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Abstract

Long lasting mechanical vibrations applied to the skin induce a reversible decrease in the perception of vibration at the stimulated skin site. This phenomenon of vibrotactile adaptation has been studied extensively. Yet, there is still no clear consensus on the mechanisms leading to vibrotactile adaptation. In particular, the respective contribution of (i) changes affecting mechanical skin impedance, (ii) peripheral processes, and (iii) central processes is largely unknown. Here, we used direct electrical stimulation of nerve fibers to bypass mechanical transduction processes and, thereby, explore the possible contribution of central vs. peripheral processes to vibrotactile adaptation. Three experiments were conducted. In the first, adaptation was induced using mechanical vibration of the fingertip (51 or 251 Hz vibration delivered for 8 minutes, at 40x the detection threshold). In the second, we attempted to induce adaptation using transcutaneous electrical stimulation of the media...

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Peripheral vs. central determinants of vibrotactile adaptation

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Klöcker A, Gueorguiev D, Thonnard JL, Mouraux A. Peripheral vs. central determinants of vibrotactile adaptation. *J Neurophysiol* 115: 685–691, 2016. First published November 18, 2015; doi:10.1152/jn.00519.2015.—Long-lasting mechanical vibrations applied to the skin induce a reversible decrease in the perception of vibration at the stimulated skin site. This phenomenon of vibrotactile adaptation has been studied extensively, yet there is still no clear consensus on the mechanisms leading to vibrotactile adaptation. In particular, the respective contributions of *1*) changes affecting mechanical skin impedance, *2*) peripheral processes, and *3*) central processes are largely unknown. Here we used direct electrical stimulation of nerve fibers to bypass mechanical transduction processes and thereby explore the possible contribution of central vs. peripheral processes to vibrotactile adaptation. Three experiments were conducted. In the first, adaptation was induced with mechanical vibration of the fingertip (51- or 251-Hz vibration delivered for 8 min, at $40\times$ detection threshold). In the second, we attempted to induce adaptation with transcutaneous electrical stimulation of the median nerve (51- or 251-Hz constant-current pulses delivered for 8 min, at $1.5\times$ detection threshold). Vibrotactile detection thresholds were measured before and after adaptation. Mechanical stimulation induced a clear increase of vibrotactile detection thresholds. In contrast, thresholds were unaffected by electrical stimulation. In the third experiment, we assessed the effect of mechanical adaptation on the detection thresholds to transcutaneous electrical nerve stimuli, measured before and after adaptation. Electrical detection thresholds were unaffected by the mechanical adaptation. Taken together, our results suggest that vibrotactile adaptation is predominantly the consequence of peripheral mechanoreceptor processes and/or changes in biomechanical properties of the skin.

adaptation; afferent pathways; mechanoreceptors; touch; vibration

IN 1930, Kampik showed that 1 h of constant mechanical vibration applied to the skin induces hypoesthesia, specifically, a reversible decrease in the perception of vibration at the stimulated site (Kampik 1930). This phenomenon has been defined as vibrotactile adaptation and is generally characterized by an increase of vibrotactile detection threshold or a reduction of vibrotactile sensibility (Francisco et al. 2011; Gescheider and Wright 1969; Hahn 1966).

The phenomenon of vibrotactile adaptation has been used extensively to study the mechanoreceptor systems responsible for the detection and transmission of vibrations applied on the skin, and the results obtained have provided support for the two-channel theory (Hahn 1968; Hollins et al. 1990), according to which the transduction of low-frequency vibrations (10–60 Hz) is preferentially achieved by rapidly adapting type I (RA) and slowly adapting type I (SAI) mechanoreceptors whereas the transduction of high-frequency vibrations (200–300 Hz) is preferentially achieved by rapidly adapting type II Pacinian (RAII/PC) mechanoreceptors. Indeed, studies have shown that vibrotactile adaptation induced with low- or high-frequency vibrations may preferentially affect the detection threshold of low- and high-frequency test stimuli, respectively, thus suggesting the existence of two distinct sensory channels with distinct frequency bandwidths.

Several non-mutually exclusive hypotheses have been put forward to explain the mechanisms of vibrotactile adaptation. Hahn suggested that changes affecting mechanical skin impedance (e.g., change in skin elasticity) could contribute to vibrotactile adaptation by impacting the transmission of vibrations through the skin and thereby reduce the mechanical stimulation of mechanoreceptors (Hahn 1966). Several authors have proposed that vibrotactile adaptation probably involves transient changes in ionic conductance at the level of the mechanoreceptors, leading to axonal hyperpolarization and, thereby, a reduced ability of the mechanoreceptors to generate action potentials following mechanical vibrations (Ribot-Ciscar et al. 1996). Gescheider and Wright advanced a two-factor hypothesis in which both changes in mechanical skin impedance and changes in the peripheral nervous system would account for vibrotactile adaptation (Gescheider and Wright 1969). Finally, neurophysiological investigations in animals have suggested that both changes at the peripheral level (e.g., increased spiking threshold of mechanoreceptors) and/or changes at the central level (e.g., reduced synaptic transmission) contribute to the phenomenon of vibrotactile adaptation (Bensmaia et al. 2005; Burke and Applegate 1989; Leung et al. 2005; O'Mara et al. 1988; Whitsel et al. 2003).

In the present study, we used direct electrical stimulation of afferent nerve fibers to bypass mechanical transduction processes and thereby explore the possible contribution of peripheral and central processes to vibrotactile adaptation. In a first series of two experiments, we compared directly the effects of mechanical vibrotactile adaptation vs. repeated and sustained transcutaneous electrical nerve stimulation on mechanical vibrotactile detection thresholds. We hypothesized that changes in threshold due to mechanically induced variations in skin impedance or mechanoreceptor transduction processes would be induced only by mechanical adaptation whereas changes in vibration threshold due to processes occurring at the level of the central nervous system would be induced by both mechan-

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ical and electrical adaptation. Furthermore, we hypothesized that if the detection of low- and high-frequency vibrations involves distinct sensory receptors or pathways, adaptation induced by low- or high-frequency vibrations could exert a differential effect on low- and high-frequency detection thresholds.

Finally, central changes induced by sustained vibrotactile adaptation could be dependent on subtle characteristics of the afferent input generated by mechanical vibrations that would not be reproduced by repeated electrical stimulation. For this reason, we conducted a third experiment in which we assessed the effect of low- and high-frequency mechanical adaptation of the fingertip on the detection of transcutaneous electrical nerve stimuli delivered to the same fingertip. In this experiment, we hypothesized that if mechanical adaptation induces changes at the central level these changes should affect not only the detection threshold of mechanical stimuli but also the detection threshold of electrical stimuli bypassing mechanoreceptor transduction.

MATERIALS AND METHODS

All experiments were approved by the local Ethical Committee (Comité d'Ethique hospital-facultaire des Cliniques universitaires Saint Luc, Brussels), and subjects gave their written informed consent.

Experiment 1: Effect of low-frequency mechanical and electrical adaptation on detection of low- and high-frequency vibrations. Thirteen subjects took part in *experiment 1* (7 men, 6 women; 29 ± 3 yr, all right handed). Each subject participated in two successive sessions: a low-frequency (51 Hz) mechanical adaptation session and a low-frequency (51 Hz) electrical adaptation session. The order of the two sessions was counterbalanced across participants. Furthermore, in half of the participants mechanical adaptation was applied to the left hand and electrical adaptation was applied to the right hand and in the other half mechanical adaptation was applied to the right hand and electrical adaptation was applied to the left hand. Each session was divided into three successive parts: *1*) estimation of baseline vibrotactile detection threshold to short-lasting low-frequency (51 Hz) and high-frequency (251 Hz) sinusoidal mechanical vibrations applied to the index fingertip, *2*) 8 min of low-frequency (51 Hz) mechanical or electrical adaptation, and *3*) estimation of adapted vibrotactile detection thresholds to the same short-lasting low- and high-frequency mechanical vibrations (Fig. 1*A*). Before the start of the experiment, subjects were seated and blindfolded and their arm was comfortably installed on a support. During the entire experiment, participants listened to white noise delivered through earphones at a comfortable level. This ensured that auditory input did not contribute to the detection of the vibrotactile stimuli.

Baseline and adapted detection thresholds to low- and high-frequency mechanical vibrations were estimated by an interlaced adaptive staircase procedure (Fig. 1*C*) performed immediately before and immediately after adaptation, respectively. The tested fingertip was placed against an 8-mm-diameter probe of a mechanical vibrator (Measurement Exciter Type 4810, Brüel & Kjaer), palm facing downward. The test stimuli lasted 500 ms and consisted of 51-Hz or 251-Hz sinusoidal vibrations of varying amplitude, applied normally against the index fingertip. The interstimulus interval varied randomly between 2 and 3 s. This, combined with the fact that the stimulus was not cued by a warning signal and the fact that a large number of stimuli were not detected, ensured that the participants could not predict when to expect the occurrence of the test stimulus. Participants were instructed to press a button with the other hand as soon as they perceived a vibration. If a detection was reported during the interstimulus interval, the stimulus was considered as detected and the
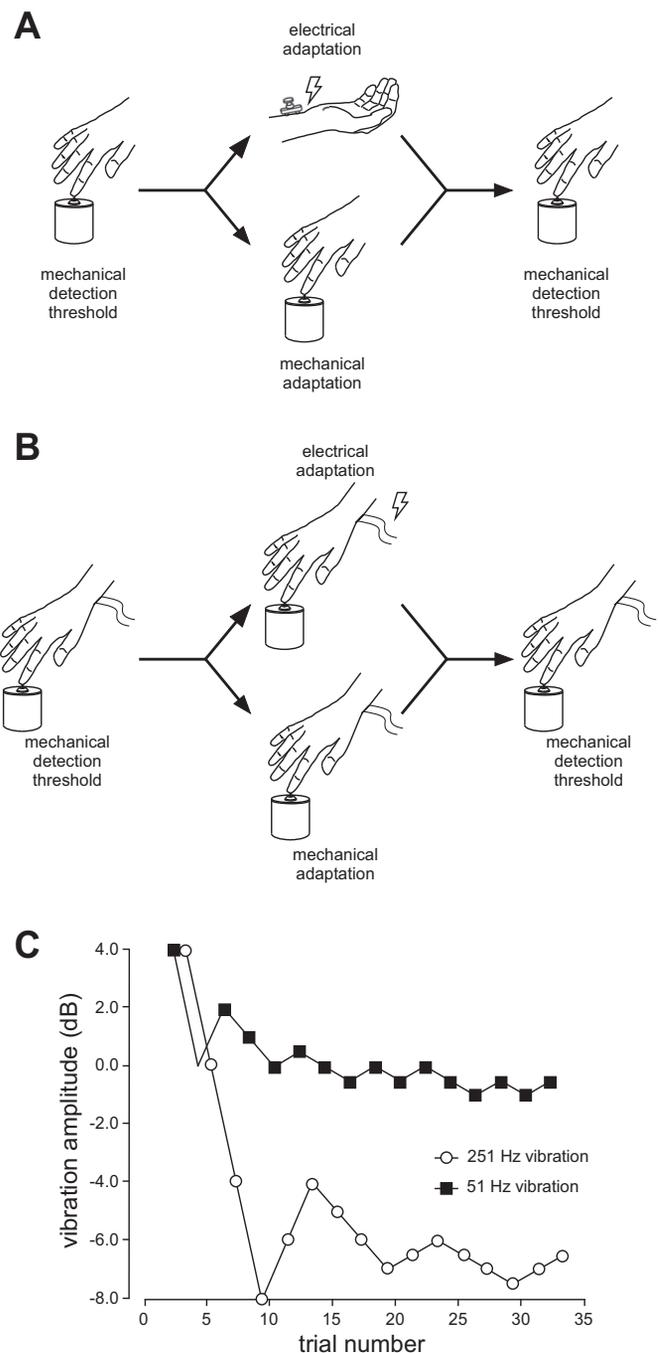
Fig. 1. *A*: in *experiments 1* and *2*, the detection threshold to short-lasting low-frequency (51 Hz) and high-frequency (251 Hz) sinusoidal mechanical vibrations applied to the index fingertip was assessed before and after application of 8 min of low-frequency (51 Hz) or high-frequency (251 Hz) mechanical or electrical adaptation. *B*: in *experiments 1* and *2*, differences in the effects of mechanical and electrical adaptation could have been due to the fact that participants maintained their fingertip on the mechanical stimulator during mechanical adaptation whereas they were requested to change the position of the hand during electrical adaptation. To address this question, a control experiment was conducted in which electrical adaptation was delivered while participants maintained their fingertip on the mechanical stimulator. *C*: in all experiments, an interlaced staircase procedure was used to estimate the detection threshold to low- and high-frequency mechanical vibrations delivered to the index fingertip.

amplitude of the following stimulus of the same category was decreased by 4 dB. If not, the stimulus was considered as undetected and the amplitude was increased by 4 dB. After the first three staircase reversals of each category, the amplitude of the staircase step was divided by two, thereby reaching a final step size of 0.5 dB. A total of 33 trials were obtained for each of the two interleaved staircases. The threshold was defined as the mean of the vibration amplitude of the two last turnover points. The entire threshold estimation procedure lasted ~2 min.

Low-frequency mechanical vibrotactile adaptation was achieved by application of a pure 51-Hz sinusoidal vibration to the index fingertip over 8 min, delivered with the mechanical stimulator also used to deliver the test vibrotactile stimuli. The fingertip thus remained against the probe of the mechanical stimulator during the entire experiment. The amplitude of the vibration was set to 40 times the amplitude of the baseline low-frequency vibrotactile detection threshold. The chosen duration and vibration amplitude were based on previous studies showing that vibrotactile adaptation is successfully induced with such parameters (Hahn 1968; Hollins et al. 1990).

Low-frequency electrical adaptation consisted of transcutaneous electrical stimulation (TES) of the median nerve at the level of the wrist for 8 min with a constant-current electrical stimulator (Digitimer Constant Current Stimulator, DS7) and bipolar felt pad electrodes positioned at the level of the wrist so as to stimulate the median nerve (8-mm diameter). During the stimulation, the hand rested on the table, palm facing upward. This position was chosen to ensure optimal and stable electrical stimulation of the median nerve. The intensity of stimulation was set to 1.5 times the detection threshold to a single 500-μs constant-current square-wave pulse. The position of the electrodes was adjusted until the stimulus elicited a clear sensation that included the index fingertip, i.e., until the stimulus activated nerve fascicles innervating the index fingertip. The stimulation consisted of trains of 500-μs pulses separated by a 1.5-ms interpulse interval. These trains of stimuli were modulated by a repeating boxcar function, such that within each train periods of stimulation alternated with periods without stimulation of equal duration, with a periodicity of 51 Hz. The intensity of the adapting stimulus was chosen in order to induce a clear sensory response without eliciting any motor response. When participants received electrical adaptation, they were requested to delineate, at the end of the experiment, the area within which the electrical stimulation had been felt by drawing this area on a picture representation of the hand. In all participants, this area included the index fingertip.

Experiment 2: Effect of high-frequency mechanical and electrical adaptation on detection of low- and high-frequency vibrations. Twelve subjects participated in *experiment 2*, nine of which had also participated in *experiment 1* (4 men, 8 women; 30 ± 3 yr, all right handed). This experiment was identical to *experiment 1* with the exception that the frequency of the mechanical and electrical stimulation used to induce adaptation was 251 Hz instead of 51 Hz.

Experiment 3: Effects of low- and high-frequency mechanical adaptation on detection of electrical stimuli. Ten subjects participated in *experiment 3* (3 men, 7 women; 32 ± 4 yr, all right handed). As for *experiments 1* and *2*, *experiment 3* consisted of two successive sessions: a low-frequency (51 Hz) mechanical adaptation session and a high-frequency (251 Hz) mechanical adaptation session. Again, the order of the two sessions was counterbalanced across participants. Each session was also divided into three parts: *1*) estimation of baseline electrical detection threshold, *2*) 8 min of low- or high-frequency mechanical adaptation, and *3*) estimation of adapted electrical detection thresholds (Fig. 2*A*).

Baseline and adapted electrical detection thresholds were estimated with a staircase procedure, as illustrated in Fig. 2*B*. Constant-current electrical stimuli were delivered as a single 500-μs square-wave pulse with two adhesive electrodes pasted on the index fingertip (6 × 11-mm Ambu Blue Sensor NF ECG Electrodes, NF-50-K/12/EU; 5-mm interelectrode distance). The intensity of the first stimulus was
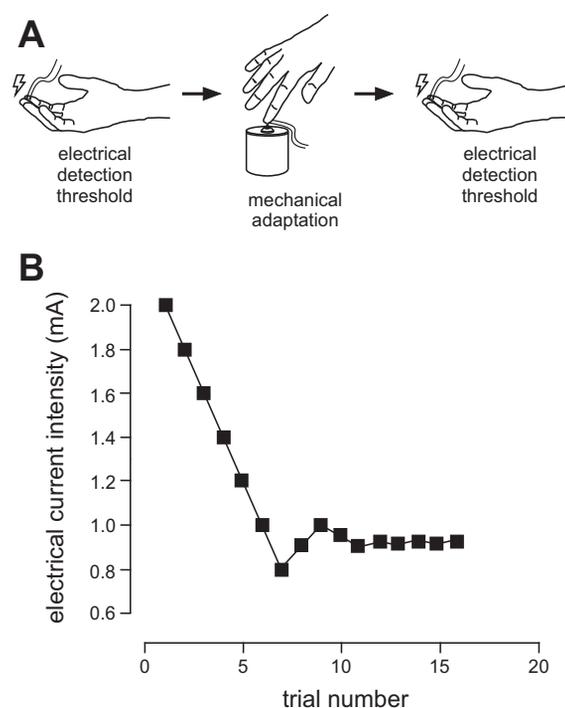

Fig. 2. *A*: in *experiment 3*, the detection threshold to single short-lasting electrical square-wave pulses delivered to the index fingertip was assessed before and after 8 min of mechanical adaptation. *B*: a single staircase procedure was used to estimate the detection thresholds.

set to 2.00 mA. This stimulus was detected by all participants. The interstimulus interval varied randomly between 1 and 3 s. Participants were instructed to report when they perceived the stimulus. As in *experiments 1* and *2*, detecting or not detecting the stimulus determined the intensity of the following stimulus. The initial step size was set to 0.20 mA. After the first staircase reversals, the step was reduced to 0.10 mA, 0.05 mA, and 0.02 mA. The staircase was interrupted after the occurrence of three staircase reversals at this final step size. The threshold was defined as the mean intensity of the two last turnover points. The entire threshold estimation procedure lasted ~2 min.

As in *experiments 1* and *2*, mechanical vibrotactile adaptation was achieved by applying a pure 51-Hz or 251-Hz sinusoidal vibration to the index fingertip during 8 min at 40 times the amplitude of the vibrotactile detection threshold (defined prior to the baseline electrical detection threshold).

Control experiments. In *experiments 1* and *2*, mechanical adaptation was delivered while participants maintained their index fingertip against the mechanical stimulator used to assess mechanical vibrotactile detection thresholds, whereas electrical adaptation was delivered with the hand resting on a table, palm facing upward, in order to reliably position the felt pad stimulation electrodes. To examine whether differences between the effects of mechanical adaptation and the effects of electrical adaptation could have been due to moving the hand after electrical adaptation but not after mechanical adaptation, we performed a first control experiment in which electrical adaptation was delivered without moving the hand, i.e., with the index maintained against the probe of the mechanical stimulator (Fig. 1*B*). To make this possible, electrical stimulation was delivered with 30 × 22-mm self-adhesive electrodes (30 × 22-mm Ambu Blue Sensor NF ECG Electrodes, NF-50-K/12/EU; 15-mm interelectrode distance) pasted over the median nerve, at the level of the wrist. The electrodes were positioned before the beginning of the experiment. The effects of low-frequency and high-frequency electrical adaptation on low- and high-frequency mechanical detection thresholds were assessed in 10
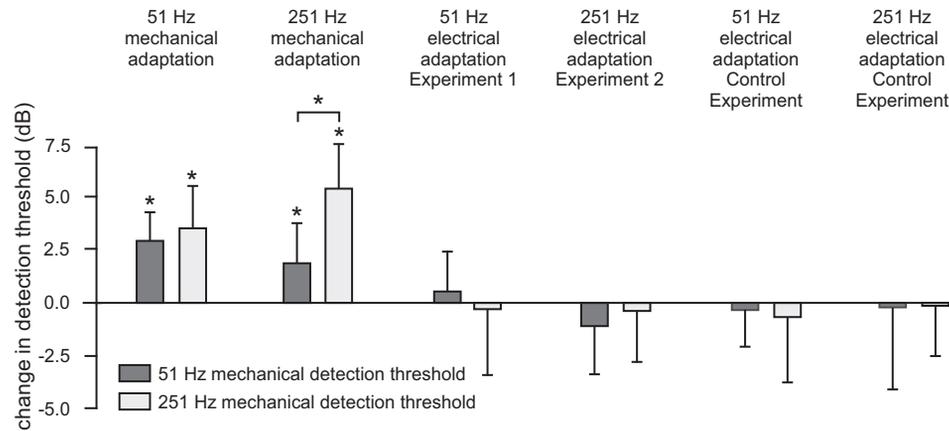
Fig. 3. Group-level average ($\pm$SD) change in mechanical detection thresholds induced by 8 min of mechanical or electrical adaptation (*experiment 1*, *experiment 2*, and control experiment). Low-frequency (51 Hz) mechanical adaptation induced a significant increase of vibrotactile detection threshold to both low (51 Hz)- and high (251 Hz)-frequency mechanical vibrations. High-frequency (251 Hz) mechanical adaptation also increased low- and high-frequency detection thresholds, but this effect was significantly greater for high-frequency (251 Hz) vibrations compared with low-frequency (51 Hz) vibrations. Contrasting with the effects of mechanical adaptation, electrical adaptation at 51 Hz and 251 Hz did not exert any effect on mechanical detection thresholds. Significant changes in detection thresholds relative to baseline are marked by an asterisk. Significant differences in the change in detection threshold across conditions are marked by a horizontal line ($P < 0.05$).

(7 men, 3 women; 25 $\pm$ 4 yr, 9 right handed) and 8 participants (4 men, 4 women; 24 $\pm$ 3 yr, 7 right handed), respectively.

A second control experiment was conducted to assess whether the intensity of the percept generated by the mechanical adapting stimulus differed from the intensity of the percept generated by the electrical adapting stimulus. Seven participants took part in this experiment (3 men, 4 women; 30 $\pm$ 6 yr, 6 right handed). After the electrical detection thresholds were estimated with the same adaptive procedure as in *experiments 1* and *2*, 10 trains of low-frequency and high-frequency electrical stimulation lasting 10 s were applied to the median nerve in separate sessions separated by at least 4 h. The intensity was set at 1.5 times the detection threshold, i.e., the intensity used to deliver the electrical adaptation stimulus in *experiments 1* and *2*. In two other sessions, 10 low-frequency and high-frequency mechanical vibrations lasting 10 s were applied to the index fingertip, at an intensity corresponding to 40 times the low-frequency and high-frequency vibrotactile detection threshold, i.e., the intensity used to deliver the mechanical adaptation stimulus in *experiments 1* and *2*. In each session, participants were requested to rate the intensity of each stimulus using a 0–10 numerical rating scale.

Statistical analyses. In *experiments 1* and *2*, the effects of mechanical and electrical adaptation on mechanical vibration detection thresholds were assessed by a repeated-measures ANOVA with the factors "time" (before vs. after adaptation), "adaptation modality" (mechanical vs. electrical adaptation), and "detection frequency" (detection of low- vs. high-frequency vibrations). To assess the specific effects of mechanical and electrical adaptation, a repeated-measures ANOVA with the factors "time" and "detection frequency" was then used for each modality of adaptation.

In *experiment 3*, the effects of low- and high-frequency mechanical adaptation on the detection of electrical stimuli were assessed by a repeated-measures ANOVA with the factors "time" (before vs. after adaptation) and "adaptation frequency" (low- vs. high-frequency mechanical adaptation).

All statistical analyses were conducted with IBM SPSS (version 21). Significance level was set at $P < 0.05$.

RESULTS

Intensity of sensation elicited by mechanical and electrical adaptation. The average intensity of the sensation elicited by the low-frequency mechanical adaptation stimulus was not significantly different from the intensity of the sensation elic-

ited by the low-frequency electrical adaptation stimulus ($z = -1.18$, $P = 0.24$; Wilcoxon signed-rank test). The sensation elicited by high-frequency mechanical adaptation was perceived as significantly less intense than the sensation elicited by high-frequency electrical adaptation ($z = -2.20$, $P = 0.028$).

Effect of low-frequency mechanical and electrical adaptation on detection of low- and high-frequency vibrations. After mechanical adaptation at 51 Hz, the mechanical detection threshold increased similarly for 51-Hz vibrations and 251-Hz vibrations, indicating that adaptation had a similar effect on the ability to perceive low- and high-frequency vibrations (Fig. 3). In contrast, both mechanical detection thresholds appeared to be unaffected by electrical adaptation (Fig. 3). This was confirmed by the three-way repeated-measures ANOVA (Table 1), which showed a significant interaction between the factors "time" (before vs. after adaptation) and "adaptation modality" (mechanical vs. electrical adaptation) ($F = 22.10$, $P = 0.001$).

Table 1. *Three-factor repeated-measures ANOVA results of experiments 1 and 2*

Independent Variables	Experiment 1	Experiment 2
Adaptation modality	$F_{(1,11)} = 24.85$ $P < 0.001^*$	$F_{(1,11)} = 54.29$ $P < 0.001^*$
Time	$F_{(1,11)} = 10.86$ $P = 0.007^*$	$F_{(1,11)} = 41.05$ $P < 0.001^*$
Detection frequency	$F_{(1,11)} = 5.30$ $P = 0.042^*$	$F_{(1,11)} = 9.78$ $P = 0.010^*$
Adaptation modality $\times$ time	$F_{(1,11)} = 22.10$ $P = 0.001^*$	$F_{(1,11)} = 35.89$ $P < 0.001^*$
Adaptation modality $\times$ detection frequency	$F_{(1,11)} = 2.43$ $P = 0.147$	$F_{(1,11)} = 9.72$ $P = 0.010^*$
Time $\times$ detection frequency	$F_{(1,11)} = 0.02$ $P = 0.881$	$F_{(1,11)} = 13.83$ $P = 0.003$
Adaptation modality $\times$ time $\times$ detection frequency	$F_{(1,11)} = 1.77$ $P = 0.211$	$F_{(1,11)} = 3.13$ $P = 0.105$

$^*P < 0.05$.

Table 2.   *Two-factor repeated-measures ANOVA results of experiments 1 and 2*

Independent Variables	Experiment 1		Experiment 2	
	Electrical adaptation	Mechanical adaptation	Electrical adaptation	Mechanical adaptation
Time	$F_{(1,11)} = 0.00$ $P = 0.987$	$F_{(1,12)} = 52.26$ $P < 0.001*$	$F_{(1,11)} = 1.57$ $P = 0.236$	$F_{(1,11)} = 95.19$ $P < 0.001*$
Detection frequency	$F_{(1,11)} = 7.95$ $P = 0.017*$	$F_{(1,12)} = 2.95$ $P = 0.111$	$F_{(1,11)} = 17.5$ $P = 0.002*$	$F_{(1,11)} = 2.08$ $P = 0.177$
Time × detection frequency	$F_{(1,11)} = 0.83$ $P = 0.381$	$F_{(1,12)} = 0.18$ $P = 0.2047$	$F_{(1,11)} = 0.59$ $P = 0.460$	$F_{(1,11)} = 14.18$ $P = 0.003*$

$*P < 0.05$.

For mechanical adaptation, the follow-up two-way ANOVA showed a main effect of "time" (before vs. after adaptation: $F = 52.26$, $P < 0.001$) and no interaction between the factors "time" and "detection frequency" ($F = 0.18$, $P = 0.205$) (Table 2).

In contrast, for electrical adaptation delivered with felt pad electrodes (*experiment 1*) as well as self-adhesive electrodes (control experiment), the two-way ANOVA showed no effect of "time" (*experiment 1*: $F = 0.00$, $P = 0.987$; control experiment: $F = 1.09$, $P = 0.324$) and no interaction between "time" and "detection frequency" (*experiment 1*: $F = 0.83$, $P = 0.381$; control experiment: $F = 0.05$, $P = 0.836$).

Taken together, the results of *experiment 1* show that low-frequency mechanical adaptation induces a similar increase in the detection threshold for low- and high-frequency mechanical vibrations whereas low-frequency electrical adaptation has no significant effect on the detection of both low- and high-frequency mechanical vibrations. Furthermore, the results of the control experiment show that the lack of effect of low-frequency electrical adaptation observed in *experiment 1* was not due to an unaccounted effect of moving the hand to deliver the electrical stimulus.

Effect of high-frequency mechanical and electrical adaptation on detection of low- and high-frequency vibrations. After mechanical adaptation at 251 Hz, the mechanical detection threshold was increased for both 51-Hz vibrations and 251-Hz vibrations. However, the increase in threshold was greater for 251-Hz vibrations, indicating that high-frequency mechanical adaptation has a stronger effect on the ability to perceive high-frequency vibrations compared with low-frequency vibrations (Fig. 3). In contrast, and similarly to *experiment 1*, both low- and high-frequency mechanical detection thresholds appeared to be unaffected by electrical adaptation (Fig. 3). This was confirmed by the three-way repeated-measures ANOVA (Table 1), which showed a significant interaction between the factors "time" (before vs. after adaptation) and "adaptation modality" (mechanical vs. electrical adaptation) ($F = 35.89$, $P < 0.001$) but also a significant interaction between the factors "adaptation modality" and "detection frequency" ($F = 9.72$, $P = 0.010$) and between the factors "time" and "detection frequency" ($F = 13.83$, $P = 0.003$). There was, however, no significant interaction between the three factors ($F = 3.13$, $P = 0.105$).

For mechanical adaptation, the two-way ANOVA showed a significant main effect of "time" ($F = 95.19$, $P < 0.001$) and a significant interaction between the factors "time" and "detection frequency" ($F = 14.18$, $P = 0.003$) (Table 2). Post hoc pairwise comparisons showed that both the 51 Hz and the 251 Hz detection thresholds were increased but that this increase

was significantly greater for the detection of 251-Hz vibrations compared with 51-Hz vibrations (Fig. 3). In contrast, for electrical adaptation delivered with felt pad electrodes (*experiment 2*) as well as self-adhesive electrodes (control experiment), the two-way ANOVA showed no effect of "time" (*experiment 2*: $F = 1.57$, $P = 0.236$; control experiment: $F = 0.03$, $P = 0.880$) and no interaction between the factors "time" and "detection frequency" (*experiment 2*: $F = 0.59$, $P = 0.460$; control experiment: $F = 0.14$, $P = 0.716$).

Taken together, the results of *experiment 2* show that high-frequency mechanical adaptation induces a significant increase in the detection threshold for both low- and high-frequency vibrations but that this increase in threshold is greater for high-frequency vibrations. In contrast, high-frequency electrical adaptation has no significant effect on the detection of both low- and high-frequency mechanical vibrations. Furthermore, the results of the control experiment show that the lack of effect of high-frequency electrical adaptation observed in *experiment 2* was not due to an unaccounted effect of moving the hand to deliver the electrical stimulus.

Effects of low- and high-frequency mechanical adaptation on detection of electrical stimuli. As shown in Fig. 4, mechanical adaptation at 51 Hz and 251 Hz had no effect on the detection threshold to transcutaneous electrical stimuli delivered to the index fingertip. The two-way repeated-measures ANOVA showed no main effect of "time" ($F = 2.30$, $P =$
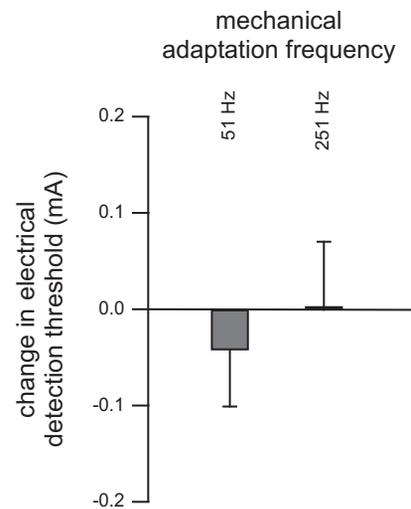

Fig. 4. Group-level average change in electrical detection threshold induced by 8 min of mechanical adaptation. Low-frequency (51 Hz) and high-frequency (251 Hz) mechanical adaptation had no significant impact on the detection threshold of single short-lasting square-wave electrical pulses delivered to the index fingertip.

0.164), no main effect of "adaptation frequency" ($F = 0.06$, $P = 0.831$), and no interaction between the two factors ($F = 1.82$, $P = 0.210$).

DISCUSSION

The results of our study can be summarized as follows. First, we confirm that mechanical vibration of the index fingertip induces vibrotactile adaptation, as evidenced by the increased detection thresholds to both low-frequency (51 Hz) and high-frequency (251 Hz) vibrations. Second, we show that low-frequency mechanical adaptation induces a similar increase in the detection thresholds to low- and high-frequency vibrations whereas high-frequency mechanical adaptation has a stronger effect on the detection of high-frequency vibrations. Third, we show that direct, repeated, and sustained electrical stimulation of the nerve trunk conveying sensory information from the index fingertip does not induce adaptation and, conversely, that mechanical adaptation of the index fingertip does not affect the ability to detect the sensation elicited by direct electrical stimulation of that fingertip.

Differential effect of low- and high-frequency mechanical adaptation on ability to detect low- and high-frequency vibrations. Low-frequency (51 Hz) mechanical adaptation was equally effective in raising the threshold for low-frequency (51 Hz) and high-frequency (251 Hz) vibrations. In contrast, high-frequency (251 Hz) mechanical adaptation induced a much stronger increase in the detection threshold for high-frequency vibrations than for low-frequency vibrations. The observed differential effect of low- and high-frequency mechanical adaptation provides further support to the notion that vibrotactile adaptation at different frequencies may involve changes in distinct sensory channels, in particular PC and non-PC mechanoreceptors.

Vibrations at 251 Hz may be expected to elicit strong responses within PC receptors, as this corresponds to their peak of optimal sensitivity (Fleming and Luo 2013). In contrast, non-PC receptors may be expected to elicit little or no response at 251 Hz, as this is clearly above the range of frequencies to which they respond predominantly. Therefore, 251 Hz mechanical adaptation may be hypothesized to preferentially affect the sensitivity of PC receptors and thereby preferentially affect the ability to detect high-frequency vibrations. In contrast, considering the large bandwidth of PC receptors, vibrations at 51 Hz may be hypothesized to elicit strong responses in both PC and non-PC receptors. Therefore, 51 Hz adaptation would affect the sensitivity of both PC and non-PC receptors and thereby affect equally the ability to detect low- and high-frequency vibrations. Hollins et al. reported similar findings with 10-Hz and 50-Hz adapting and test vibrotactile stimuli (Hollins et al. 1990). The 50-Hz adapting frequency was equally effective in raising the thresholds to 10-Hz and 50-Hz vibrations. In contrast, the 10-Hz adapting stimulus was more effective in raising the threshold to 10-Hz stimuli compared with the 50-Hz vibration thresholds. Hollins et al. also explained their results within the context of PC and non-PC mechanoreceptors. Specifically, they interpreted that 50-Hz adaptation affected similarly both classes of receptors whereas 10-Hz adaptation had a stronger effect on non-PC receptors compared with PC receptors (Hollins et al. 1990).

Our results showing a similar effect of low- and high-frequency adaptation contrast with findings obtained with sin-gle-unit recordings from the ulnar and median nerves of macaque monkeys (Bensmaia et al. 2005) highlighting that the amount of adaptation increases as the adapting frequency is increased, independently of the type of mechanoreceptor (SAI, RA, PC).

Finally, Leung et al. assessed the time course of adaptation and recovery from adaptation in SAI, RA, and PC mechanoreceptors (Leung et al. 2005). They found that the time required to induce adaptation and the time required to recover from adaptation were reduced compared with the results of studies using psychophysical methods to assess changes in detection threshold (Gescheider and Wright 1969; Hollins et al. 1990, 1991). This led the authors to conclude that changes at the level of the central nervous system could contribute to the change in detection threshold. However, as they could also be explained by the use of different methods to induce adaptation (e.g., differences in the diameter of the vibrating probe, differences in vibration amplitude), these differences in recovery times should be interpreted with caution.

Lack of adaptation induced by direct electrical stimulation of sensory afferents. Contrasting with the marked effect of both low-frequency and high-frequency mechanical adaptation, sustained electrical stimulation of the median nerve over 8 min did not induce any measurable change in the ability to detect vibrotactile stimuli delivered to the fingertip. These findings are in line with the results of Burke and Applegate (1989) showing that 10 min of electrical stimulation of a digital nerve at 200 Hz does not alter the responses to natural stimuli applied to the pulp of the stimulated phalanx.

Importantly, the intensity of the sensation elicited by low-frequency sustained electrical stimulation of the median nerve was similar to the intensity of the sensation elicited by low-frequency mechanical adaptation, and the intensity of the sensation elicited by high-frequency electrical adaptation was, on average, greater than the intensity of the sensation elicited by high-frequency mechanical adaptation. This indicates that the sustained afferent input generated by mechanical adaptation was not more intense than the sustained afferent input generated by electrical adaptation.

Past studies have compared the compound sensory nerve action potential (CSNAP) and somatosensory-evoked potentials (SEPs) elicited by electrical and mechanical fingertip stimulation (Hashimoto et al. 1990; Krarup and Trojaborg 1994). Even though these studies suggest that the CSNAP recorded at the level of the wrist in response to electrical stimulation of the fingertip is triphasic while the CSNAP elicited by mechanical stimulation is polyphasic, the morphology and scalp topography of the SEPs elicited by electrical and mechanical stimulation were similar (Hashimoto et al. 1990; Krarup and Trojaborg 1994). It can therefore be hypothesized that the sustained afferent input generated by an electrical and a mechanical stimulation generate grossly similar responses at the level of the central nervous system.

For these reasons, the differential effect of mechanical vs. electrical adaptation observed in our study suggests that vibrotactile adaptation predominantly results from changes occurring at the peripheral level, such as changes in the biomechanical properties of the skin or changes in mechanoreceptor transduction processes (Gescheider and Wright 1969; Hahn 1966; Ribot-Ciscar et al. 1996).

Lack of effect of mechanical adaptation on ability to detect electrical stimuli delivered to adapted fingertip. Sustained electrical stimulation of the median nerve and sustained vibrotactile stimulation of the index fingertip could exert different effects at the level of the central nervous system. Indeed, adaptation mechanisms occurring at the level of the central nervous system could be dependent on a number of aspects differentiating the input generated by the mechanical stimulation of mechanoreceptors from the input generated by the direct and unspecific electrical activation of afferent nerve fibers. For example, unlike the input generated by vibrotactile stimulation of the fingertip, the input generated by the electrical stimulus was not restricted to a specific category of sensory afferents (RA and PC afferents), nor was it restricted to a specific location on the index fingertip.

Therefore, a possible explanation for the finding that sustained electrical stimulation does not induce vibrotactile adaptation (*experiments 1* and *2*) could be that, unlike sustained vibrotactile stimulation, sustained electrical stimulation does not induce adaptation at the level of the central nervous system.

To address this alternative interpretation, we conducted a third experiment in which we show that mechanical adaptation affecting the ability to detect vibrotactile stimuli does not affect the ability to detect electrical stimuli applied directly to the index fingertip. This finding provides further support to the notion that changes at the level of the central nervous system do not contribute to the phenomenon of vibrotactile adaptation.

At the peripheral level, mechanical vibrotactile stimuli can be expected to activate preferentially specific classes of mechanoreceptors (i.e., RA and/or PC). In contrast, electrical stimuli probably activate all large-diameter afferents indistinguishably since it has been shown in microneurography that the different classes of mechanoreceptors have similar conduction velocities (Kakuda 1992; Mackel 1988). Consequently, there is no reason to assume that small differences in diameter within any subclass of mechanoreceptor afferents would separate them with regard to transcutaneous electrical thresholds. However, although at the peripheral level the afferents activated by mechanical and electrical stimulation may be expected to differ, at the cortical level it is likely that mechanical vibrotactile stimuli and electrical stimuli activate largely overlapping neuronal populations (Saal and Bensmaia 2014). Consequently, if mechanical adaptation exerts an effect on the responsiveness of cortical neurons processing mechanical vibrotactile stimuli, this change in cortical responsiveness would be expected to affect both the ability to detect mechanical vibrotactile stimuli delivered to the adapted fingertip and the ability to detect sensations generated by the direct electrical activation of mechanoreceptor afferents innervating the adapted fingertip.

Conclusions. Taken together, our psychophysical results, assessing directly the effect of bypassing peripheral transduction processes with direct electrical stimulation of sensory afferents, indicate that vibrotactile adaptation relies predominantly on changes occurring at the peripheral level and question the possible contribution of changes occurring at the level of the central nervous system.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: A.K., D.G., and A.M. conception and design of research; A.K. and D.G. performed experiments; A.K., D.G., and A.M. analyzed data; A.K., D.G., and A.M. interpreted results of experiments; A.K., D.G., and A.M. prepared figures; A.K., D.G., J.L.T., and A.M. drafted manuscript; A.K., D.G., J.L.T., and A.M. edited and revised manuscript; A.K., D.G., J.L.T., and A.M. approved final version of manuscript.

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