Supplementary Methods

Participants and stimuli. None of the subjects had a history of neurological disease and all were free of calluses at the fingerpads. Thirteen subjects participated in 2, four in 4, two in 1, and one in 3 sessions, yielding a total of 141 threshold measurements (102 at the finger, 39 at the lip). Fifteen subjects (ages 18-40 yr, 7 females) participated in the SSEP experiments, 10 of whom also participated in the grating orientation task (GOT). In each session, threshold was measured three times: before, during, and after cutaneous anesthesia of the right hand or right foot. Testing sessions lasted about 1 and 1/2 hr and were separated by at least 24 hr.

Stimuli consisted of a set of eight hemispherical plastic domes with gratings cut into their surfaces, resulting in parallel bars and grooves of equal widths at each dome (Tactile Acuity Gratings, MedCore, www.med-core.com; Supplementary Fig. 1a, b). Since cutaneous spatial resolution is relatively insensitive to force\(^1\) and the spatial profile for the neural response to complex surfaces are relatively insensitive to the depth of indentation\(^2\), stimuli were applied with moderate force (resulting in approximately 2 mm of skin displacement). Testing sites were either the distal pad of the left index finger (n = 19) or in different sessions in the same subjects the glabrous skin of the lower lip left of the midline (n = 13). The order in which sites were tested was counterbalanced between subjects to minimize sequence effects. Gratings were applied by two different investigators, one of whom, examining 7 subjects at the finger and 6 at the lip, was blind to the research hypothesis.
Procedure. Subjects were comfortably seated and blindfolded (Supplementary Fig. 1c). For finger testing sessions a cast immobilized the left arm and hand, exposing only the palmar surface of the left index finger fixated by adhesive tape. Hence, movement of the skin at the testing sites was minimized by hand fixation for tests at the index finger. Prior to each session, each subject was taught the task by visual demonstrating the stimuli. At the beginning of each block for each spatial period, gratings were applied ten times to familiarize subjects with the stimulus. On a given trial, the gratings were applied perpendicularly to the surface for 1.5 sec with the ridges and grooves randomly oriented in one of two orthogonal directions (i.e., perpendicular or parallel to the axis of the finger or lip) and subjects had to identify the alignment. Subjects were required to verbally report or signal their responses when testing at the lip. After each trial, feedback on responses was provided. Trials with movement of the test site or in which subjects failed to respond in time were deemed invalid and repeated after stimulus re-selection. Starting with the grating with the broadest spatial period and thereafter continuing in a descending groove width order, subjects were required to identify and report the stimulus orientation (two alternative forced-choice paradigm) in blocks of 30 trials per grating until performance approached chance (50% correct responses). Selection of the stimulus orientation in each block was chosen from a random table.

A subgroup of subjects received training 24 hr prior to threshold measurements. The site of training (finger or lip) always corresponded to the testing site on the following day. Training consisted of two successive GOT
Determinations at the respective test site (i.e., finger or lip) with an interval of 60 minutes.

**Deafferentation.** Deafferentation was achieved by inducing an ischemic nerve block (INB) at the right lower forearm or right leg. The experimenter elevated the subjects arm or leg for 3 min to drain the venous blood. A conventional sphygmomanometer, 7.5 cm wide, was placed just distal to the cubital fossa (n = 19) or the knee (n = 6) inflated to 220 mm Hg, and the arm or leg was returned to the horizontal position. The tourniquet pressure was kept constant during the experiment until the end of GOT-testing during INB. Low-threshold mechanoreceptive function (perception threshold to light touch) at the distal pad of the second finger or toe was assessed using von Frey filaments (Aesthesiometer, Stoelting Co, Wood Dale, IL, USA). Filaments were applied in a descending order of magnitude to assess the level at which the sensation disappeared. Anesthesia was defined as the time when light-touch perception was abolished (in 5 of 5 successive trials) when tested with a 4.56-mm diameter filament, which caused a visible skin indentation (target force 4 N; > 50 times upper threshold limit). GOT-testing during INB commenced immediately after onset of anesthesia. The mean duration (range) of tourniquet inflation was similar between sessions being 33 (20 to 39) and 34 (27 to 43) min with INB at the right arm for finger and lip sessions, respectively, and 36 (25 to 44) min at the leg. In all trials, subjects rated the intensity and affective reaction to the tourniquet-induced discomfort on a visual analogue scale (VAS) ranging from 0 to 250. This measurement has been shown to have good internal consistency, reliability, as well as objectivity, and can discriminate between the sensorial and affective components of pain\(^3\). According to
this measure, there was no significant difference (intensity: $F_{2, 14} = 0.2$, $P = 0.9$; affective: $F_{2, 13} = 0.5$, $P = 0.6$) in the level of discomfort between finger (mean ± s.e.m. intensity 163.4 ± 9.4, affective descriptor 104.0 ± 15.4), lip (intensity 165.6 ± 10.4, affective descriptor 111.4 ± 17.2) and leg (intensity 176.6 ± 30.8, affective descriptor 139.2 ± 43.2) sessions.

As an additional control to mimic increased attention by focusing on the left hand, in a separate set of experiments, the tourniquet was placed around the right forearm of naïve subjects ($n = 8$) and inflated only to 20 mm Hg. This caused only minimal alteration in sensory perception (reduction of light touch threshold in 4 subjects by one or two von Frey filaments sizes) in half of the subjects.

**Somatosensory evoked potentials.** Somatosensory evoked potentials (SSEPs) are EEG signals generated in response to peripheral nerve stimulation. They convey information on the excitability of neuronal structures in different relays of the somatosensory pathway. We recorded SSEP from two silver/silver chloride surface electrodes overlying the median nerve at the wrist (sensory nerve action potentials, [SNAP], bandpass 100 – 2000 Hz, sampling rate 4 kHz)$^4$, and from silver/silver chloride electrodes secured to the scalp with collodion (average of 200 - 400 trials, timebase 120 ms, bandpass 0.5 - 2000 Hz, sampling rate 10 kHz, impedance < 1 KΩ) placed 2 cm posterior to C4 (overlying postcentral gyrus, approximately area 3, C4’) and over P4 of the standard 10-20 system referred to an midfrontal electrode 2 cm posterior to Fpz and to linked earlobe electrodes. The SNAP provides information on the magnitude of the afferent volley carried through the median nerve. The $P_{15}$ component is a potential generated by the ascending afferent volley in the cerebral lemniscal pathway$^5$ and the $N_{20}$ and $N_{20-25}$.
components (termed N1 and P1 in this report) are generated in S1. SSEPs were recorded following electrical stimuli delivered through ring electrodes placed around left digits II, III, and IV (constant voltage rectangular pulse of 0.2 ms duration, stimulation intensity 2 - 3 times sensory threshold, stimulation frequency randomized between 1 - 3 Hz, two runs before, during and after the end of anesthesia). Trials with EMG artifacts were rejected offline. In each experimental session (right hand INB (n = 10), right foot INB (n = 7)), we recorded six runs consisting of 600 trials each: two runs at baseline, two during ischemia, and two following tourniquet deflation.

For the analysis, the peak of the first major cortical negativity (N20) and the peak-to-peak amplitude of the parietal N20/P25 and P29/N30 complexes were measured. In addition, in 5 of 10 subjects we could consistently identify and measure positive deflections in channels referred to the earlobes with a mean peak latency of 16.1 ms (range 15.0 – 18.1) which we will term P15 and which reflects a subcortical neural response generated by the ascending afferent volley in cerebral lemniscal pathways (Fig. 2a of main manuscript).

Data analysis and statistics. GOT threshold was defined as the level at which responses were 75% correct and was determined by interpolating between groove widths spanning 75% correct responses (unless performance was precisely at a 75% correct response rate) according to Van Boven et al. Performance at this level is midway between chance and perfect performance and is a standard psychophysical threshold criterion. Since thresholds were based on normally distributed (Shapiro-Wilk test of Normality), binomial data with homogeneous
variances (Bartlett's Chi-Square) ANOVA for repeated-measures was used to assess differences between measurements before, during, and after the intervention. To compare SSEP amplitudes between the measurements at different timings, three-way repeated–measures ANOVA with time, INB site and SSEP components as factors was used. Conditioned by a significant p-value, individual pair-wise comparisons were performed using the Tukey-Kramer procedure. Results were considered significant at a level of $P < 0.05$. Variance is expressed as SEM.