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No perceptual prioritization of non-nociceptive vibrotactile and visual stimuli presented on a sensitized body part

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High frequency electrical conditioning stimulation (HFS) is an experimental method to induce increased mechanical pinprick sensitivity in the unconditioned surrounding skin (secondary hyperalgesia). Secondary hyperalgesia is thought to be the result of central sensitization, i.e. increased responsiveness of nociceptive neurons in the central nervous system. Vibrotactile and visual stimuli presented in the area of secondary hyperalgesia also elicit enhanced brain responses, a finding that cannot be explained by central sensitization as it is currently defined. HFS may recruit attentional processes, which in turn affect the processing of all stimuli. In this study we have investigated whether HFS induces perceptual biases towards stimuli presented onto the sensitized arm by using Temporal Order Judgment (TOJ) tasks. In TOJ tasks, stimuli are presented in rapid succession on either arm, and participants have to indicate their perceived order. In case of a perceptual bias, the stimuli presented on the attended side are systematically reported as occurring first. Participants performed a tactile and a visual TOJ task before and after HFS. Analyses of participants' performance did not reveal any prioritization of the visual and tactile stimuli presented onto the sensitized arm. Our results provide therefore no evidence for a perceptual bias towards tactile and visual stimuli presented onto the sensitized arm.

Cutaneous tissue injury induces increased pain sensitivity (hyperalgesia) within the injured area ("primary" hyperalgesia) and also in the surrounding non-injured skin ("secondary" hyperalgesia). Secondary hyperalgesia is thought to be the result of central sensitization, defined by the International Association for the Study of Pain (IASP) as "an increased responsiveness of nociceptive neurons in the central nervous system to their normal or subthreshold afferent input"¹. Secondary hyperalgesia can also be induced experimentally, for example, after capsaicin treatment² or by high frequency electrical stimulation (HFS), which consists of five 1-second trains of painful electrical stimuli delivered on the skin^{3,4}. By using these methods, studies have showed that secondary hyperalgesia is characterized by increased pain sensitivity to mechanical pinprick stimuli but not heat stimuli^{5,6}; and by increased pinprick evoked potentials (PEPs)⁷.

Interestingly, previous studies have reported an increase in brain responses measured by event related potentials (ERPs) to non-nociceptive vibrotactile and visual stimuli presented into the area of secondary hyperalgesia^{8,9} 20 minutes after the end of HFS. This increase cannot be explained in terms of central sensitization as it is currently defined by the IASP¹ (for a debate about the concept of central sensitization please refer to^{10,11}) and may be considered a corollary HFS-induced effect involving supra-spinal cognitive mechanisms⁹, possibly attentional ones.

Attention allocated towards a particular stimulus or location typically leads to a *perceptual bias*, meaning that the processing of attended stimuli is speeded up at the detriment of unattended ones^{12,13}. We hypothesized that HFS would increase attentional allocation towards the sensitized arm and consequently induce a perceptual bias towards the sensitized body part leading to a prioritization of the processing of the stimuli applied onto that body part. Indeed, if the aim of sensitization is to protect the body from further injury and promote healing, one might expect that, after inducing sensitization, all sensory stimuli presented on the sensitized body part could

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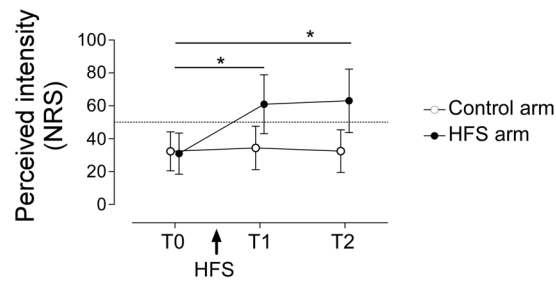


Figure 1. The perceived intensity of the pinprick stimuli was measured at each time point on a numerical rating scale (NRS) anchoring the value of 50 for the transition between the non-painful and painful sensations. The perception of mechanical pinprick stimuli was increased at T1 (20 minutes after HFS) and T2 (45 minutes after HFS) as compared to T0 for stimuli applied on the HFS, but not on the control arm. Asterisks denote a $p < 0.001$.

potentially constitute a threat to monitor. The possibility that HFS promotes the voluntary (endogenous) allocation of spatial attention towards the sensitized body location would also explain why after HFS the ERP vertex negative component (e.g. the negative peak recorded at approximately 150–200 ms at Cz, sometimes referred to as N1 or N2) elicited by sensory stimuli of several modalities was increased^{8,9,14–17}. Indeed, previous studies have reported a larger vertex negativity in response to sensory stimuli presented within the focus of attention^{18–23}. Our hypothesis, that HFS would prompt an endogenous attentional deployment towards the stimulated arm leading to a perceptual bias, was tested by using a temporal order judgment (TOJ) task, a well-established method to assess perceptual biases^{12,13,24–26}.

In TOJ tasks, pairs of stimuli are presented in rapid succession at different temporal delays (i.e. at different SOAs for stimulus onset asynchronies between the stimuli of the pair) and participants have to indicate which of the two stimuli they perceived as presented first. Perceptual changes in TOJ tasks, reflected in the tendency to report the stimuli presented on one side as occurring before the stimuli presented on the other side, are interpreted in terms of *prior entry*. The priority entry law states that attended stimuli are perceived prior to unattended stimuli^{12,25,27}, and that unattended stimuli have to be presented before attended stimuli in order to be perceived as simultaneous. In TOJ tasks, the Point of Subjective Simultaneity (PSS) is the parameter used to characterize prior entry. The PSS corresponds to the threshold of the psychometric function fitting the participants' responses (defined in terms of probability of responding that one of the stimuli was perceived as first at each presented SOA), and characterizes the SOA at which the two stimuli have an equal chance of being perceived as presented first (for a review, see²⁵). Shifts in PSS pinpoint changes in stimulus processing due to perceptual biases. We included in our study two TOJ tasks on pairs of vibrotactile stimuli applied onto the sensitized and control arm, and on pairs of visual stimuli flashed on either arm. We used an adaptive TOJ task, which has the advantage of selecting the SOAs between the two stimuli on the basis of the performance of the participant (Bayesian approach), thereby allowing a smaller number of trials^{28,29} without reducing the precision of the outcome (see³⁰). Participants' performance was measured immediately before HFS (T0) and twice after HFS, at 20 (T1) and at 45 (T2) minutes after the end of sensitization, in line with the experimental design used in previous studies (e.g.^{16,31}). Perceptual biases were indexed by significant deviations of the PSS from 0 or significant changes across time points.

Results

Secondary hyperalgesia. A pre-requisite of our experimental question was that HFS effectively induced secondary hyperalgesia, a manifestation of central sensitization. A first analysis showed that this was the case (see Fig. 1), as confirmed by the significant '*Time * Side*' interaction ($F(1,16) = 29.284$, $p < 0.001$, $\eta_p^2 = 0.647$). Post-hoc t-tests revealed a significant increase in the perceived intensity of the stimuli applied onto the HFS arm (T0 vs. T1: $t(16) = -6.559$, $p < 0.001$; T0 vs. T2: $t(16) = -6.550$, $p < 0.001$), but not onto the control arm (T0 vs. T1: $t(16) = -1.046$, $p = 0.311$; T0 vs. T2: $t(16) = -0.046$, $p = 0.964$).

TOJ tasks. Participants did not report any change in the perceived brightness of the visual stimuli or intensity of the vibrotactile stimuli across blocks and no difference between the two arms at any of the time points. Vibrotactile stimuli were never perceived as painful.

T-tests did not reveal any significant difference from 0 for the PSS at any of the time points (all $|t| < 1.302$, all $p > 0.210$). Furthermore, PSS values did not change across time points, neither during the visual TOJ ($F(1,17) = 1.715$, $p = 0.195$, $\eta_p^2 = 0.092$), nor during the vibrotactile TOJ ($F(1,17) = 0.809$, $p = 0.426$, $\eta_p^2 = 0.107$). Similar results were observed for values characterizing the slope of the fitting functions (visual TOJ: $F(1,17) = 0.547$, $p = 0.584$, $\eta_p^2 = 0.031$; vibrotactile TOJ: $F(1,17) = 0.356$, $p = 0.729$, $\eta_p^2 = 0.010$). Data at the group level are illustrated in Fig. 2 (panel A).

We performed additional Bayesian analyses to estimate the probability that HFS did not induce a significant perceptual bias, in other words to support the null-hypothesis H_0 . In contrast with frequentist statistics, which only allow the conclusion that there is no evidence supporting the alternative hypothesis H_1 (in our case that HFS leads to a perceptual bias), Bayesian statistics can quantify the probability that H_0 is true (i.e. that HFS does not lead to a perceptual bias) as compared to H_1 (i.e. that HFS leads to a perceptual bias)^{32,33}.

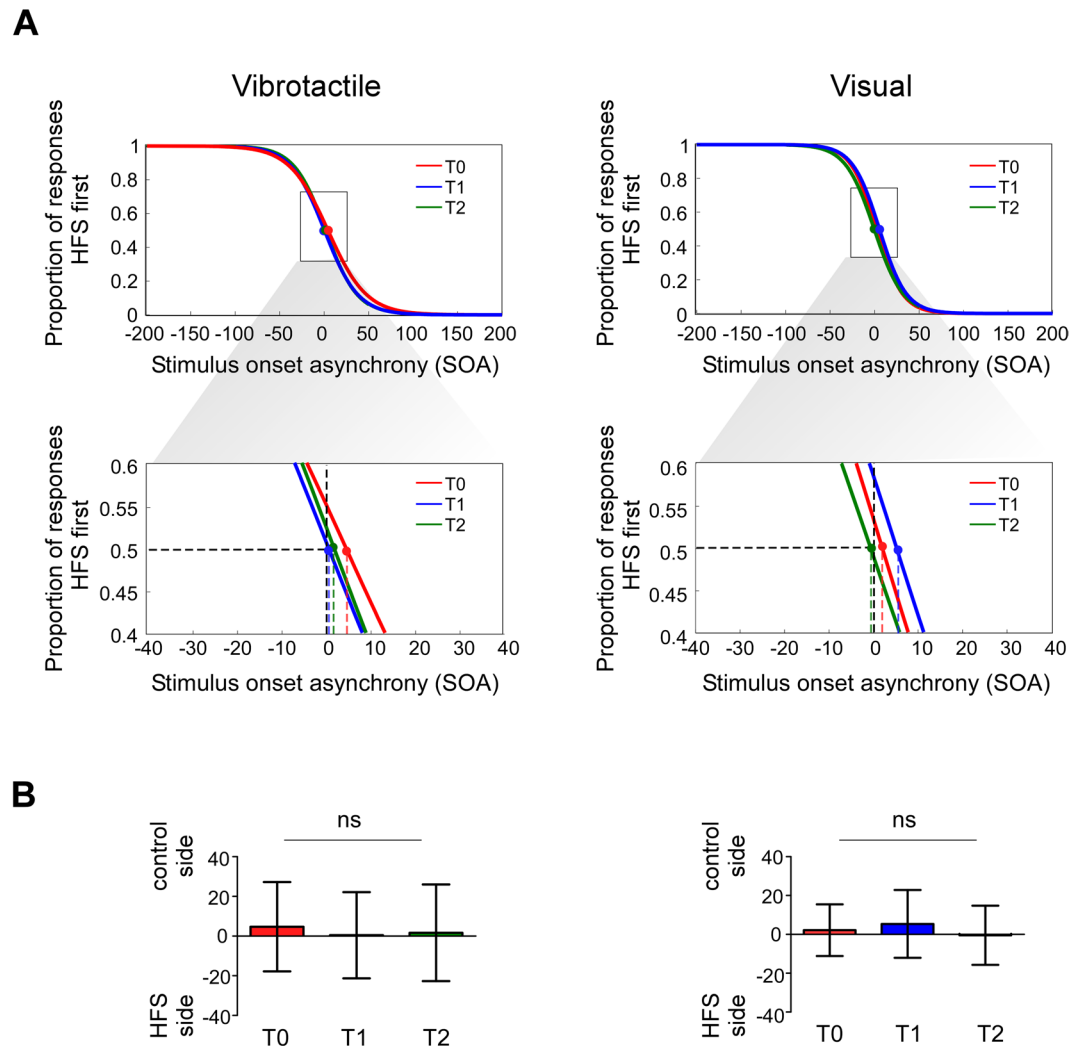


Figure 2. Panel A. Group level results. Data were fitted with a logistic function. The proportion of trials in which the stimulus applied onto the HFS arm was reported as occurring first was plotted as a function of the Stimulus Onset Asynchrony (SOA). Negative values indicate that the HFS side was stimulated first. The black dotted lines in the lower part of the panel correspond to the coordinates ($x = 0$; $y = 0.5$) representing the SOA at which the two stimuli have equal chance to be perceived first i.e. they represent the absence of any perceptual bias. For each time point, i.e. T0, T1 and T2, PSS values were compared against zero to disclose the presence of a perceptual bias. No significant shift emerged (i.e. none of the values was significantly different from zero). Panel B. Histograms represent PSS values. Upwards values show how many milliseconds the stimulus applied onto the control arm had to precede those applied onto the HFS arm to be perceived as occurring first.

The Bayesian one-sample t-tests supported the null hypothesis (i.e. bias absent) at all time points for the tactile (T0: $BF_{01} = 2.924$, $BF_{10} = 0.342$; T1: $BF_{01} = 4.102$, $BF_{10} = 0.244$; T2: $BF_{01} = 3.964$, $BF_{10} = 0.252$, ‘*moderate evidence*’), and the visual TOJ (T0: $BF_{01} = 3.338$, $BF_{10} = 0.300$; T1: $BF_{01} = 1.988$, $BF_{10} = 0.503$; T2: $BF_{01} = 4.081$, $BF_{10} = 0.245$, ‘*moderate evidence*’), although the evidence for the visual TOJ at T1 was less compelling (‘*anecdotal evidence*’; a graphical representation and the detailed statistics can be found in the supplementary file, and an explanation of the labels ‘*moderate*’ and ‘*anecdotal*’ can be found in the methods section). The Bayesian repeated measures ANOVA on the PSS values in the tactile TOJ provided evidence in support of the null model H_0 (‘*Time*’ $BF_{01} = 3.911$, $BF_{10} = 0.256$, ‘*moderate evidence*’). The same analysis in the visual TOJ revealed the same tendency, but with less clear-cut results (‘*Time*’ $BF_{01} = 2.091$, $BF_{10} = 0.478$, ‘*anecdotal evidence*’).

Therefore, in order to investigate differences between the two modalities, we carried out a 3×2 Bayesian ANOVA, using the ‘*Time*’ (T0, T1 and T2) and the ‘*Modality*’ (Vibrotactile, Visual) as factors. The results strongly supported the null-model that HFS did not induce perceptual biases (Interaction ‘*Time***Modality*’ $BF_{01} = 10.777$, $BF_{10} = 0.024$, ‘*strong evidence*’), all the details of this analysis and the results of the same frequentist ANOVA can be found in the supplementary file).

Discussion

In this study we have investigated whether HFS induced an endogenous attentional deployment towards the hyperalgesic arm leading to a perceptual bias towards the stimuli presented on that arm. A perceptual bias towards the HFS arm should have led participants to prioritize the stimuli applied on the sensitized arm, resulting in a PSS shift towards the control arm. We did not observe any significant change in PSS after HFS suggesting that HFS does not induce a perceptual bias to non-nociceptive stimuli delivered to the sensitized body part.

It is unlikely that our findings can be explained by a lack of sensitivity of the TOJ task. There is extensive literature showing that TOJ tasks can detect perceptual biases^{12,13,25,28,34–42}. These biases can be generated by *exogenous* shifts of attention when lateralized non-target stimuli are presented shortly before the pair of target stimuli (e.g.^{29,38,42}), but also by *endogenous* shifts of attention when participants voluntarily allocate spatial attention towards a location, either in response to a cue pointing in that direction or due to increased motivation to attend to the location (e.g.^{13,39–42}). In more detail, TOJ studies in several sensory domains have shown that unilateral non-target stimuli presented a few milliseconds before the pair of TOJ target stimuli bias the PSS towards the uncued side, i.e. they trigger exogenously a bias, leading to a prioritization of the stimuli presented on the cued side at the expense of the stimuli presented on the uncued side (e.g.^{12,29,38,42–44}). Other studies have pointed out that endogenous attentional changes, like the ones we were expecting after HFS, can lead to significant perceptual biases towards the attended location or modality, resulting in a prioritization of stimuli presented at the attended body site (e.g.^{13,24,39–42,45}). Taken together these results indicate that TOJ tasks are sensitive in detecting perceptual biases induced by exogenous and endogenous shifts in spatial attention. Notably, the lack of evidence for a perceptual bias in the present study for vibrotactile and visual stimuli does not exclude the possibility that there could be a perceptual bias for mechanical pinprick stimuli.

Does the lack of perceptual bias after HFS allow us to conclude that HFS does not influence spatial attention? Several studies have reported an enhancement of the vertex negativity for stimuli presented within the focus of spatial attention^{18–23} and the same increase was observed in previous HFS studies^{8,9,14–17}. Therefore it is possible that HFS increases spatial attention towards the sensitized arm leading to a larger negative ERP peak, but without inducing any significant perceptual bias. Importantly, several attentional mechanisms and pathways have been characterized and their recruitment often depends on the kind of task and the relevance of the stimuli (for reviews in different sensory domains see^{46–49}). A functional magnetic resonance study has evidenced that the execution of a tactile TOJ task activated the inferior parietal cortex, the superior and middle frontal gyri, and also the pre-motor cortices⁵⁰. Instead, spatial attention directed to tactile or visual stimuli modulates activity in the corresponding sensory regions, the insula and the cingulate cortex besides the frontal-parietal attentional networks^{51–57}. It is therefore possible that the two tasks do not engage the same cortical structures.

To conclude, we have found that HFS does not induce a perceptual bias towards non-nociceptive stimuli presented onto the HFS-treated arm. This suggests that the mechanism underlying the previously reported enhancement of brain responses elicited by non-nociceptive visual and vibrotactile stimuli is most likely different from the one mediating the prioritization of stimuli.

Methods

Participants. Eighteen healthy volunteers took part in the experiment (mean age 23.39, range 19–41, 7 men). Sample size was estimated on the basis of previous studies reporting an increase of the ERPs after HFS-induced sensitization (e.g.^{14,16,58}). Exclusion criteria comprised having already participated in an HFS experiment, cardiac, neurologic and psychiatric complaints, history of chronic pain or ongoing pain, acute pain on the day of testing, usual intake of psychotropic medication, and intake of centrally active and analgesic drugs (e.g. NSAIDs) on the day of testing or on the day preceding the test. All participants were naïve to the aims of the study and were right handed according to the Flinders questionnaire⁵⁹. The experimental procedure was approved by the local ethic committee (Commission d’Ethique Biomédicale Hospitalo-Facultaire de l’Université catholique de Louvain) in agreement with the Declaration of Helsinki and was carried out in accordance with the corresponding guidelines and regulations. All participants signed an informed consent form prior to the experimental session and received financial compensation for their participation.

Stimuli and materials. *Visual stimuli* were presented by means of two white light emitting diodes (LED) with a 17-lm luminous flux, a 6.40-cd luminous intensity, 5-ms duration and a 120° diffusion angle (GM5BW97330A, Sharp Corporation, Japan). They were perceived as brief flashes. LEDs were attached onto the arms by means of medical tape approximately 1 cm from the area of the volar forearm where HFS was applied and on the homologue area on the control arm. This location was chosen according to a previous study⁹ and on the basis of the average reported spread of secondary hyperalgesia⁶ (Fig. 3A). The exact location was marked on the skin at the beginning of the experimental procedure to ensure correct and constant positioning of the LEDs throughout the blocks. Before starting the experiment, we enquired whether stimuli were perceived as equally bright. In case of a negative response, the LED perceived as less intense was slightly moved along the medial line on the volar forearm until the stimuli were perceived as equally bright. A third yellow LED, equidistant from the arms at approximately 40 cm from the trunk (min. 0.7-cd luminous intensity at 20-mA, 120° diffusion angle, Multicomp, Farnell element14, UK) was used as fixation point during the task. At the end of each block we asked whether the stimuli were perceived as having the same luminosity during the block.

Tactile stimuli were generated by two vibrotactile transducers driven by standard audio amplifiers (TL-002-14R Haptuator Redesign, Tactile Labs, Inc., Montreal, Canada) secured to the arms by means of gauze. The stimuli lasted 10 ms, and were vibrating at 440 Hz. The stimulators were attached onto the arms approximately at 1.5 cm from the stimulated area, in line with previous studies^{6,8} (see also the comment for the visual stimuli). Also in this case, the exact location was marked on the skin at the beginning of the experiment and kept constant across the blocks. At the beginning of the experiment we checked whether the perceived intensity of the stimuli

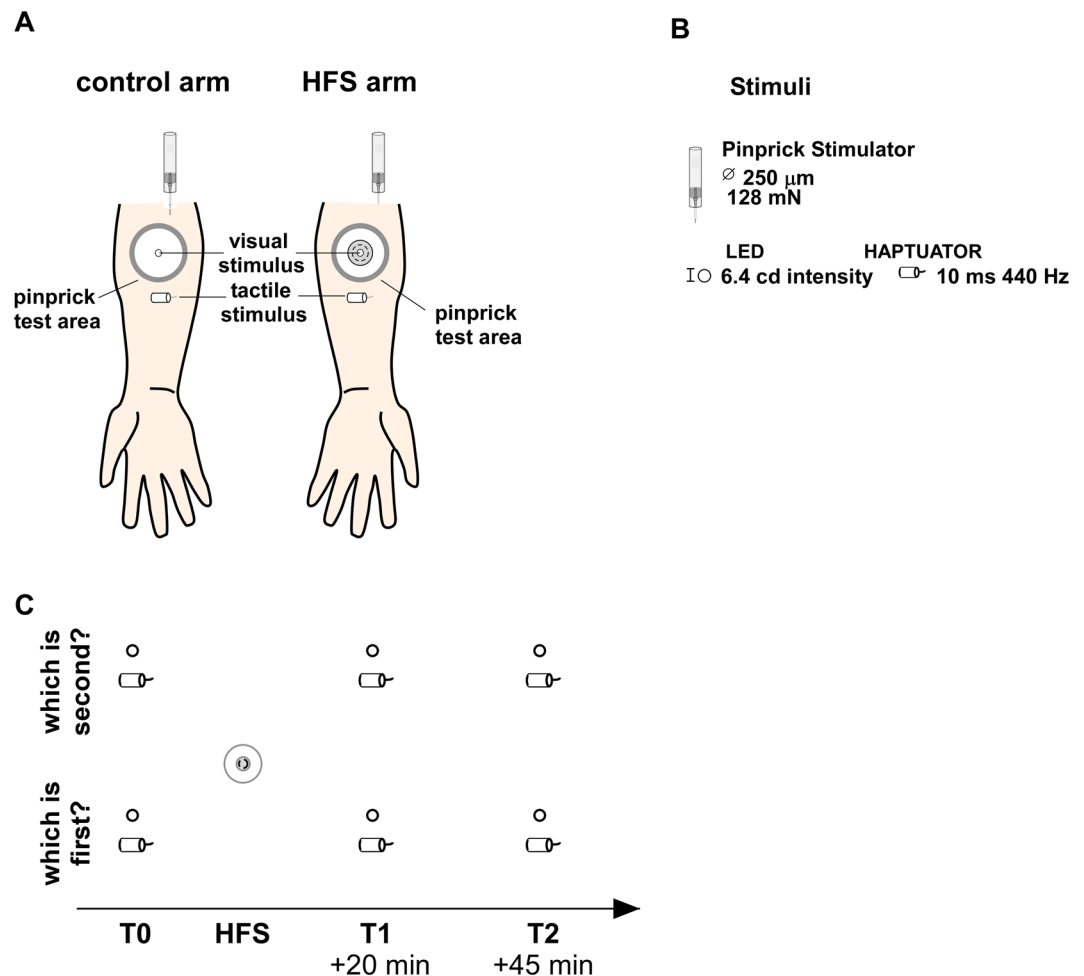


Figure 3. Experimental procedure. Panel A. Participants received, at different SOAs, pairs of either visual or vibrotactile stimuli on either forearm. Secondary hyperalgesia was tested by using pinprick stimuli. The location where visual and tactile stimuli were applied was established on the basis of previous studies^{8,9}. Panel B. Details of the stimuli. Panel C. Participants were asked to report verbally which arm was perceived as stimulated first (or second). Tasks were performed before applying HFS (T0), 20 minutes (T1) and 45 minutes (T2) after HFS.

was the same between the arms. In case of a negative response, the haptuator perceived as less intense was slightly moved along the medial line on the volar forearm until the stimuli were perceived as equally intense.

Secondary hyperalgesia was induced by HFS of the skin using a specifically designed electrode made of 16 blunt stainless steel pins with a diameter of 0.2 mm protruding 1 mm from the base^{3,60}. The pins were placed in a circle with a diameter of 10 mm and served as cathode. The stainless steel reference electrode, the anode, was placed surrounding the cathode and had an inner diameter of 22 mm and an outer diameter of 40 mm. HFS consisted of five trains of 100 Hz electrical stimuli (pulse width 2 ms) that lasted 1 second each and were repeated at a 10 s interval. The pulses were generated by a constant-current electrical stimulator (DS7A, Digitimer Ltd, Welwyn Garden City, UK). The duration of the whole procedure was 50 seconds. HFS was applied on the volar forearm skin of either the dominant or non-dominant arm, which was counterbalanced across participants. The intensity of stimulation was adjusted individually at 20 times the absolute detection threshold to a single pulse. The average threshold for the single pulse detection was 0.25 ± 0.09 mA, and the average intensity used for the sensitization procedure was 4.9 ± 1.8 mA.

Procedure. The experiment was conducted in a dimly lit room. During the experiment, participants sat comfortably on a chair with their chin positioned on a chin rest in order to minimize head movement towards one of the arms. The arms were positioned palms up on a table in front of them. The distance between the arms was kept constant at approximately 30 cm. Visual and tactile stimuli were presented in pairs on either arm. At the beginning of the procedure, the experimenter who placed the haptuators and the LEDs on the skin was blind to the side of HFS stimulation.

At the beginning of the experiment, a familiarization phase composed of 4 short blocks (2 for the visual and 2 for the tactile TOJ) was run. In each block, 10 pairs of stimuli were presented for each modality. After familiarization, the actual experiment was started. The visual and tactile TOJs were performed in 4 separate blocks (2 for the visual and 2 for the tactile TOJ), each of which was composed of 40 trials. This number was chosen in

accordance with previous studies having measured reliable parameters and having successively found PSS shifts using 20 to 40 trials^{28,29,61–63}. A trial started with the illumination of the yellow fixation point. After 500 ms, the pair of stimuli was presented. During the familiarization phase, SOAs between the two stimuli were of ± 145 and ± 200 ms for the visual TOJ, and ± 150 and ± 200 ms for the tactile TOJ. All participants correctly understood and performed the task. During the actual experiment twenty possible SOAs were defined for the visual TOJ task (± 200 , ± 145 , ± 90 , ± 75 , ± 60 , ± 45 , ± 30 , ± 15 , ± 10 , ± 5 ms), and 22 for the tactile TOJ task (± 400 , ± 200 , ± 150 , ± 90 , ± 75 , ± 60 , ± 45 , ± 30 , ± 15 , ± 10 , ± 5 ms). Negative values indicate that the left-sided stimulus was presented before the right-sided one, positive values indicate the reverse. The SOA was chosen at each trial on the basis of the participant's performance in all previous trials, according to the adaptive PSI method⁶⁴ (implemented through the Palamedes Toolbox⁶⁵). The adaptive PSI method adopts a Bayesian framework where parameters of interest are estimated without probing extensively all the predefined SOAs an equal number of times. Starting from pre-defined priors relative to the threshold and the slope of the logistic function fitting the participant's responses (that we set as 0 ± 20 for the threshold and 0.06 ± 0.6 for the slope; see²⁸), the PSI algorithm updates at each trial the joint distribution of the slope and the threshold and chooses the subsequent SOA to minimize the expected entropy of the posterior distribution. In such a way, the number of trials needed to achieve a stable estimate of the parameters under exam can be reduced. In one block participants had to report verbally which side was perceived as stimulated first ('*which is first?*'), in the other which was perceived as stimulated second ('*which is second?*'). The condition '*which is second?*' allows limiting the influence of response/decisional biases over perceptual biases^{12,25,66}. No instruction was given regarding response speed. Participants' responses were encoded manually by the experimenter and no feedback about the accuracy of the response was provided. A new trial started 2000 ms after the response was encoded.

The TOJ tasks were performed at three time points: before HFS (T0), 20 (T1) and 45 (T2) minutes after HFS. The order of the sensory modalities was counterbalanced across participants, the order 'which is first', 'which is second' was randomized.

Measures. The presence of HFS-induced secondary hyperalgesia was assessed using a calibrated pinprick stimulator exerting a force of 128 mN (MRC Systems, Heidelberg, Germany). Participants were asked to rate the average sensation elicited by 3 consecutive stimuli applied at different locations onto the skin surrounding the area onto which HFS was applied and by 3 stimuli applied onto the homologue area of the contralateral non-sensitized arm. Ratings were provided on a Numerical Rating Scale (NRS) ranging from 0 to 100, and participants were informed that the number of 50 represented the transition from the non-painful to the painful domain of sensation. The extremes of the scale were described as 'I did not feel anything' (NRS = 0) and 'pain as bad as I can imagine' (NRS = 100). Half of the participants received the pinprick stimuli before the beginning of each block, the other after each block.

Data were fitted with a logistic function, which allowed us to derive the parameters of interest: the α and the β (as in²⁸). The α defines the *threshold* of the function and characterizes in the present study the Point of Subjective Simultaneity (PSS) corresponding to the SOA at which two stimuli are reported as perceived first equally often. In the present study the logistic function was fitted on the probability of reporting the stimuli presented at the HFS side. Therefore, the PSS reflects the SOAs at which the probability of responding HFS as first stimulated arm equals 50%. The β defines the *slope* of the logistic function, namely, it describes the precision of the participants' responses. Considering that the aim of this study was to investigate perceptual biases, our main outcome was the analysis of the threshold (the α), i.e. the PSS. Results of the slope (the β) are reported for completeness.

Figure 3 shows the experimental procedure.

Statistical analysis. *Frequentist analysis.* Statistical analyses were conducted using IBM Statistics SPSS 19 (Armonk, NY: IBM 22 Corp.).

Mechanical hyperalgesia. The presence of secondary hyperalgesia was assessed by comparing the perceived intensity of the average of the three mechanical stimuli applied at each time point by means of a repeated-measure ANOVA with '*Time*' (T0, T1, T2) and '*Side*' (control vs. HFS) as within-subject factors.

Perceptual bias. Before analyzing TOJ values, the PSS and slope values of the '*which is first?*' and '*which is second?*' conditions were averaged for each modality and each time period. In order to match the data of the two groups of participants according to the side of HFS the values of participants who received HFS onto the right arm were 'flipped', i.e. multiplied by -1. T-tests against zero were used to disclose significant perceptual biases (PSS significantly different from zero). A one-way repeated-measure ANOVA using the factor '*Time*' was then conducted, separately for each modality, to assess changes of PSS and slope values across time for each modality. Greenhouse-Geisser corrections of degrees of freedom were used in case of violation of sphericity. Effect sizes were estimated by means of partial Eta squared (η^2_p). Contrasts were used when necessary.

Bayesian analysis. Bayesian analysis on the PSS values were performed with JASP⁶⁷. An advantage of the Bayesian approach over the frequentist approach consists in comparing the evidence for the null (H_0) and alternative (H_1) models, in our case that HFS did not lead to a perceptual bias (H_0) and that HFS induced a bias (H_1)^{32,68}. The strength of evidence for one model or the other is quantified by the Bayes factor of B_{10} for H_1 and B_{01} for H_0 . For instance, a B_{10} of 7 indicates that the data are 7 times more likely under H_1 than under H_0 . Conventionally, it is considered that values between 1 and 3 indicate '*anecdotal*' evidence, from 3 to 10 '*moderate*', from 10 to 30 '*strong*' and above 30 '*very strong*'⁶⁹. Bayesian analyses were performed, as for the frequentist approach, for t-tests and repeated measure ANOVAs separately for modality. An additional 3×2 ANOVA, using both '*Time*' and

'Modality' as factors was carried out to compare possible differential effects of HFS on the modality (see results section). Given the lack of a priori knowledge on the effect sizes, a default Cauchy prior was used (0.707). Results using wider priors are presented in the supplementary material. The datasets and the design are available on the Open Science Framework platform.

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Author Contributions

D.M.T. conceived the research, all authors discussed the design, D.M.T. and L.F. collected and analysed the data, D.M.T. and E.N.V.D.B. discussed the results, all authors wrote and discussed the paper, and all authors approved the final version.

Additional Information

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