bias*$^{+d}$ and a significant difference ($p < 0.05$) between *baseline* versus the three biased conditions. This shows that the information carried by the electrotactile feedback was exploited in the sensory integration process with a considerable weight. Introducing a delay in the feedback did not affect this (f_{mt} in *bias*$^{+d}$: 90.0 ± 7.9%; not significantly different from *bias*$^+$). Conversely, the force at the first turn was not significantly different across the conditions ($p = 0.22$). The time from the onset of force generation in the matching task to the first turn was 0.55 ± 0.11 s (*bias*$^-$), 0.44 ± 0.09 s (*baseline*), 0.45±0.08 s (*bias*$^+$), and 0.45 ± 0.07 s (*bias*$^{+d}$). One way ANOVA detected a significant difference across the groups ($p = 0.011$), however after applying Bonferroni post hoc test we only found a significant difference between *bias*$^+$ and *bias*$^-$. The estimated average relative weight of electrotactile feedback ($W_{electro}; Eq.\ 9$) was 0.69 ± 0.29, which implies that the weight of natural force feedback was 0.31 ± 0.29. This implies that the subjects, on average, relied more on the electrotactile feedback than on natural feedback when selecting the appropriate muscle activation level during the matching task. The high variability in this weight across subjects, however, showed that this behavior was not consistently observed in all subjects, as the range of relative weights was 0.14-0.99 (figure 6). The estimated weights of electrotactile feedback across subjects was significantly correlated ($r^2 = 0.75, p < 0.001$) with the improvement in the precision of the matching task plateau force when including electrotactile feedback (*natural feedback only* versus *baseline*). This is in accordance with MLE that predicts that a precise source of information would be assigned a high weight. The top and right panel in figure 6 displays fitted distributions of matching task plateau forces across conditions for two representative subjects. These examples illustrate the meaning of values at different ends of the spectrum for the two axes ($W_{electro}$ and variance ratio). The high variance ratio (0.92) for subject No.12 implies that the fitted distributions for the *natural feedback only* and *baseline* conditions had approximately the same variance. On the other hand, for subject No. 8, the variance was much smaller for the *baseline* condition; hence a low variance ratio (0.35). For this subject, the high $W_{electro}$ (0.90) reflects a clear shift in the mean value of the fitted distributions to the *bias*$^+$, *baseline*, and *bias*$^-$ conditions, whereas these distributions are largely overlapping for subject No.12.

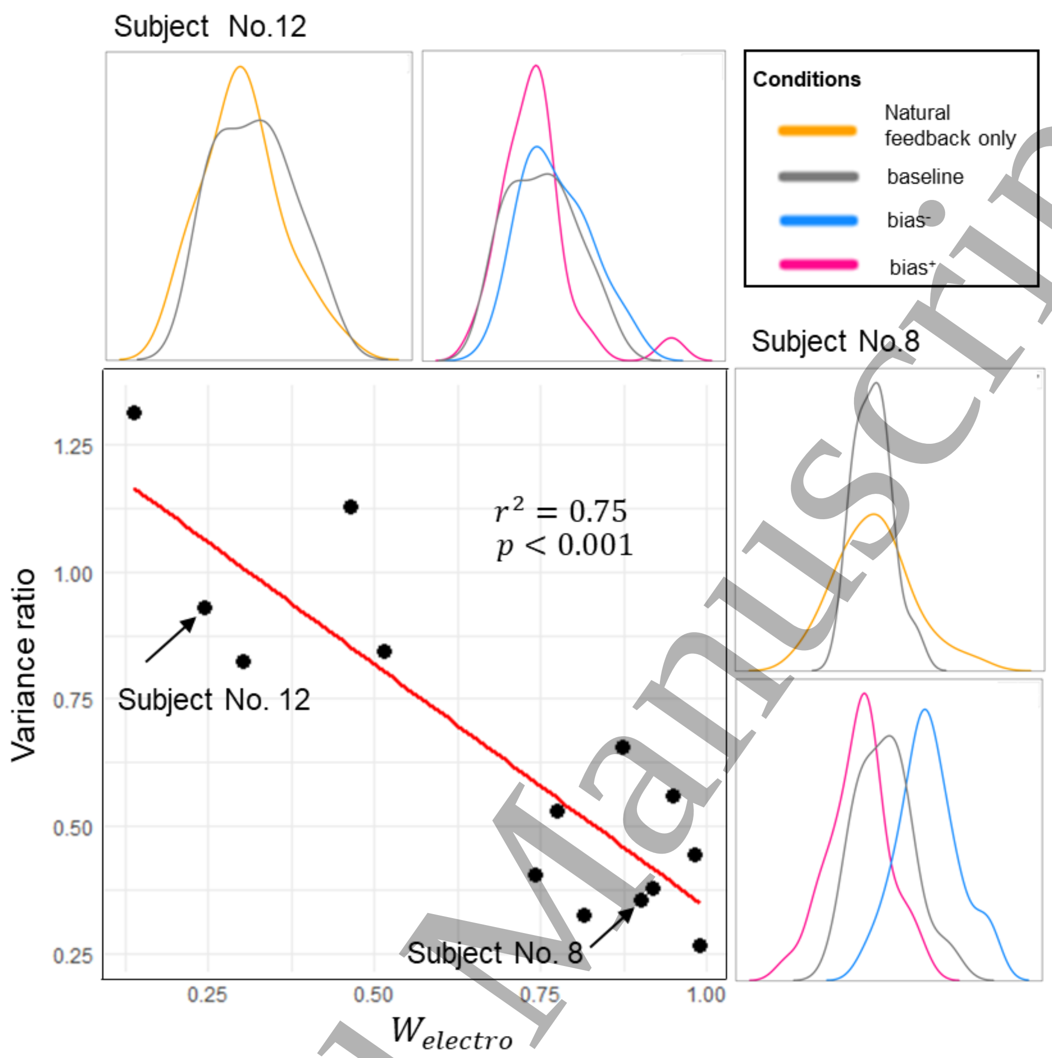

Figure 6. Scatterplot between the estimated $W_{electro}$ and the ratio of the variance of the matching task plateau forces in the baseline and *natural feedback only* conditions. The red line indicates the best linear fit. The top and right panel displays fitted distributions (obtained by applying *kernel density estimator)* of matching task plateau forces across conditions for two representative subjects (No. 8 and 12). The high variance ratio (0.92) for subject No.12 indicates the equal variance of the fitted distributions for the *natural feedback only* and baseline. Contrariwise, for subject No. 8, a low variance ratio (0.35) and high $W_{electro}$ (0.90) reflects a clear shift in the mean value of the fitted distributions to the *bias*$^+$, *baseline*, and *bias*$^-$ conditions, whereas these distributions are largely overlapping for subject No.12.

The average range between sensation and discomfort threshold reported by the subjects was 3.67 ± 0.64 mA (main experiment) and 3.47 ± 0.42 mA (pilot experiment). From the data collected in the main experiment, linear regression analysis indicated a significant correlation between the weight of electrotactile feedback and this range ($Beta = 0.871, p < .001, r^2 = .758$). Conversely, there were no significant relations between this weight and the subject's MVC, JND or the variance of plateau force during *natural feedback only* condition.

Discussion

In this study, abled-bodied volunteers performed a grasp force matching task while receiving electrotactile stimulation with a pulse train frequency proportional to the generated grasp force. Careful manipulation of the electrotactile feedback in a range that was unnoticeable by the subjects, showed that the feedback was integrated in the neural process of estimating the generated grasp force in a way that is compatible with MLE. The latter model is typically used to describe the way redundant natural feedback sources are fused by the nervous system to generate a state estimate [17–20]. Moreover, the results demonstrated that in this integration the electrotactile feedback outweighed the natural feedback for most subjects. In other words, when faced with incongruent information in the natural and electrotactile force feedback, the nervous system tended to rely mostly on the electrotactile feedback. The electrotactile stimulation evokes a tingling sensation on the forearm, which is normally not associated with grasp force. Nevertheless, with minimal training (<5 min), the central nervous system adopted this source of information in a new context and judged it more reliable than the natural source. This is a remarkable finding since the generation of a range of forces is a common element in many every-day tasks, and it could have been expected that the central nervous system would not dramatically alter the degree to which it relies on the natural grasp force feedback.

The pilot experiment indicated that the presence of electrotactile stimulation does not impair the perceived reliability of the natural force feedback. Instead, it can be speculated that the high reliance on electrotactile feedback reflects that it provided a less ambiguous source of information compared to natural force feedback. In natural feedback, the grasp force estimate is obtained from many sources including tactile receptors sensing the mechanical deformation of the tissue and Golgi tendon organs detecting forces generated by muscles [41,42]. Each of these two classes of feedback comprise hundreds or thousands individual receptors, whose individual activity may vary substantially across repetitions. For example, even a slight shift in the position of the force transducer during grasping would imply a redistribution of the force across the palm and fingers, thereby activating the individual tactile receptors differently. Furthermore, the redundancy of the forearm muscles imply that one grasp force magnitude can be generated by many combinations of muscle activation patterns. This is not merely a theoretical option, but it is well-established that the central nervous system actively exploits different solutions when repeating the same motor tasks [43,44]. Consequently, the activation of individual Golgi tendon organs would be expected to vary across repetitions, even in the simple task of grasping a gripper [45]. Finally, the information on the overall grasping force, which is the actual task relevant variable, must be estimated by the brain from such an intrinsically variable activation of a network of receptors. Conversely, the electrotactile feedback provides a simpler and more stable representation of the net grasp force, since the task relevant information is transmitted directly, encoded in the stimulation frequency, via the same group of nerves activated in a synchronous manner.

The fact that subjects reacted in a systematic way to changes in the relation between grasp force and electrotactile stimulation frequency that were not noticed indicates multiple streams of neural processing for this signal. In one stream, the stimulation is consciously sensed as a tingling on the forearm with a resolution that is limited by JND. In the literature regarding sensory substitution feedback, this is normally assumed to be the only stream by which the feedback can be processed [25]. Furthermore, exploiting this stream is assumed to imply a substantial cognitive load since the sensation of tingling must be actively re-interpreted as the modality that is encoded in the feedback (in this case grasp force) [30]. The findings of this study, however, show that the information from electrotactile feedback is also processed subconsciously and that the resolution of this stream might not be limited by JND. This is similar to the processing of natural feedback, as the CNS continuously receives and processes information, most of which is never brought to our conscious attention. Nevertheless, this information can be exploited, as shown previously in the experiments from which our protocol drew inspiration (tactile and proprioceptive sensory feedback) [17,19], and other studies (visual feedback) [46]. The electrotactile feedback is also transmitted through the natural sensory pathway (skin afferents) with an advantage that the afferents are stimulated in a way which directly encodes the task relevant information (net grasping force). As the results of the present study demonstrate, this combination seems to be particularly effective approach of closing the control loop, as in most subjects the electrotactile feedback improved the precision of the force-matching task when added to the existing natural feedback. Previous studies indicated that the cognitive load of a prosthetic control task increases with supplementary tactile feedback [47,48], suggesting that primarily cognitive processing was exploited for control. The present study indicates that sensory substitution, if implemented to facilitate subconscious integration, could lead to a non-invasive feedback that improves performance while minimizing the added cognitive load. However, the translation of this insight into clinical applications is a challenging step, which requires a non-trivial transition from hand to prosthesis control, and this will be thus explored in future work.

The outcome of this study has several important implications for the design of artificial feedback for restoration of sensation for prosthesis users. First, several studies have explored invasive stimulation of nerves that innervated receptors in the amputated hand to evoke natural phantom sensations [10–13]. Compared to non-invasive sensory substitution feedback, this method is commonly believed to have the advantage of evoking sensations that are intuitively associated with prosthesis actions at the cost of a more complex implementation involving e.g. surgery. This study, however, indicates that non-invasive sensory substitution can also evoke sensations that are intuitive in the sense that they are processed subconsciously by the central nervous system. Additionally, the electrotactile feedback had a substantial impact on the state estimate, and in most subjects, it actually dominated over the natural feedback. Importantly, this subconscious processing of the feedback was maintained when a time-lag representing the delay for mechanical activation of the prosthesis was simulated (Figure 5).

Second, although most subjects relied primarily on electrotactile feedback in the grasp force task, three subjects exhibited weights of electrotactile feedback <0.5 (Figure 6). A previous study showed a large variability in such weights for natural feedback sources across subjects [19], indicating that such variations may be expected. However, across all subjects the electrotactile weights were significantly correlated with the magnitude of the range between sensation and discomfort threshold. This suggests that subjects who relied mainly on natural force feedback were those with lowest tolerance towards electrotactile stimulation. This implies that, the stimulation intensities used during the experiment for subjects with low electrotactile weights were relatively close to the sensation threshold, which may have implied that the evoked stimulation pattern was transmitted to the central nervous system via a small number of individual nerves. Accordingly, the subjective sensation of the stimulation was weak, which might have decreased both conscious and subconscious perception of the frequency modulation, reducing thereby the perceived reliability of this feedback source. It is likely that a longer training period with exposure to stimulation prior to determination of the discomfort threshold could have familiarized these subjects to the sensation of electrotactile stimulation, thereby allowing them to tolerate higher stimulation intensities. In this way, it can be hypothesized that higher weights of electrotactile feedback could have been achieved even in those subjects, but such effects are to be determined in future studies.

Finally, the proposed experimental scheme may be an efficient way to objectively compare different feedback coding schemes. Artificial feedback may be provided as vibrotactile or electrotactile stimulation and encoded in stimulation frequency, amplitude and location. Furthermore, the encoding may be based on linear or non-linear relations between the feedback variable and the stimulation parameters. Various combinations of these settings for feedback systems have been presented previously [24], but their efficiencies are rarely compared and there are several examples of contradictory findings [25]. This may be related to different experimental protocols for assessment. We believe that estimating the weight of the feedback relative to its natural counterpart provides an objective and meaningful measure of its effect. Previous studies have estimated the weight of artificial somatosensory feedback relative to visual feedback by blurring the vision to different degrees [21,22]. This is an effective solution for demonstrating that the integration follows the principles of MLE, but the obtained values of the weights of the feedback are less easy to interpret in an intuitive way. Specifically, the approach outlined in this study predicts if the feedback is considered either more or less reliable than the natural feedback it seeks to replace, instead of providing the weight relative to visual feedback superimposed on a certain amount of noise. In this context, it is important to acknowledge that the current experimental protocol cannot be performed by amputees, since they lack a natural sense of grasping force. For this reason, the experimental paradigm needs to be adjusted in order to verify if the feedback scheme identified as being superior in able-bodied individuals is equally effective in amputee subjects.

When attempting to match the target force, all subjects followed similar strategies. A rapid increase in the force to approximate the target force followed by slow adjustments (Figure 3). It is likely that the first phase reflects feedforward control since the force at the first turn was not significantly different from the target force in any condition (Figure 5). The significant difference in plateau forces, however, suggest that feedback control was used after the first turn to fine-tune the generated force in a more careful way. Although the forces at first turn were not significantly different from the target, it exhibited the same trends as those observed for the plateau force in most conditions (Figure. 5). This may reflect that the first turn is not a perfect estimate of the switch between control strategies. Instead, it is likely that some subjects simply slowed down the increase in the feedforward-based force when beginning to assess the feedback without necessarily making a turn.

Conclusion

In conclusion, this study shows that electrotactile stimulation on the surface of the skin with a frequency related to the net grasp force is processed subconsciously according to the principles of MLE and that the integration is thus not limited by JND. Furthermore, the weight assigned to the electrotactile feedback, and thus its impact on the state estimate, exceeds that of natural grasp force feedback. These findings have important implications for the understanding and design of the methods for the restoration of somatosensory feedback based on the principle of sensory substitution.

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