

# 2 **Touch inhibits cold: non-contact cooling reveals a novel thermotactile gating mechanism**

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14

## **Abstract**

16 Skin stimuli reach the brain via multiple neural channels specific for different stimulus  
18 types. These channels interact in the spinal cord, typically through inhibition. Inter-  
channel interactions can be investigated by selectively stimulating one channel and  
20 comparing the sensations that result when another sensory channel is or is not  
concurrently stimulated. Applying this logic to thermal-mechanical interactions proves  
22 difficult, because most existing thermal stimulators involve skin contact. We used a novel  
non-tactile stimulator for focal cooling (9mm<sup>2</sup>) by using thermal imaging of skin  
24 temperature as a feedback signal to regulate exposure to a dry ice source. We could then  
investigate how touch modulates cold sensation by delivering cooling to the human hand  
dorsum in either the presence or absence of light touch. Across three signal detection  
26 experiments, we found that sensitivity to cooling was significantly reduced by touch. This  
reduction was specific to touch, since it did not occur when presenting auditory signals  
28 instead of the tactile input, making explanations based on distraction or attention  
unlikely. Our findings suggest that touch inhibits cold perception, recalling interactions of  
30 touch and pain previously described by Pain Gate Theory. We show, for the first time, a  
thermotactile gating mechanism between mechanical and cooling signals.

## 32 **1. Introduction**

34 The neural pathways that conduct information about a specific stimulus type from the  
35 skin to the brain are considered distinct somatosensory channels. These channels are  
36 thought to interact, for example by inhibitory synaptic connections in the spinal cord [1-  
37 5], and also supraspinally [6, 7]. For instance, touch reduces pain, and pain relieves itch  
38 [1-5, 8-10]. To study these interactions, researchers have selectively stimulated a target  
39 sensory channel and compare either neural responses or reported sensations when  
40 another sensory channel either is or is not stimulated. This research strategy has  
41 remained elusive for cold sensation because most cold stimulation devices inevitably  
42 require contact with the skin. Possible interactions between cold and touch could  
therefore only be investigated with controllable non-tactile stimulators [11].

Pain gating studies have shown that touch inhibits pain [1-3]. Different subpopulations of  
44 A $\delta$ -fibres are thought to mediate both non-noxious cooling, and also heat pain in humans  
45 [2, 3, 12-17]. Additionally, recent studies have found robust and overlapping responses to  
46 both mechanical and cooling inputs in the mouse primary somatosensory cortex (SI) [18,  
47 19]. In humans, SI BOLD activity can discriminate between warm and cold thermotactile  
48 stimuli applied to the hand [20]. Altogether, these results suggest that non-noxious cold  
may interact with tactile signals, for example, through gating mechanisms analogous to  
50 those previously reported for nociceptor signals.

Green and colleagues have reported that touch attenuates cold sensations in humans  
52 [21, 22]. They found more intense cold sensations when *making* tactile contact with an  
53 object already pre-cooled, a scenario they called dynamic touch, compared to when  
54 *maintaining* tactile contact with a thermally-neutral object that is then cooled to the same  
55 temperature, which they called static touch. However, both conditions in this study  
56 involved some degree of tactile input. In other words, skin cooling was not fully  
57 dissociated from touch. Understanding how touch modulates cold sensation would ideally  
58 involve comparing cold sensations with and without touch.

We have therefore studied detection of focal cooling with and without tactile stimulation,  
60 by using a novel non-tactile cooling stimulator [11]. We found that touch consistently  
61 decreased sensitivity to non-tactile cooling, recalling the interaction of touch and pain  
62 described by Pain Gate Theory [1-3].

## **2. Material and methods**

### 64 **(a) Participants and ethics**

A total of 36 healthy volunteers participated with ethical permission, 12 in each of 3  
66 experiments (Experiment 1: 9 females, mean age: 25.92 years  $\pm$  5.57 SD; Experiment 2:  
67 9 females, mean age: 28.33 years  $\pm$  6.74 SD; 9 females; Experiment 3: 11 females, mean  
68 age: 25.5 years  $\pm$  5.88 SD). The sample size was determined by a power calculation, as  
69 follows. We estimated an effect size of 0.857 (Cohen's *d*) for the effect of touch on  
70 sensitivity to cooling, based on a previous study using a similar experimental design but  
71 showing that touch reduced sensitivity to pain [2]. For a one-tailed t-test, a significance  
72 level of 0.050, and a power level of 0.80, ten participants are required, but we decided to  
73 test 12 participants, for comparability with previous studies [2]. We defined *a priori*  
74 criteria to avoid floor and ceiling effects: overall response accuracy above 95% or below  
75 50% in any condition would entail excluding the participant. In fact, no participant was  
76 excluded.

78 The research was approved by UCL Research Ethics Committee (ID number: ICN-PH-PWB-0847/010), and specific risk management protocols were approved and implemented with respect to thermal stimulation.

## 80 **(b) Experimental set-up**

82 The experimental apparatus was similar to that described in [omitted for blind review] (figures 1a & b).

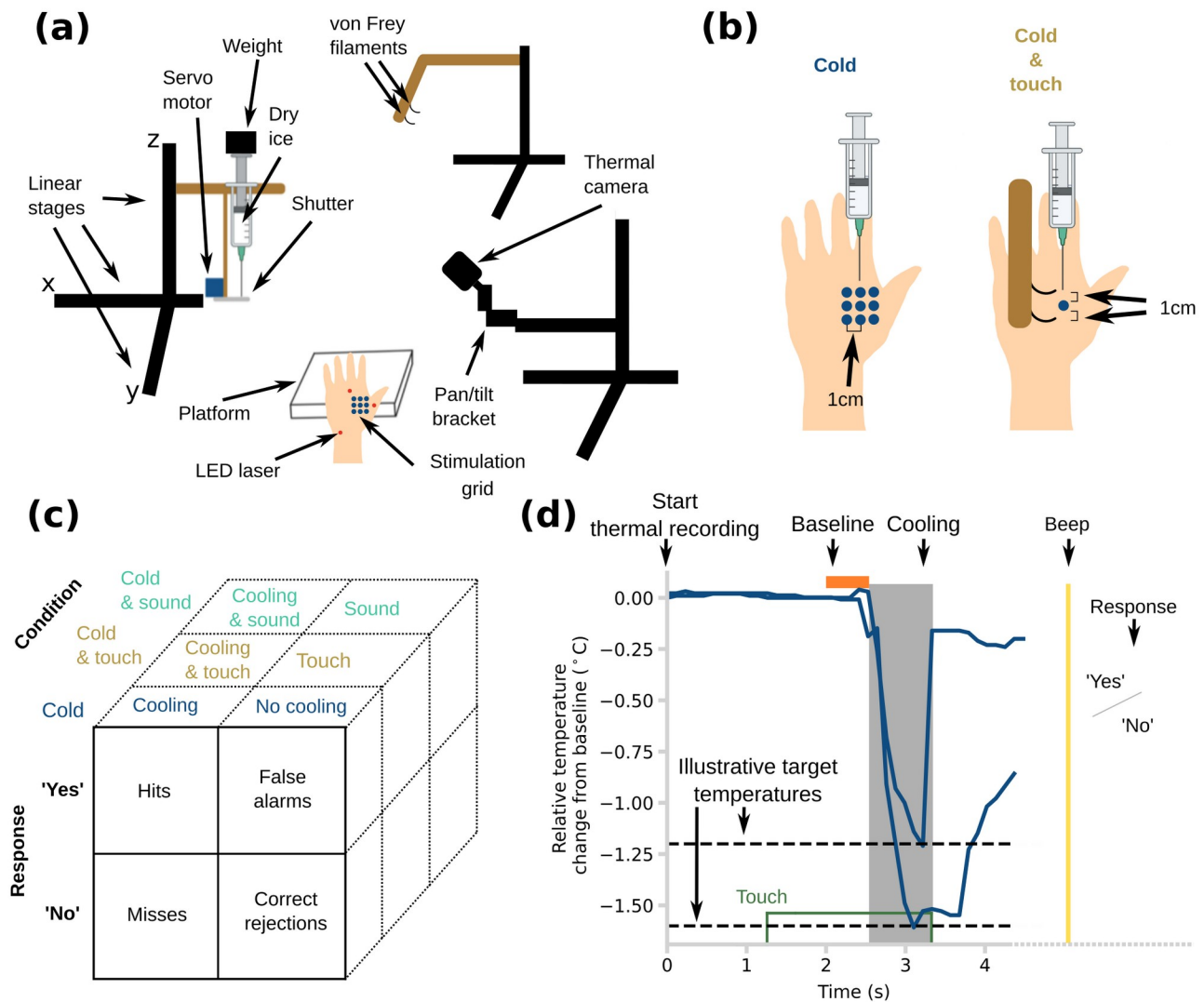
84 A tactile stimulus was delivered by two von Frey monofilaments [23] (bending force: 1 gram-force, diameter: 0.4 mm, length: 15 mm), aligned proximodistally, and each 1 cm from the cooling point (figures 1a & b). The position of the monofilaments was controlled 86 by a computerised XYZ stage (Zaber Technologies Inc.) (figure 1).

88 Thermal tactile stimuli were delivered to the back of the left hand using a custom stimulator allowing controlled exposure to a small dry ice source. Nine skin locations, forming a 3x3 grid with 1 cm spacing, were thermally stimulated in pseudorandom order. 90 The same location was restimulated with cooling only after at least 3 other locations had been visited, ensuring a minimum of 30 s for thermal recovery at each site between 92 cooling events. On each trial, the distance between the dry ice nozzle and the skin was chosen based on the desired skin temperature decrease, using calibration values from a 94 previous study [11]. A thermal camera on a pan/tilt head and additional XYZ stage (ROB-14391, SparkFun Electronics) viewed the stimulated skin region, and measured the actual 96 temperature decrease on each trial.

98 To standardise skin temperature across participants and minimise variation in baseline skin temperatures, an infrared lamp (Infrasec IR2 250W bulb, Tungstram) controlled by a dimmer was used to gently warm participants' hands at the beginning and during breaks. 100 Windows and doors were closed to minimise airflows and thermal fluctuations in the room. A curtain blocked the participant's view of hand and all apparatus.

102 The experiments followed a signal detection theory paradigm. In each trial, participants judged whether a temperature change was or was not present. In Experiments 1 and 2, a 104 speech recognition algorithm was used to transform the participants' responses (either 'Yes' or 'No') from voice to text (IBM Watson, IBM). Vocal responding was chosen because 106 pandemic management protocols in place at the time mandated minimising manual contacts with surfaces. In Experiment 3, participants pressed 'Yes' and 'No' keys on a 108 keypad (Pauk10, Targus International LLC).

110 In Experiments 1 and 2, the duration of possible stimulation was indicated with a tone (frequency: 400 Hz). In Experiment 3, the duration of possible stimulation was indicated 112 by an LED (red LEDs, VCC) placed on the curtain between the participant's eyes and the stimulated hand. The LED light was controlled by an Arduino Uno. In this experiment, 114 some conditions involved auditory stimuli accompanying thermal stimuli. These were tones with a frequency of 500 Hz, a loudness of 50 dB at the position of the participant, 116 delivered from micro-loudspeakers bracketing the thermal location. The aim of this experiment was to show whether the reduction in sensitivity to cooling was specific to 118 touch or might also involve general factors such as distraction by any ongoing stimulus. We set the auditory intensity to be five times reported auditory threshold values [i.e., 10dB at 500 Hz; 24], since our tactile stimuli were also approximately five times 120 previously reported detection threshold values of 0.2 gf [25].



122

**Figure 1. Experimental set-up, trial structure and design.** (a) An illustration of the set-up with the main components including the mechanical stimulator. (b) Comparison between 'Cold' and 'Cold & touch' conditions (c) Table showing definitions of hits, misses, false alarms, and correct rejections for each trial type and condition based on response data. (d) Schematic displaying events on each trial including 2 illustrative thermal traces, with different target temperatures and from different participants. The traces show change of temperature from the mean of a baseline period of 0.5 s immediately before the thermal onset/tone onset. The grey shaded area indicates the period of thermal exposure which was accompanied throughout by a tone.

### 132 (c) Experimental design and task

At the beginning of all experiments, there were 4 training trials to familiarise participants with the trial structure and the task (2 cooling and 2 no cooling trials). Participant were instructed to focus on the thermal stimulus and respond 'Yes' or 'No' after a beep to the question: 'Was there a temperature change during the tone?'. The question was presented after each stimulation by either a computer-generated voice (Experiments 1 & 2) or on-screen text (Experiment 3).

Each experiment involved an initial staircase to select stimulation levels, followed by a signal detection paradigm. A broadly similar exposure protocol and trial structure was used in each case. The staircase procedure estimated the temperature decrease, in the

140

142 absence of touch, which each participant could detect with a probability of approximately  
143 0.80, called percent-correct point henceforth.

144 In all experiments, the staircase procedure followed a 3-down/1-up rule. This rule was  
145 applied following the first negative response ('No'). The step sizes were fixed at +0.1°C  
146 for the down step and -0.14°C for the up step. The boundaries of the staircase were  
147 established at -0.2°C and -2°C. Cooling thresholds of healthy humans lie within this range  
148 [11, 26, 27] and the performance of the stimulator was also optimised for this range [11].  
149 The staircase algorithm followed the carry-on rule when the staircase value surpassed the  
150 established boundaries [28, 29].

At the start of each staircase trial (figure 2a), the thermal camera started recording to  
151 obtain baseline measurements of skin temperature. After 1.5 s, a tone or LED light  
152 alerted the participant, and the stimulator shutter opened at the same time, exposing the  
153 participant's skin to the nearby dry ice. When the temperature of the skin in the ROI  
154 reached the value assigned by the staircase algorithm, the stimulator shutter closed, the  
155 tone or light terminated, and a further beep (duration: 0.2 s; frequency: 100 Hz) indicated  
156 that participants should respond. Participants were instructed to answer the same  
157 question formulated in the training trials. If the temperature was not reached after a  
158 timeout period of 10 s, the trial was considered failed and immediately repeated in  
159 another position of the stimulation grid. To refill the stimulator with dry ice and maintain  
160 participants' engagement, there were 2-min breaks every 6-8 min. In all experiments,  
161 there were 2 parallel, interleaved staircases: one became progressively colder starting  
162 from -0.2°C with respect to baseline skin temperature and the other became  
163 progressively less cold starting from -1.2°C. Both staircases were stopped after 12  
164 reversals (figure 2b) [28, 29].

165 Experiments 1 and 2 used a signal detection paradigm for two different stimulus types,  
166 *Cold* and *Cold & touch*, tested in randomly interleaved order (figure 1b & c). In  
167 Experiment 3, there was one signal detection with three conditions: *Cold*, *Cold & touch*  
168 and *Cold & sound*. Each condition consisted of 27 trials in which cooling was present  
169 interleaved with 27 trials in which cooling was absent (but other elements of stimulation  
170 such as touch and sound were present according to condition). This design allowed us to  
171 use signal detection theory [31] (figure 1c) to compare sensitivity and bias of cooling  
172 detection with vs. without associated touch or sound.

173 The structure of trials in the signal detection paradigm was similar in all experiments  
174 (figure 1c). First, the thermal imaging acquisition began and the thermal camera took a  
175 baseline skin temperature for 0.5 s. Then, for trials involving touch stimulation, the von  
176 Frey filaments were moved to touch the skin around the designated cooling stimulation  
177 point (figure 1b). For trials involving sound rather than touch, a 500 Hz tone began  
178 playing. Next, 2 s later, the shutter of the dry-ice source opened, in cooling (i.e., signal  
179 present) trials only (figure 1c). In no-cooling (i.e., signal absent) the shutter was moved to  
180 create a comparable noise from the shutter servo-motor, but did not open or expose the  
181 source. In experiments 1 and 2, a tone started to alert the participant that cooling might  
182 occur. In Experiment 3, the alert was given by an LED, rather than a tone. The thermal  
183 camera continually monitored skin temperature in a region of interest under the dry-ice  
184 source, and compared this to a baseline measure taken from the first 0.5 s of each trial.  
185 Timestamps for individual thermal images showed that this sampling loop operated at  
186  $7.24 \pm 1.44$  Hz. When instantaneous ROI temperature reached the target decrease from  
187 baseline estimated as each participant's 80% detection threshold by the initial staircase  
188 (see above), the stimulator shutter closed, the alerting tone terminated (experiments 1 &  
189 2) or the LED light turned off (experiment 3). The duration of each cooling stimulation  
190 was recorded and used to replay non-cooling, stimulus absent trials with matched

192 durations. After cooling ended, a brief beep instructed participants to judge whether there  
194 had been a temperature change during the tone, exactly as in the initial staircase.  
196 Participants either said 'Yes' or 'No' in Experiments 1 and 2, or pressed a corresponding  
key in Experiment 3 (figure 1b). The intertrial interval was 8 s. To refill the stimulator with  
dry ice and maintain the participant's engagement, there were 2 minute breaks every 6-8  
minutes.

198 As in the initial staircase, failed trials – principally those where the target temperature  
was not achieved within the 10 s timeout period – were repeated at a random point in the  
200 block. Out of 4538 trials, a total of 176 trials (3.7%; mean of 4.9 failed trials per  
participant) were classified as failed trials. The majority of the failed trials were due to  
202 participant movement, which could be corrected immediately after a failed trial thanks to  
the LED lasers.

#### 204 **(d) Data Analysis and Statistics**

The initial staircase was used to calculate the target temperature change for cooling  
206 signal detection in each experiment. The mean temperature change from baseline was  
estimated from the reversals of each, ignoring the first 3 reversals. A reversal was  
208 defined as a trial in which the response of the participant changed relative to the previous  
trial (figure 2b). The target temperature change values from the interleaved ascending  
210 and descending staircases were averaged to produce a final estimate (figure 2b).

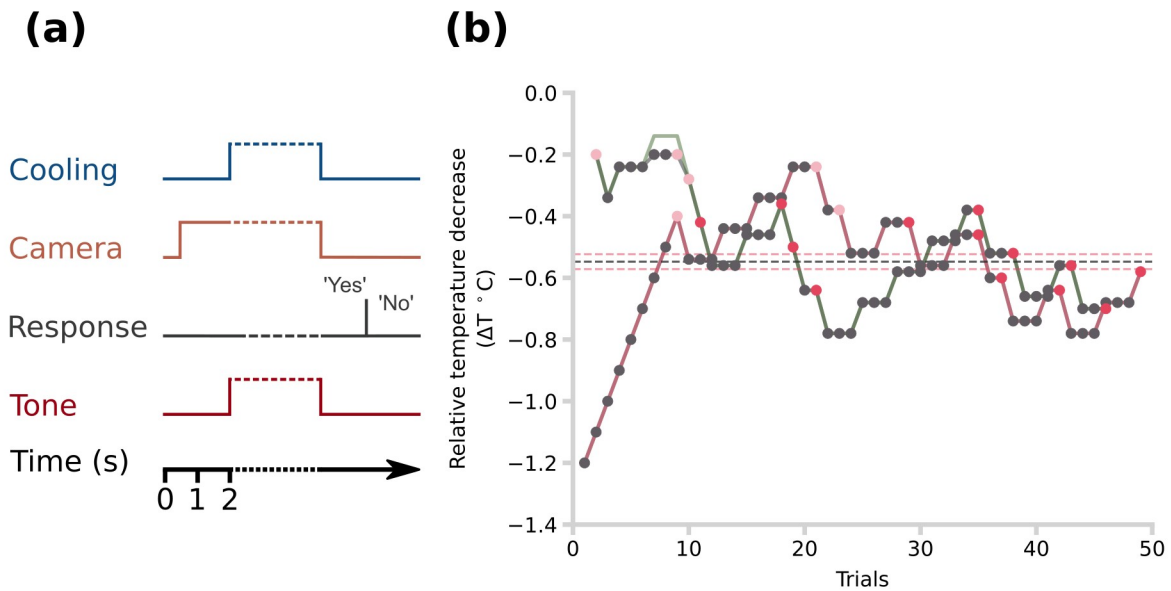
For each experiment, the percent correct response, the hit and false alarm rates were  
212 calculated for each participant in each condition. The sensitivity to cooling ( $d'$ ) and the  
response bias ( $c$ ) were then calculated using signal detection theory and a standard  
214 loglinear method [30-33], which adjusts  $d'$  and  $C$  when hit/false alarm rates are 1 or 0. In  
total, 0% (0/36) of hit rates were 1 and 33% of false alarm rates were 0 (12/36).

216 We hypothesised that the sensitivity in the 'Cold & Touch' condition would be less than  
the sensitivity in the 'Cold' condition, based on Gate Control Theory [1-3]. Therefore, we  
218 compared  $d'$  across conditions with one-tailed tests. As we did not have prior predictions  
about the bias, we compared values of  $C$  across conditions with two-tailed paired t-tests.  
220 For experiment 3, our predictions focussed on the effects of touch and of sound on  
cooling detection. Consistent with the previous experiments, the  $d'$  of 'Cold & touch'  
222 condition was compared to the 'Cold' condition with a one-tailed test, whereas the  
sensitivities and the  $d'$  of the 'Cold & sound' condition were compared to the 'Cold'  
224 condition with two-tailed tests.

### 3. Results

#### 226 **(a) Touch decreases the sensitivity to focal cooling**

The initial staircases for experiment 1 estimated that the smallest temperature decrease  
228 from baseline could be detected with 80% accuracy was  $-0.80^{\circ}\text{C} \pm 0.25^{\circ}\text{C}$  standard  
deviation. For experiments 2 and 3, the corresponding values were  $-1.12^{\circ}\text{C} \pm 0.54^{\circ}\text{C}$  and -  
230  $1.27^{\circ}\text{C} \pm 0.37^{\circ}\text{C}$ , respectively.



232 **Figure 2. Staircase procedure.** (a) Schematic of the temporal sequence of events in a trial  
234 during the staircase procedure. People responded either 'Yes' or 'No' to the question: 'Was there  
236 any temperature change during the tone?' (b) An example percent-correct point estimation with a  
238 staircase procedure from one participant. The red line follows the value tracked by the staircase  
240 algorithm for the descending branch, whereas the green line follows the value tracked for the  
242 ascending branch. The black line follows the relative temperature decrease that participants were  
244 exposed to at each trial and it is overlaid with the green and red lines for most of the procedure.  
The black dots indicate the trials in which the participant said 'Yes'. The light red dots indicate the  
first three trials in which the participant said 'No'. These initial trials were excluded. The red dots  
indicate the subsequent trials in which the participant said 'No'. The average of these  
temperatures was taken as the final percent-correct value. The red horizontal dashed lines are the  
percent-correct points for the descending and ascending staircases. The black line shows the  
mean of these values.

The results of experiment 1 showed that concurrent tactile stimuli ('Cold & touch') significantly reduced sensitivity compared to cooling alone (*Cold & touch*  $d'$ :  $1.25 \pm 0.69$ ; *Cold*  $d'$ :  $1.97 \pm 0.66$  standard deviation; difference:  $0.72 \pm 0.52$ ; one-tailed paired-sample t-test;  $t_{11} = 4.51$ ;  $p = 0.00004$ ; Cohen's  $d = 1.05$ ) (figure 3a). Experiment 2 replicated this result, though with a lower effect size: (*Cold & touch*  $d'$ :  $1.63 \pm 0.85$ ; *Cold*  $d'$ :  $1.90 \pm 0.64$ ; difference:  $0.27 \pm 0.43$ ; one-tailed paired-sample t-test;  $t_{11} = 2.09$ ;  $p = 0.03$ ;  $d = 0.36$ ) (figure 3c).

252 Participants had a tendency to say 'No' in both conditions, producing a negative response  
254 bias (*Cold & touch*:  $-0.46 \pm 0.47$ ; *Cold*  $C$ :  $-0.42 \pm 0.45$ ). There was no significant  
256 difference between the two conditions (difference in  $C$ :  $0.04 \pm 0.34$ ; two-tailed paired-  
258 sample t-test,  $t_{11} = 0.43$ ;  $p = 0.67$ ;  $d = 0.10$ ) (figure 3b). In experiment 2, participants  
again had a tendency to say 'No' in both conditions (*Cold & touch*:  $-0.14 \pm 0.59$ ; *Cold*  $C$ :  $-0.05 \pm 0.56$ ). There was no significant difference between the two conditions (difference in  $C$ :  $0.09 \pm 0.3$ ; two-tailed paired-sample t-test;  $t_{11} = 0.99$ ;  $p = 0.34$ ;  $d = 0.16$ ) (figure 3d).

## 260 (b) Distraction is unlikely to explain the thermotactile gate

262 In experiment 3, sensitivity was calculated for each of the three conditions (*Cold*  $d'$ :  $1.88 \pm 0.61$ ; *Cold & touch*  $d'$ :  $1.64 \pm 0.74$ ; *Cold & sound*  $d'$ :  $1.75 \pm 0.80$ ) (figure 3a). Sensitivity was again significantly reduced when non-tactile cooling was accompanied by

264 concurrent tactile stimuli (*Cold & touch* vs *Cold*: difference  $d$ 's:  $0.25 \pm 0.39$ ; one-tailed  
paired-sample t-test;  $t_{11} = 2.09$ ;  $p = 0.03$ ;  $d = 0.36$ ). There was no significant reduction  
266 when non-tactile cooling was accompanied by a sound (*Cold & sound* vs *Cold*: difference  
 $d$ 's:  $0.13 \pm 0.62$ ; one-tailed paired-sample t-test;  $t_{11} = 0.70$ ;  $p = 0.25$ ;  $d = 0.18$ )).

268 Participants had a bias to respond 'No' in all three conditions (C values *Cold*:  $-0.42 \pm 0.48$ ;  
*Cold & touch*:  $-0.26 \pm 0.49$ ; *Cold & sound*:  $-0.17 \pm 0.60$ ) (figure 3b). Planned comparison  
270 testing showed no significant effect of concurrent tactile stimuli (*Cold & touch* vs *Cold*  
difference:  $-0.16 \pm 0.33$ ; two-tailed paired-sample t-test;  $t_{11} = -1.57$ ;  $p = 0.15$ ;  $d = -0.32$ ).  
272 However, response bias was significantly changed when non-tactile cooling was  
accompanied by a sound as compared to the unimodal cooling condition (*Cold & Sound*  
274 vs *Cold*: difference:  $-0.24 \pm 0.24$ ; two-tailed paired-sample t-test;  $t_{11} = -3.33$ ;  $p = 0.007$ ;  $d =$   
 $-0.45$ ). That is, the presence of a sound increased the probability of 'Yes' responses,  
276 whether cooling stimuli were actually present or not.

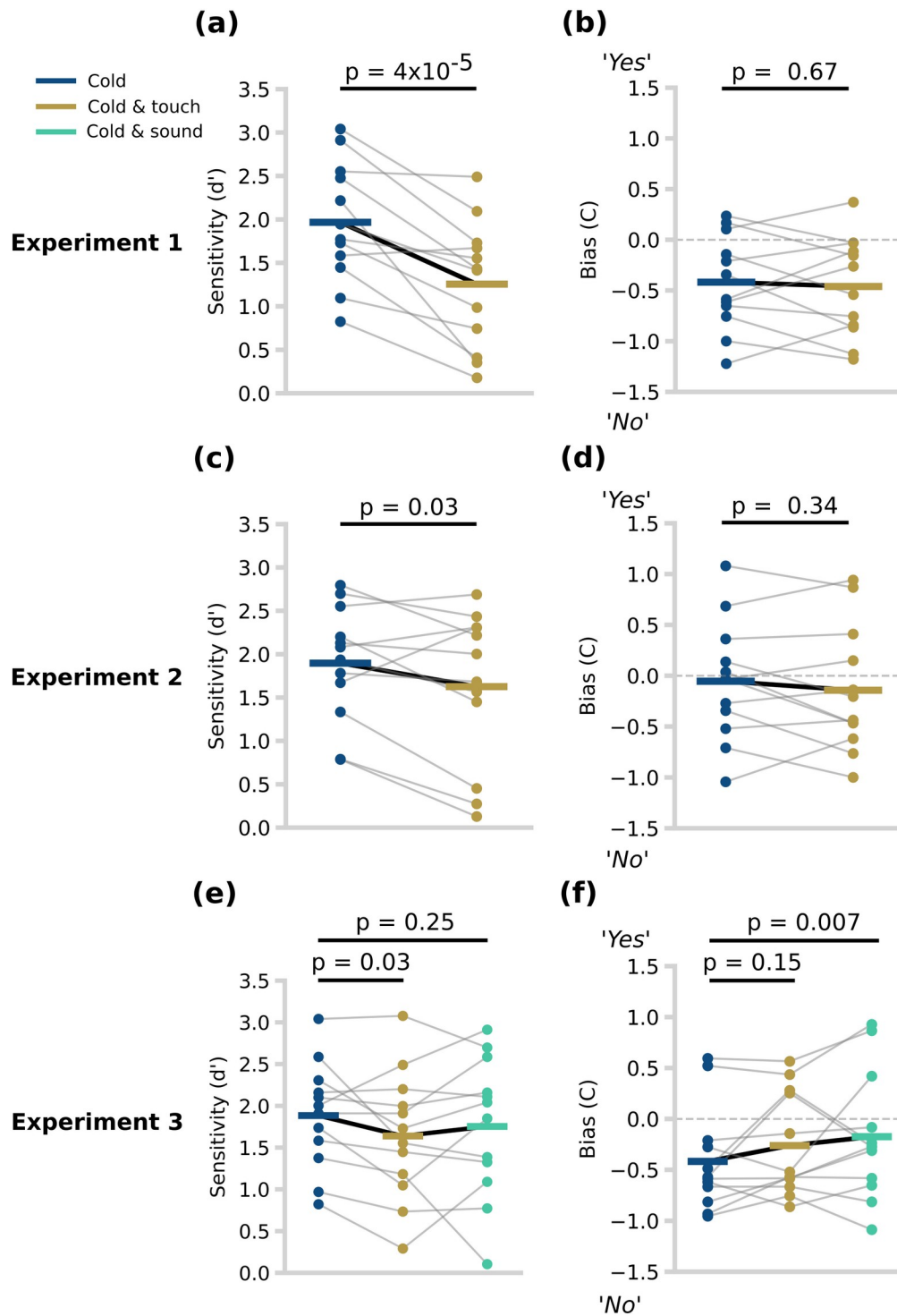
Finally, because the *Cold & touch* and *Cold* conditions were present in all three  
278 experiments, we additionally performed a planned comparison between these two  
conditions after pooling across experiments. This confirmed that sensitivity was reduced  
280 by touch (*Cold & touch*  $d'$   $1.51 \pm 0.79$ , *Cold*  $d'$   $1.92 \pm 0.64$ , difference  $0.41 \pm 0.50$ ,  
 $t(35)=4.85$ ,  $p<0.001$  one-tailed, Cohen's  $d=0.57$ ). Pooled analysis of bias showed no  
282 significant difference between conditions (*Cold & touch*  $d'$   $-0.29 \pm 0.54$ , *Cold*  $d'$   $-0.30 \pm$   
 $0.53$ , difference  $0.01 \pm 0.34$ ,  $t(35)=-0.13$ ,  $p=0.55$  one-tailed, Cohen's  $d=-0.01$ ).

## 284 **4. Discussion**

We investigated the effect of touch on the detection of focal, non-tactile cooling, using a  
286 novel stimulation method that provides non-contact cooling under controlled  
experimental conditions, and without mechanoreceptor stimulation [11]. Thus, we could  
288 measure the sensitivity to focal, non-tactile cooling with and without touch. To our  
knowledge, this has not been attempted previously. We found that sensitivity to non-  
290 tactile cooling was significantly reduced when it was accompanied by touch. Crucially,  
this effect was specific to mechanoreceptor input, rather than reflecting a general  
292 distraction effect of additional stimulation, since detection of cooling was not decreased  
by a concomitant auditory stimulus balanced for duration and intensity with our tactile  
294 stimuli. We suggest our results reflect a previously-overlooked interaction between  
cooling and tactile signals. We speculate that this interaction may be analogous in its  
296 mechanisms and consequences to the well-known interaction between touch and pain  
described by Gate Control Theory [1-3].

298 The Gate Control Theory states that non-painful tactile input can suppress pain [1].  $A\beta$   
afferent signals are thought to inhibit pain signals carried by  $A\delta$ - and C- fibres within the  
300 spinal cord, thus reducing the central transmission of the signals that determine  
perceived pain intensity [2, 3]. Cold sensations are also mediated both by  $A\delta$ - and C-  
302 fibres [15-16], with  $A\delta$ -fibres predominantly responsible for non-noxious cold and C-fibres  
for noxious cold. A similar gating mechanism may underlie the reduction we observed in  
304 sensitivity to non-noxious cooling caused by touch. Specifically, SAI- $A\beta$  fibres activated by  
static touch may activate inhibitory interneurons, which in turn decrease the transmission  
306 of cooling-sensitive  $A\delta$ - and C-fibres.





308 **Figure 3. Sensitivity and bias across experiments and conditions.** (a) The sensitivities ( $d'$ )  
310 in Experiment 1. Each datapoint (coloured dot) is the sensitivity of each participant during the  
312 signal detection paradigm. The light grey lines join the datapoints belonging to the same  
314 participant. The horizontal, coloured lines represent the mean of the sensitivities. (b) The  
response biases (C) in Experiment 1. The dashed, horizontal, grey line follows  $y = 0$ . A negative  
value indicates a tendency to say 'No', whereas a positive value indicates a tendency to say 'Yes'.  
(c) The sensitivities ( $d'$ ) in Experiment 2. (d) The response biases (C) in Experiment 2. (e) The  
sensitivities ( $d'$ ) in Experiment 3. (f) The response biases (C) in Experiment 3.

318 Tactile sensation is mediated by multiple mechanoreceptor types, and their associated  
319 afferent fibres, which may function as independent sensory channels or submodalities [4].  
320 Which of these various touch channels might underlie this cold/touch interaction? Green  
321 and colleagues previously reported that “dynamic touch” attenuates cold sensation  
322 compared to “static touch”. Both of their conditions involved mechanical contact with the  
323 thermal stimulator, but the type of contact was quite different. Dynamical touch  
324 comprised synchronised changes in both contact force and temperature, for example  
325 when a cold object makes new contact with the skin. The static touch condition involved  
326 ongoing contact pressure from a stimulator which then changed in temperature [21, 22].  
327 In contrast, our design made thermal and mechanical stimulation completely  
328 independent. Further, the transient onset of mechanical contact in Green et al.’s dynamic  
329 touch experiments would presumably activate multiple classes of mechanosensitive  
330 fibres [34-37]. In contrast, we used two focal mechanical stimuli (i.e. von Frey filaments  
331 that 2 s before cooling. Together with previous experiments, our results suggest that the  
332 interaction between cooling and tactile inputs might depend on the spatiotemporal profile  
333 of mechanical force. Future research should compare the effects of different tactile stimuli  
334 on sensitivity to non-tactile cooling.

334 Spatiotemporal stimulus properties may influence the interaction of thermotactile signals  
335 in the nervous system that are not fully understood. Strikingly, sensations of wetness,  
336 which are clearly distinguishable from our thermotactile sensations, might emerge from  
337 the integration of cooling and tactile signals [6]. For instance, rate of temperature  
338 decrease strongly influences wetness perception even in the absence of moisture [38,  
339 39].

340 A recent study in mice [7] found that the threshold to detect either a cooling or a tactile  
341 stimulus decreased when they were presented simultaneously. This might reflect a  
342 thermotactile interaction with the opposite sign of the one reported here. There are  
343 several differences between these two studies. First, the studies were conducted on  
344 different species. Second, the mouse study delivered the thermal stimulus with a contact  
345 stimulator, whereas we have used a non-contact stimulator capable of dissociating  
346 cooling from mechanical signals. Third, the thermotactile stimuli had different  
347 spatiotemporal features. In the mouse study, the tactile stimulus was vibratory and  
348 covered the entire dorsal surface of the forepaw throughout the entire experimental  
349 session, while the contact thermal stimulus covered the ventral surface of the paw. In our  
350 studies, the thermal stimulus had an area of 10.9 mm<sup>2</sup> [11] and was delivered to the  
351 dorsal surface of the hand. The tactile stimuli bracketed the thermal stimulus, and had a  
352 diameter of 0.503 mm<sup>2</sup>. Therefore, the difference in the direction of the effect could be  
353 due to differences in the cooling and tactile stimuli. Future research should study the  
354 mechanism underlying differences in perceptual output across stimuli space as this might  
355 reveal overlooked receptors, fibre types and pathways. For example, the suppressive  
356 effect of touch on cold sensitivity that we have found should be investigated with  
357 parametric variations of the both thermal and tactile stimulus area.

358 The brain has limited resources for processing sensory information. Therefore, it could be  
359 that touch is simply a distraction for detecting cooling and the effect we observe is due to  
360 attentional shift rather than to a gating mechanism. In our study, we minimised  
361 attentional effects in four ways. First, the tactile stimulus was never relevant to the task.  
362 Second, in all trials there was either a tone or a light that alerted the participant when  
363 temperature changes might occur. Temporal expectancy was therefore balanced across  
364 conditions and independent of the presence of touch. Third, our tactile stimulus was  
365 designed to avoid shifts in *spatial* attention, since the two monofilament stimuli were  
366 centred on the cooling location. Finally, the filaments always touched the skin 2 s before  
the onset of cooling and then remained static until the end of cooling. New events attract

368 attention transiently ("exogenous attention") for around 200 ms [40], but sustained  
stimuli may not attract attention (e.g., we tend to ignore tactile input from our clothes).

370 Further, experiment 3 included a condition with an auditory stimulus to control for  
attentional, arousal and distraction effects of multisensory stimulation. We found no  
372 evidence that the concurrent sound modulated sensitivity to cooling, though we found  
that the sound did induce a shift towards more liberal response bias. In contrast,  
374 concomitant touch did not significantly influence response bias in any experiments. Some  
participants in experiment 3 spontaneously volunteered that they had found difficult to  
376 stay alert and engaged on trials without a tone. We therefore speculate that the tone may  
have had attentional effects. Since experiments 1 and 2 included a tone on all trials, the  
378 effects of touch on cooling detection would be independent of any such attentional  
effects. Further, we found that touch inhibited sensitivity to cooling across all three  
380 experiments, despite differences in other aspects of the trial structure, such as the  
alerting signals used. Therefore, it seems unlikely the inhibitory effect of touch on  
382 sensitivity to cooling we found is due to attentional mechanisms.

We note some limitations of our methods and results. First, we cannot know exactly what  
384 classes of afferents are activated by our dry-ice cooling, nor by our monofilament tactile  
stimulation. The hypothesised inhibitory interaction between tactile and thermal signals  
386 has not been confirmed directly by neurophysiological data. Our hypothesis that A $\beta$   
fibres interneuronally inhibit transmission of signals by A $\delta$  fibres therefore remains  
388 speculative. Future microneurographic studies could attempt to record from individual  
afferents of these classes during stimulation using our experimental conditions, and then  
390 relate behavioural effects to firing patterns. However, microneurography is limited to  
opportunistic sampling from peripheral afferents, so cannot reliably identify changes in  
392 afferent signals due to spinal interactions. Animal studies could successfully study spinal  
interactions between specific signals [41], but present limitations for studying conscious  
394 experience.

Second, we cannot completely exclude some incidental mechanical effect of dry-ice  
396 cooling, due to convection currents. We measured the force on the skin generated by  
downward airflow through our cooling apparatus at 0.53 mN [11]. This is below published  
398 threshold values for activating slowly adapting SAI and SAII units (1.3 mN and 7.5 mN,  
respectively) [42, 43], suggesting the forces generated by convection are negligible.  
400 Further, any mechanical effect from dry-ice thermal sensation should be similar in all our  
experimental conditions, so cannot readily explain differences between touch-present and  
402 touch-absent conditions. Third, while the inhibitory effect of touch on sensitivity to  
cooling was present across all three experiments, it varied somewhat in size. The reasons  
404 for this variation are not clear. The three experiments were performed in two different  
laboratory rooms, and at two different seasons, so contextual factors might have  
406 contributed to variability in effect size. Future, larger studies might provide a more stable  
estimate of mean effect size, and a clearer picture of why the effect size may vary across  
408 individuals.

In conclusion, we report an apparently novel interaction in thermotactile somatosensation.  
410 Specifically, touch reduces detection sensitivity for focal, non-tactile cooling. Classic  
views of cortical somatosensation suggest that signals for each submodality ascend  
412 independently to primary cortex. Only then, in secondary and associative cortical regions,  
is somatosensory information integrated across different submodalities to produce an  
414 overall percept [44, 45]. These cortical interactions are often linked to causal inference  
computations [46], and to a general prior of objects having parallel multisensory  
416 attributes [47]. An alternative view suggests that perception is shaped by multiple  
interactions between afferent signals at each step along the ascending somatosensory

418 pathway. In particular, elaborate patterns of interaction in the spinal cord can be  
420 identified by anatomical studies [4, 5], potentially explaining the robust finding of tactile  
422 gating of nociceptive afferent signalling, leading to reduced pain levels [1-3]. Our findings  
424 add a novel interaction between touch and temperature to this interaction-based view,  
and contribute to our understanding of inter-channel interactions in somatosensation. Our  
study could also lead to potential applications in areas such as clothing design, and  
wearable technology. Further perceptual and neurophysiological studies are required to  
confirm the precise neural mechanism of the interaction we have identified.

426 **Data accessibility.** The data shown in this manuscript and the code for collecting,  
428 analysing and visualising it can be found in the following link:  
<https://github.com/iezgrom/publication-touch-inhibits-cold>. More information around the  
430 non-tactile cooling stimulator including additional data and code can be found in a  
previous study [11].

432 **Declaration of AI use.** We have not used AI-assisted technologies in creating this  
article.

434 **Authors' contributions.** I.E.R.: data curation, formal analysis, funding acquisition,  
investigation, methodology, software, validation, visualization, writing—original draft,  
436 writing—review and editing; M.C.: investigation, methodology, writing—review and  
editing; P.H.: conceptualization, funding acquisition, resources, methodology, project  
administration, validation, supervision, writing—review and editing.

438 **Conflict of interest declaration.** We declare we have no competing interests.

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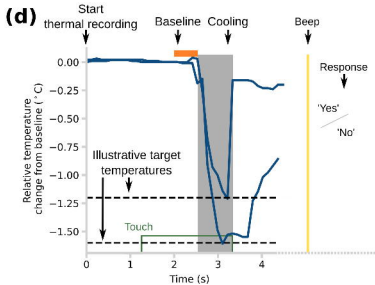
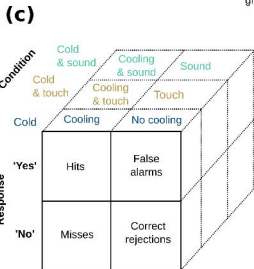
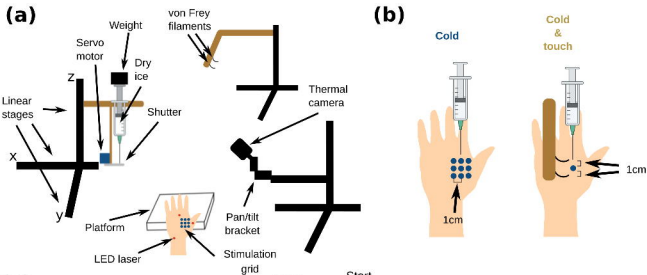
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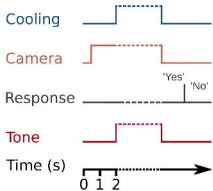
## References

- 448 1. Melzack R, Wall PD. Pain Mechanisms: A New Theory: A gate control system modulates sensory input  
from the skin before it evokes pain perception and response. *Science*. 1965 Nov 19;150(3699):971-9.
- 450 2. Mancini F, Beaumont AL, Hu L, Haggard P, Iannetti GD. Touch inhibits subcortical and cortical  
nociceptive responses. *Pain*. 2015 Oct 1;156(10):1936-44.
- 452 3. Mancini F, Nash T, Iannetti GD, Haggard P. Pain relief by touch: a quantitative approach. *Pain*. 2014  
Mar 1;155(3):635-42.
- 454 4. Abraira VE, Ginty DD. The sensory neurons of touch. *Neuron*. 2013 Aug 21;79(4):618-39.
- 456 5. Abraira VE, Kuehn ED, Chirila AM, Springel MW, Toliver AA, Zimmerman AL, Orefice LL, Boyle KA, Bai L,  
Song BJ, Bashista KA. The cellular and synaptic architecture of the mechanosensory dorsal horn. *Cell*.  
2017 Jan 12;168(1):295-310.
- 458 6. Filingeri D, Fournet D, Hodder S, Havenith G. Why wet feels wet? A neurophysiological model of  
human cutaneous wetness sensitivity. *Journal of neurophysiology*. 2014 Sep 15;112(6):1457-69.
- 460 7. Schnepel P, Paricio-Montesinos R, Ezquerra-Romano I, Haggard P, Poulet JF. Cortical cellular encoding  
of thermotactile integration. *Current Biology*. 2024 Apr 22;34(8):1718-30.
- 462 8. Bautista DM, Wilson SR, Hoon MA. Why we scratch an itch: the molecules, cells and circuits of itch.  
*Nature neuroscience*. 2014 Feb;17(2):175-82.
- 464 9. Feng J, Luo J, Yang P, Du J, Kim BS, Hu H. Piezo2 channel-Merkel cell signaling modulates the  
conversion of touch to itch. *Science*. 2018 May 4;360(6388):530-3.
- 466 10. Yosipovitch G, Duque MI, Fast K, Dawn AG, Coghill RC. Scratching and noxious heat stimuli inhibit itch  
in humans: a psychophysical study. *British Journal of Dermatology*. 2007 Apr 1;156(4):629-34.
- 468 11. Ezquerra-Romano I, Chowdhury M, Leone CM, Iannetti GD, Haggard P. A novel method to selectively  
elicit cold sensations without touch. *Journal of Neuroscience Methods*. 2023 Feb 1;385:109763.
- 470 12. Mouraux A, Guerit JM, Plaghki L. Non-phase locked electroencephalogram (EEG) responses to CO2  
laser skin stimulations may reflect central interactions between A $\delta$ - and C-fibre afferent volleys.  
*Clinical neurophysiology*. 2003 Apr 1;114(4):710-22.
- 472

- 474 13. Mouraux A, Iannetti GD, Plaghki L. Low intensity intra-epidermal electrical stimulation can activate A $\delta$ -nociceptors selectively. *Pain*. 2010 Jul 1;150(1):199-207.
- 476 14. Campero M, Serra J, Ochoa JL. C-polymodal nociceptors activated by noxious low temperature in human skin. *The Journal of physiology*. 1996 Dec 1;497(2):565-72.
- 478 15. Campero M, Serra J, Bostock H, Ochoa JL. Slowly conducting afferents activated by innocuous low temperature in human skin. *The Journal of physiology*. 2001 Sep;535(3):855-65.
- 480 16. Paricio-Montesinos R, Schwaller F, Udhayachandran A, Rau F, Walcher J, Evangelista R, Vriens J, Voets T, Poulet JF, Lewin GR. The sensory coding of warm perception. *Neuron*. 2020 Jun 3;106(5):830-41.
- 482 17. Yarnitsky D, Ochoa JL. Warm and cold specific somatosensory systems: psychophysical thresholds, reaction times and peripheral conduction velocities. *Brain*. 1991 Aug 1;114(4):1819-26.
- 484 18. Milenkovic N, Zhao WJ, Walcher J, Albert T, Siemens J, Lewin GR, Poulet JF. A somatosensory circuit for cooling perception in mice. *Nature neuroscience*. 2014 Nov;17(11):1560-6.
- 486 19. Vestergaard M, Carta M, Güney G, Poulet JF. The cellular coding of temperature in the mammalian cortex. *Nature*. 2023 Feb 23;614(7949):725-31.
- 488 20. Jung Y, Walther DB. Neural representations in the prefrontal cortex are task dependent for scene attributes but not for scene categories. *Journal of Neuroscience*. 2021 Aug 25;41(34):7234-45.
- 490 21. Green BG, Schoen KL. Evidence that tactile stimulation inhibits nociceptive sensations produced by innocuous contact cooling. *Behavioural brain research*. 2005 Jul 1;162(1):90-8.
- 492 22. Green BG. Temperature perception on the hand during static versus dynamic contact with a surface. *Attention, Perception, & Psychophysics*. 2009 Jul;71(5):1185-96.
- 494 23. Weinstein S. Intensive and extensive aspects of tactile sensitivity as a function of body part, sex and laterality. In *The First Int'l symp. on the Skin Senses*, 1968.
- 496 24. Van Hemel SB, Dobie RA, editors. *Hearing loss: Determining eligibility for social security benefits*.
- 498 25. Bowden JL, McNulty PA. Age-related changes in cutaneous sensation in the healthy human hand. *Age*. 2013 Aug;35:1077-89.
- 500 26. Hafner J, Lee G, Joester J, Lynch M, Barnes EH, Wrigley PJ, Ng K. Thermal quantitative sensory testing: a study of 101 control subjects. *Journal of Clinical Neuroscience*. 2015 Mar 1;22(3):588-91.
- 502 27. Rolke R, Baron R, Maier CA, Tölle TR, Treede RD, Beyer A, Binder A, Birbaumer N, Birklein F, Bötefür IC, Braune S. Quantitative sensory testing in the German Research Network on Neuropathic Pain (DFNS): standardized protocol and reference values. *Pain*. 2006 Aug 1;123(3):231-43.
- 504 28. Garcia-Pérez MA. Forced-choice staircases with fixed step sizes: asymptotic and small-sample properties. *Vision research*. 1998 Jun 1;38(12):1861-81.
- 506 29. Prins N. *Psychophysics: a practical introduction*. Academic Press; 2016 Jan 4.
- 508 30. Green DM, Swets JA. *Signal detection theory and psychophysics*. New York: Wiley; 1966 Jan 1.
- 510 31. Macmillan NA, Creelman CD. *Detection Theory: A User's Guide* Lawrence Erlbaum Associates. New York. 2005;73.
- 512 32. Hautus MJ. Corrections for extreme proportions and their biasing effects on estimated values of  $d'$ . *Behavior Research Methods, Instruments, & Computers*. 1995 Mar;27:46-51.
- 514 33. Stanislaw H, Todorov N. Calculation of signal detection theory measures. *Behavior research methods, instruments, & computers*. 1999 Mar;31(1):137-49.
- 516 34. Johansson RS, Flanagan JR. Coding and use of tactile signals from the fingertips in object manipulation tasks. *Nature Reviews Neuroscience*. 2009 May;10(5):345-59.
- 518 35. Manfredi LR, Baker AT, Elias DO, Dammann III JF, Zielinski MC, Polashock VS, Bensmaia SJ. The effect of surface wave propagation on neural responses to vibration in primate glabrous skin. *PloS one*. 2012 Feb 13;7(2):e31203.
- 520 36. Saal HP, Bensmaia SJ. Touch is a team effort: interplay of submodalities in cutaneous sensibility. *Trends in neurosciences*. 2014 Dec 1;37(12):689-97.
- 522 37. Saal HP, Delhaye BP, Rayhaun BC, Bensmaia SJ. Simulating tactile signals from the whole hand with millisecond precision. *Proceedings of the National Academy of Sciences*. 2017 Jul 11;114(28):E5693-702.
- 524 38. Filingeri, D., Redortier, B., Hodder, S. and Havenith, G., 2013. The role of decreasing contact temperatures and skin cooling in the perception of skin wetness. *Neuroscience letters*, 551, pp.65-69.
- 526 39. Merrick C, Rosati R, Filingeri D. The role of friction on skin wetness perception during dynamic interactions between the human index finger pad and materials of varying moisture content. *Journal of Neurophysiology*. 2022 Mar 1;127(3):725-36.
- 528 40. Posner MI. Orienting of attention. *Quarterly journal of experimental psychology*. 1980 Feb;32(1):3-25.
- 530 41. Seki, K., Perlmutter, S. I., & Fetz, E. E. (2003). Sensory input to primate spinal cord is presynaptically inhibited during voluntary movement. *Nature neuroscience*, 6(12), 1309-1316.
- 532 42. Cahusac PM, Noyce R. A pharmacological study of slowly adapting mechanoreceptors responsive to cold thermal stimulation. *Neuroscience*. 2007 Aug 24;148(2):489-500.
- 534 43. Zheng W, Nikolaev YA, Gracheva EO, Bagriantsev SN. Piezo2 integrates mechanical and thermal cues in vertebrate mechanoreceptors. *Proceedings of the National Academy of Sciences*. 2019 Aug 27;116(35):17547-55.

- 536 44. Serino A, Haggard P. Touch and the body. *Neuroscience & Biobehavioral Reviews*. 2010 Feb  
1;34(2):224-36.
- 538 45. Mountcastle, V. B. (1997). The columnar organization of the neocortex. *Brain: a journal of neurology*,  
120(4), 701-722.
- 540 46. Körding, K. P., Beierholm, U., Ma, W. J., Quartz, S., Tenenbaum, J. B., & Shams, L. (2007). Causal  
inference in multisensory perception. *PLoS one*, 2(9), e943.
- 542 47. Ho HN, Watanabe J, Ando H, Kashino M. Mechanisms underlying referral of thermal sensations to sites  
of tactile stimulation. *Journal of Neuroscience*. 2011 Jan 5;31(1):208-13.



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