Title: **Selective attention gates the interactive crossmodal coupling between cortical sensory systems**

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Abstract

Cortical sensory systems often activate in parallel, even when stimulation is experienced through a single sensory modality[1–3]. Critically, the functional relationship between co-activated cortical systems is unclear: Co-activations may reflect the interactive coupling between information-linked cortical systems or merely parallel but independent sensory processing. Here, we report causal evidence that human somatosensory cortex (S1), which co-activates with auditory cortex during the processing of vibrations and textures[4–9], interactively couples to cortical systems that support auditory perception. Acute manipulation of S1 activity using transcranial magnetic stimulation (TMS) impairs auditory frequency perception when subjects simultaneously attend to auditory and tactile frequency, but not when attention is directed to audition alone. Auditory frequency perception is unaffected by TMS over visual cortex thus confirming the privileged coupling between the somatosensory and auditory cortical systems in temporal frequency processing[10–13]. Our results provide a key demonstration that selective attention can enhance the functional coupling between cortical systems that support different sensory modalities. The gating of crossmodal coupling by selective attention may critically support multisensory interactions and feature-specific perception.

Attending to a stimulus feature that can be redundantly signalled through different senses can activate multiple cortical sensory systems. For example, the auditory cortex can be activated by visual stimulation even in the absence of sounds, particularly when attending to stimulus features that are associated with sounds[14,15]. Such co-activation of sensory systems is thought to reflect a number of attention-based operations including the selection, refinement, and binding of sensory representations[16]. Critically, the functional relationship between co-activated cortical systems remains ambiguous. Co-activation could reflect an interactive coupling between the cortical sensory regions. Alternatively, co-activation could merely reflect the parallel, but independent activation of sensory systems. Distinguishing between these possibilities would provide critical insight into the functional role of distributed activity over cortical systems that are traditionally thought to be dedicated to unisensory processing.

Somatosensory cortex (S1) often co-activates with auditory cortex[4,7,9,17]. Co-activation of these sensory cortical systems may reflect the recruitment of cortical networks that support frequency representations encoded by both touch and audition[8,18] and shared neural circuits may underlie the highly-specific perceptual interactions observed between touch and audition in the temporal frequency domain[10,19,20]. If tactile frequency perception recruits cortical systems that also support audition, the functional connectivity within these networks conceivably fluctuates systematically to enable flexible behaviour. Here, we hypothesized that S1 becomes functionally coupled to cortical systems that support audition specifically when attention is directed to tactile frequency. We used transcranial magnetic stimulation (TMS) to probe signal transmission between the somatosensory and auditory cortical systems and to characterize the dependence of this crossmodal coupling on attention state. In a state of increased crossmodal coupling, we reasoned that TMS-induced activity changes in S1 would propagate through the auditory cortical system, potentially disrupting auditory perception.

To test our hypothesis, we causally manipulated S1 activity using online TMS while participants performed a discrimination task[10–13] that required them to report which of two stimuli was perceived to be higher in frequency (Fig. 1a). Subjects (n = 15) performed the discrimination task in separate blocks that differed according to the sensory modality to which subjects directed their attention. In the unimodal auditory block (Fig. 1b, Unimodal_A), sounds were presented during both stimulus intervals (auditory-only trials),

requiring subjects to attend only to audition. In the unimodal tactile block (Fig. 1b, $Unimodal_T$), vibrations were presented during both intervals (touch-only trials), requiring subjects to attend only to touch. In the Mixed blocks (Fig. 1b, Mixed), auditory-only and tactile-only trials were randomly interleaved with crossmodal trials that comprised a sound in one interval and a vibration in the other. Randomization ensured that subjects could not predict stimulus modality during any stimulus interval in the Mixed blocks, thereby forcing subjects to attend to both modalities throughout the blocks. Crucially, by comparing performance on the auditory-only trials, which occurred in both the $Unimodal_A$ and Mixed blocks (Fig. 1b, red boxes), we tested how manipulating S1 activity using TMS impacted auditory frequency perception under states that differed only with respect to whether or not subjects also attended to tactile frequency cues. According to our hypothesis, we predicted that TMS over S1 would impair auditory perception only during the Mixed blocks. In our within-subjects design, each subject completed the same experiment in two sessions in which they received TMS over S1 or a control site (Fig. 1c). During each session, subjects initially performed the auditory and tactile discrimination task in blocks without TMS (baseline blocks) before completing the $Unimodal_A$, $Unimodal_T$, and Mixed blocks (Methods).

To establish the TMS target site in each subject, we located the hand representation in left S1 and validated this target location using multiple functional procedures (Methods). Prior to the discrimination task blocks, subjects performed a tactile detection task in which they reported on each trial whether they experienced a brief tap on the index finger of the left hand, right hand, both hands or no taps. In the absence of TMS, subjects achieved high performance (>0.90 probability correct) in all conditions (Fig. S1). Because S1 contains body representations that are predominantly contralateral, manipulating activity in left S1 using TMS should selectively impair the detection of taps on the right hand. Consistent with this prediction (Fig. 2a), online TMS delivered over left S1 significantly and systematically impaired performance on the detection task ($F_{3,42}$ = 17.6, p = 1.49e-07, η_p^2 = 0.55) by reducing performance accuracy on trials in which the tap was delivered to the right hand only (0.58 $\pm$ 0.09) and to both hands (0.39 $\pm$ 0.07). Critically, TMS-induced accuracy reductions resulted from a failure to detect taps on the right hand: Subjects reported feeling no stimulation when taps were delivered to the right hand only and they reported touch on only the left hand when taps were delivered to both hands (Fig. 2a). To quantify this lateralized TMS effect, we computed an extinction

index (EI) for each subject where positive values indicate better detection performance on the hand ipsilateral to the stimulated cortex compared to the contralateral hand (Fig. 2b). The group-averaged EI (mean EI = 0.50 $\pm$ 0.12) was significantly greater than 0 (t-test, t(14) = 4.19, p = 8.98e-04, d = 1.08) and positive EI values were observed in a significant number of individual subjects (13/15; binomial test, p = 0.003). These results demonstrate that TMS over S1 selectively disrupted the perception of simple taps on the hand contralateral to the stimulated hemisphere.

In addition to impairing stimulus detection, TMS over S1 also significantly impaired subjects' ability to discriminate tactile frequency (Fig. 2c) ($F_{2,24}$ = 11.35, p = 0.0003, η_p^2 = 0.48). In the absence of TMS, subjects successfully performed the tactile-only trials (0.80 $\pm$ 0.02). Relative to baseline performance, TMS over S1 significantly reduced performance in the Unimodal_T block (0.66 $\pm$ 0.03; t(12) = 3.75, p = 0.003, d = 1.34) and Mixed block (0.67 $\pm$ 0.04; t(12) = 3.85, p = 0.002, d = 1.25). Performance levels did not differ between the Unimodal_T and Mixed blocks (t(12) = -0.20, p = 0.84, d = 0.04). TMS also delayed response times (RT) significantly (Fig. S4) ($F_{2,24}$ = 20.69, p = 5.98e-06, η_p^2 = 0.63). Subjects took more time to respond in the Unimodal_T (844.7 $\pm$ 133.2 msec; t(12) = -4.50, p = 7.17e-04, d = 0.80) and Mixed blocks (956.7 $\pm$ 127.2 msec; t(12) = -5.64, p = 1.08e-04, d = 1.12) compared to the baseline block (527.9 $\pm$ 78.7 msec). These data indicate that manipulating S1 activity disrupted the ability of subjects to detect and discriminate tactile stimuli, thereby providing strong validation for the TMS target site over left S1.

To test the hypothesis that S1 becomes functionally coupled to cortical systems that mediate auditory frequency perception, we assessed subjects' ability to discriminate sound frequency as we causally manipulated S1 activity under different attention states. If coupling between the somatosensory and auditory systems requires the deployment of attention to tactile frequency, we predicted that TMS over S1 would impair auditory discrimination performance only in the Mixed block during which subjects attended to both tactile and auditory frequency. Auditory discrimination performance (Fig. 3a) differed significantly between the test blocks ($F_{2,24}$ = 17.68, p = 1.91e-05, η_p^2 = 0.60). In the absence of TMS, subjects reliably and accurately performed the auditory discrimination task (0.79 $\pm$ 0.02). Performance in the Unimodal_A block was nominally

lower compared to baseline (0.76 ± 0.03), but this difference did not achieve statistical significance ($t(12) = 1.75$, $p = 0.10$, $d = 0.41$). This result implies that simply applying TMS over S1 was insufficient for disrupting auditory frequency perception. Critically, performance on the auditory-only trials during the Mixed block (0.67 ± 0.02) was significantly impaired compared to performance in the baseline block ($t(12) = 5.37$, $p = 1.67e-04$, $d = 1.66$) and the $Unimodal_A$ block ($t(12) = 4.15$, $p = 0.001$, $d = 0.90$). With TMS over S1, there was nearly a 10% performance reduction on average (Fig. 3b) when comparing the $Unimodal_A$ block with the Mixed block (*Modulation index* vs 0, $t(12) = 4.15$, $p = 0.001$, $d = 1.15$). In fact, lower relative accuracies were observed in the Mixed block in nearly every subject (12/13; binomial test, p= 0.001). Importantly, in a control experiment that did not involve TMS, no significant differences were observed between auditory-only trials in $Unimodal_A$ and Mixed blocks (n = 8; Fig. S2). This control experiment result indicates that the observed decrements in auditory discrimination performance with TMS over S1 was not simply a consequence of requiring subjects to divide their attention over two senses. Instead, auditory frequency perception could be impaired only when TMS was applied over S1 as subjects attended to both tactile and auditory frequency.

TMS is associated with audible discharge sounds as well as tactile sensations on the scalp. These confounds can impact behaviour[21] and subjects may have been vulnerable to these non-specific TMS effects when they directed attention to auditory and tactile frequency. To address this possibility, we retested each subject while applying TMS over a control site (Methods). In this control experiment (Fig. 3a), auditory discrimination performance did not differ significantly between blocks ($F_{2,24} = 1.04$, $p = 0.36$, $\eta_p^2 = 0.08$; Baseline: 0.82 ± 0.01, $Unimodal_A$: 0.79 ± 0.03, Mixed: 0.81 ± 0.03). Furthermore, despite substantial inter-subject variability (Fig. 3b), there were no systematic and significant performance differences between the $Unimodal_A$ and Mixed blocks with TMS over the control site ($t(12) = -1.03$, $p = 0.31$, $d = 0.28$). Thus, the performance pattern observed with TMS over S1 also cannot be attributed to non-specific TMS effects nor to an interaction between these effects and the attention manipulations. Notably, subjects (n = 12) who performed an analogous intensity discrimination experiment (Methods) were severely impaired by TMS over both S1 ($F_{2,22} = 10.47$, $p = 0.0006$, $\eta_p^2 = 0.48$) and the control site ($F_{2,22} = 9.09$, $p = 0.001$, $\eta_p^2 = 0.45$) in the $Unimodal_A$ (S1: $t(11) = 3.37$, $p = 0.006$, $d = 1.44$; Ctrl: $t(11) = 4.15$, $p = 0.001$, $d = 1.44$) and Mixed blocks (S1: $t(11) =$

4.23, $p = 0.001$, $d = 1.73$; Ctrl: $t(1) = 3.85$, $p = 0.002$, $d = 1.38$). The ubiquity of TMS influences on performance of the intensity discrimination task reveals that auditory intensity perception may be particularly vulnerable to non-specific TMS effects, in stark contrast to auditory frequency perception. These results collectively establish the feature-dependence of TMS influences on audition and demonstrate that TMS selectively impaired auditory discrimination performance only when S1 activity was manipulated as subjects attended to auditory and tactile frequency.

Given the extensive connectivity within the sensorimotor cortical system, we considered whether impaired frequency discrimination performance resulted from TMS-induced excitability changes in motor cortex, which may have disrupted subjects' ability to generate and report perceptual decisions correctly. To test this possibility, we compared EMG activity recorded from surface electrodes on the hand (Methods) during auditory-only trials in the Unimodal_A and Mixed blocks (Fig. S3). TMS over S1 rarely produced motor evoked potentials (MEPs) and similar rates of small-amplitude MEPs were measured in the two blocks ($t(11) = 1.45$, $p = 0.17$, $d = 0.54$) which did not differ in magnitude (Wilcoxon signed-ranks test, $p = 0.53$, $d = 0.05$). Moreover, the amplitude of evoked responses was uncorrelated with task performance ($r = -0.30$, $p = 0.25$), ruling out the possibility that performance impairments in the Mixed block were due to TMS influences on motor cortex excitability.

According to the speed-accuracy tradeoff, auditory discrimination performance during the Mixed block could have been lower if subjects adopted different response criteria or performance strategies which caused them to rush their decisions. To test this possibility, we evaluated response times (Fig. S4) and found significant RT differences over the blocks ($F_{2,24} = 15.29$, $p = 5.21e\text{-}05$, $\eta_p^2 = 0.56$; Baseline: 512 ± 57msec, Unimodal_A: 681 ± 66msec, Mixed: 889 ± 103msec). Importantly, rather than rushing their decisions, subjects took significantly more time to respond in the Mixed block compared to the baseline block ($t(12) = -4.94$, $p = 3.37e\text{-}04$, $d = 1.25$) and the Unimodal_A block ($t(12) = -2.96$, $p = 0.01$, $d = 0.66$). This pattern indicates that the reduced discrimination accuracies in the Mixed block were unlikely due to subjects hurrying their decisions. Instead, the longer RTs are consistent with the interpretation that subjects' ability to discriminate auditory frequency was selectively impaired by TMS over S1 during the Mixed block.

Our main finding is that manipulating S1 activity using TMS impaired the ability to perform an auditory frequency discrimination task when subjects also attended to tactile frequency information. Manipulating attention alone or applying TMS over a control region did not produce behavioural deficits in the frequency discrimination task. These results reveal that the functional coupling between the somatosensory and auditory cortical systems is gated by directing attention to vibration frequency. We also found that TMS severely impaired auditory intensity perception regardless of attention state or TMS target. These results indicate that TMS effects on audition differ depending on whether subjects perform a task that requires them to judge stimulus frequency rather than intensity, even when baseline performance on these tasks is standardized. Given the extensive perceptual interactions between touch and audition in the temporal frequency domain[10,18,22], it is perhaps unsurprising that neural activity in S1 can influence auditory processing – our data reveal that even TMS-evoked neural signals in S1, in the absence of bottom-up stimulus-driven activity, can be transmitted to neural circuits that support audition. TMS-evoked S1 activity could propagate along a number of cortico-cortical and thalamo-cortical pathways which connect the somatosensory and auditory systems[23–25]. Presumably, neural activity is similarly routed through these networks when actual sensory inputs are processed, which result in the co-activation of the somatosensory and auditory cortical systems. Outside of the sensory cortices, auditory and tactile information can also be represented in common or overlapping neural populations in frontal regions that support working memory and decision-making[26]. Although we cannot identify which downstream neural circuits inherit the perturbations induced by TMS over S1, our results reveal the critical role of feature-based attention in dynamically regulating the crossmodal coupling within this distributed functional network. These findings are consistent with the results of earlier studies which combined brain stimulation with neuroimaging to demonstrate that attention state can modulate the coupling between fronto-parietal control networks and sensory cortex[27,28]. Our results build on these earlier findings by showing that TMS can also reveal state-dependent coupling, as indexed by highly selective behavior changes, between cortical systems that are thought to support different sensory modalities which process the same stimulus features.

How might selective attention gate the crossmodal coupling between the somatosensory and auditory systems? A prevailing view is that oscillatory dynamics in intrinsic brain

activity control the flow of information through anatomical pathways[29,30]. By modulating the effective connectivity between different neural populations and networks, such mechanisms are hypothesized to support flexible and context-dependent behaviours. Selective attention may modulate neuronal oscillations[31]: Increasing the coherence between oscillatory activity in different neuronal populations can facilitate information transmission and integration[32–34]. In our paradigm, directing attention to tactile frequency may have synchronized the intrinsic activity in S1 and the cortical networks that support frequency processing for touch and audition. This coherent network state would then enable the perturbations induced by TMS over S1 to propagate to neural populations that mediate auditory frequency processing thereby disrupting auditory perception. If similar state-dependent transmission of stimulus-evoked activity underlies the perceptual interactions between audition and touch, our results could be interpreted as evidence for the general framework that multisensory interactions result from crossmodal binding through neural coherence[35].

Sensory cortical systems that are traditionally considered to be dedicated to individual modalities often co-activate, even when the inputs are presented in a single modality[16]. These co-activations are thought to reflect the binding of information-linked neural representations via the crossmodal spread of spatial attention[36,37] or feature-based attention[38–40]. The causal manipulation of activity in one sensory system using non-invasive brain stimulation can modulate processing in a different sensory modality[41], implying an interactive connectivity between sensory cortical systems. Our results demonstrate that the interactive coupling between cortical systems which support different sensory modalities is modulated by selective attention. This gating of crossmodal coupling by selective attention may critically support multisensory interactions and feature-specific perception.

METHODS

Participants. A total of 38 subjects participated in this study. Fifteen subjects (9 males; mean age ± SD: 23.73 ± 6.49 years) participated in the frequency discrimination experiment (Experiment 1). Fifteen subjects (7 males, mean age ± SD: 25.2 ± 6.86 years) participated in the intensity discrimination experiment (Experiment 2). Eight subjects (3 males; mean age ± SD: 25 ± 4.14 years) participated in the frequency discrimination experiment without TMS (Experiment 3). Two subjects participated in both

Experiments 1 and 2. Two subjects took part in all three experiments. Two subjects participated in both Experiments 1 and 3. Five subjects were left handed, according to the Edinburgh Handedness Inventory[42]. All participants reported normal tactile and auditory sensibilities. No participant reported a neurological or psychiatric history. No subjects reported contraindications to non-invasive transcranial brain stimulation[43]. All testing procedures were performed in compliance with the policies and procedures of the Baylor College of Medicine Institutional Review Board. All participants gave their written informed consent and were paid for their participation.

Stimuli and procedures. *Stimuli.* Auditory and tactile stimuli tested in the discrimination experiments comprised sine waves (sample rate: 44.1kHz; linear ramp: 30msec) that were digitally generated in Matlab (2011b, MathWorks) and presented with Psychtoolbox-3[44] running on a MacBook Pro (model A1278; OS X 10.9.5, 2.5 GHz Core i5, 4 GB of RAM). Auditory stimuli consisted of analog signals from one channel of the auxiliary port which were amplified (PTA2, Pyle) and delivered binaurally via noise-cancelling in-ear headphones (ATH-ANC23, Audio-Technica U.S., Inc). Participants also wore noise-attenuating earmuffs (Peltor H10A Optime 105 Earmuff, 3M) over the in-ear headphones which served to attenuate the sounds associated with TMS discharge and tactile stimulation. Tactile stimuli consisted of analog signals from the other channel of the auxiliary port which were amplified (Krohn-Hite Wideband Power Amplifier, model 7500) and delivered to the subject's right index finger through an electromechanical tactor (type C-2, Engineering Acoustics, Inc.). The stimuli tested in the tactile detection task consisted of brief taps delivered through a pair of miniature electromechanical tactors (type C-FT, Engineering Acoustics, Inc.) attached to the left and right index fingers. Tactors were fastened to the distal phalanges using self-adherent cohesive wrap bandages.

General procedures. The frequency and intensity discrimination experiments (Experiments 1 and 2, respectively) each comprised 3 sessions. Each session took place on separate days (mean inter-session interval ± SD, Experiment 1: 4.5 ± 2.7 days; Experiment 2: 3.8 ± 2.2). The general organization of the sessions was the same for the frequency and intensity discrimination experiments and the general procedures are detailed using the frequency discrimination experiment as the example.

During session 1, participants were trained to perform the frequency discrimination task

in both the auditory and the tactile modalities. After the initial training period, each participant's auditory and tactile frequency discrimination thresholds (FDT_A and FDT_T) were estimated with a Bayesian adaptive threshold-tracking procedure[45] (Supplementary information). We defined FDT as the minimum change in stimulus frequency required for a comparison stimulus to be perceived as higher in frequency compared to a 200-Hz standard stimulus 80% of the time. For the intensity discrimination experiment, we estimated each participant's intensity discrimination threshold (IDT), defined as the minimum change in stimulus amplitude required for a 200-Hz comparison stimulus to be perceived as more intense than a 200-Hz reference stimulus of a fixed supra-threshold intensity 80% of the time (Supplementary information). In preliminary experiments, we identified reference amplitudes for 200-Hz auditory and tactile stimuli such that they were perceived as equally intense (Supplementary information) in order to perform the crossmodal intensity judgments (Fig. S5). In sessions 2 and 3, subjects were tested with stimuli determined according to their FDT or IDT (see below), which enabled us to standardize baseline performance across subjects and tasks.

Sessions 2 and 3 involved TMS and were identical except for the location over which TMS was applied. The order of the sessions involving TMS over the S1 site or the control site was counterbalanced across subjects. Each session began with 2 baseline blocks during which subjects performed auditory-only or tactile-only frequency discrimination trials. Performance on these blocks, which were achieved in the absence of TMS, established the consistency of FDT values estimated in session 1 and provided a baseline against which we compared discrimination performance achieved with TMS. After the subject completed the baseline blocks, we performed TMS mapping to localize the motor hotspot in the subject's left motor cortex and to estimate her resting motor threshold (RMT) (see *M1 hotspot localization and RMT estimation*). After establishing RMT, the S1 site or control site was localized (see *Localization of S1 and control sites*) and participants began behavioral testing with TMS. In sessions with TMS over S1, subjects performed a tactile detection task before the discrimination task. For the discrimination task, each participant was tested on 1 $Unimodal_A$ block (auditory-only trials), 1 $Unimodal_T$ block (tactile-only trials), and 3 Mixed blocks (auditory-only, tactile-only, and crossmodal trials). Each block contained 42 trials and block order was randomized in each subject. Subjects were provided with 5-min rest intervals between each block.

Tactile detection task. Subjects performed a 4-alternative forced choice tactile detection task with and without TMS. On each trial, a brief (5-msec) tactile tap was delivered to the index finger on either the left hand, right hand, both hands, or there was no stimulation. Subjects, who maintained fixation throughout the trials, received a visual cue indicating the trial interval during which the tap(s) could have been delivered followed by a cue indicating that the subject should respond. On each trial, subjects verbally reported whether they detected touch on the left hand only ("Left"), right hand only ("Right"), both hands simultaneously ("Both"), or no stimulation ("None"). Tactile-stimulation trials (left, right, and both) were repeated 8 times each and no-stimulation trials were repeated 4 times in random order. The amplitude of the taps was set at 120% of each subject's tactile detection thresholds, determined with an adaptive threshold tracking procedure[45] (Supplementary information). These amplitudes were chosen to standardize detection performance across subjects at ~90% in the absence of TMS (Fig. S1).

Frequency discrimination task. Participants discriminated auditory and tactile frequencies in a 2-interval, 2-alternative forced choice (2AFC) paradigm (stimulus duration: 300msec; inter-stimulus interval: 500msec). Subjects were asked to report which interval contained the stimulus perceived to be higher in frequency by button press using their left hand. Throughout the test blocks, subjects maintained their gaze on a central fixation point on a computer screen.

Trials were organized according to 3 modality conditions (auditory-only, tactile-only, crossmodal). Within each modality condition, there were 3 frequency conditions resulting in a total of 9 unique stimulus pairs in Experiment 1 (Table S1). During each unimodal block, subjects were tested on 3 stimulus pairs (all of the same modality condition) individualized according to each subject's FDT estimates: 200Hz vs 200Hz-FDT, 200Hz vs 200Hz+FDT, and 200Hz+FDT vs 200Hz+2*FDT. The average (±SD) FDT_A and FDT_T were 3 ± 2Hz and 39 ± 16Hz, respectively. These thresholds, relative to 200Hz, are consistent with published reports[10,11]. Each stimulus pair was repeated 14 times in the unimodal blocks. During the Mixed blocks, the auditory-only and tactile-only trials were interleaved with crossmodal trials that also comprised 3 stimulus pairs individualized according to FDT: (auditory frequency vs tactile frequency) 200Hz vs 200Hz-FDT_T, 200Hz vs 200Hz+FDT_T, and 200Hz+2*FDT_T vs 200Hz+FDT_T. Over 3 Mixed blocks (42

trials each), each of the 9 unimodal and crossmodal stimulus pairs were repeated 14 times. During all blocks, the stimuli comprising each stimulus pair were presented in random order on each trial and the ordering of stimulus pairs was randomized over the block. Although the primary analyses focused on the auditory-only and tactile-only trials, we confirmed that subjects achieved performance levels on the crossmodal trials that exceeded chance level (Fig. S5).

We took multiple steps to ensure that participants performed the frequency discrimination task using frequency rather than intensity cues[10–13]. First, the stimuli were equated for perceived intensity in preliminary experiments (Supplementary information). Additionally, a random jitter (±10%) was applied to the subjectively-matched amplitudes on each trial to guarantee that differences in perceived intensity did not covary with frequency differences.

Intensity discrimination task. Participants discriminated auditory and tactile intensities in a 2AFC paradigm analogous to the frequency discrimination task. On each trial, subjects reported which of two supra-threshold stimuli was perceived to be more intense (stimulus duration: 300msec; inter-stimulus interval: 500msec; stimulus frequency: 200Hz). As in the frequency discrimination experiment, each subject was tested on 9 unique stimulus pairs (Table S2). To standardize baseline performance to ~80%, stimulus amplitudes were determined according to IDT_A and IDT_T established with adaptive threshold tracking procedures (Supplementary information). The average (±SD) IDT_A and IDT_T were 16.5 ± 9.8% of the auditory reference amplitude and 10.5 ± 4.1% of the tactile reference amplitude, respectively. The reference auditory and tactile signals measured as the output of the amplifiers were 1.9V and 2.3V, respectively.

Transcranial Magnetic Stimulation. *TMS setup, neuronavigation, and stimulation parameters*. Bi-phasic pulses were delivered through a figure-of-eight coil ($D70^2$ coil, wing diameter: 70mm) connected to a Magstim $Rapid^2$ stimulator unit (The Magstim Company). The location of the TMS coil over the participant's scalp was continuously tracked during the experiment using a frameless stereotaxic neuronavigation system (Brainsight, version 2.3.1, Rogue Research, Inc).

During discrimination trials in which TMS was applied, a train of 3 pulses (inter-pulse

interval: 67ms) was delivered over the TMS target site at the start of the second stimulus interval (Fig. 1a,c). TMS intensity was determined according to each subject's RMT. Although we aimed to stimulate all subjects at 120% RMT, we reduced TMS intensity to 110% RMT in subjects (6 in Experiment 1 and 5 in Experiment 2) who reported discomfort at 120% RMT. TMS intensity, expressed as a percentage of maximum stimulator output (MSO), was 61.8 ± 5% (Experiment 1) and 65.3 ± 7.13% (Experiment 2). TMS timing was controlled by Matlab and TMS trains were triggered by TTL pulses sent via a DAQ device (model USB-1208FS, Measurement Computing Corporation).

During trials in the detection task in which TMS was applied, a pair of TMS pulses (inter-pulse interval: 40ms) was delivered over S1. Relative to the time of the tactile stimulus, the first TMS pulse preceded the tap by 10msec[46,47]. TMS pulses were presented at the same relative time on trials that did not include tactile stimulation.

Electromyography (EMG). We recorded EMG activity from the first dorsal interosseous (FDI) muscle on the right hand using the built-in EMG setup in the Brainsight system. Two pre-gelled, disposable Ag/AgCl surface electrodes (Kendall Medi-Trace mini electrodes) were positioned over the FDI muscle while a ground electrode was placed over the styloid process of the ulna bone. Before placing the EMG electrodes, the skin was scrubbed with an alcohol wipe to reduce impedance.

M1 hotspot localization and RMT estimation. For each participant, we first localized the motor hotspot, the scalp site over left motor cortex (M1) where we reliably produced motor evoked potentials (MEPs) in the right FDI with a single TMS pulse using standard methods[48]. After localizing the motor hotspot, we established the subject's RMT, defined as the lowest stimulation intensity that evoked a response in the relaxed FDI muscle of 100-μV peak-to-peak amplitude in 5 out of 10 trials. The average RMT was 53 ± 4% MSO (Experiment 1) and 56 ± 7% MSO (Experiment 2). The localization of the M1 hotspot and estimation of RMT was performed in sessions 2 and 3 and RMT values were highly consistent across days (Fig. S6).

Localization of S1 and control sites. To localize the S1 site, we positioned the TMS coil over the M1 hotspot and applied single TMS pulses at 120% RMT as we systematically moved the coil posteriorly in 5-mm increments. The S1 site was the first location in which no MEPs were produced and subjects reported no TMS-associated

sensations of muscle activity. On average, this S1 site was posterior to the M1 hotspot by 28 ± 8mm (Experiment 1) and 27 ± 7mm (Experiment 2). For TMS over the control site, the TMS coil was positioned 3cm above the inion on the midline with the handle pointing upward.

Data analysis. All statistical analyses were performed in Matlab (2011b). We performed normality tests on all data using Kolmogorov-Smirnov tests.

Tactile detection task. Our primary analysis of the detection task was aimed at characterizing lateralized effects of TMS on tactile detection. Accordingly, we defined an extinction index (EI) as:

$$EI = L_{corr} - R_{corr}$$
$$L_{corr} = \left(L_L^{TMS} + B_L^{TMS}\right) - \left(L_L^{base} + B_L^{base}\right)$$
$$R_{corr} = \left(R_R^{TMS} + B_R^{TMS}\right) - \left(R_R^{base} + B_R^{base}\right)$$

where L_{corr} and R_{corr} corresponded to baseline-corrected detection rates on the left and right hands, respectively. Baseline-corrected rates were calculated as the difference in the detection rates achieved with TMS and without TMS (base). For the TMS and base-conditions, detection rates on each hand were summed over unimanual (L or R) and bimanual (B) trials. Positive EI values indicate higher baseline-corrected detection rates on the left hand (ipsilateral to the S1 cortex receiving TMS) compared to the right hand (contralateral to the S1 cortex receiving TMS). Because S1 contains a predominantly contralateral hand representation, we predicted TMS should selectively impair detection on the right hand if TMS disrupted perception at all[46,47]. Accordingly, a subject's discrimination data were included in group-level analysis only if he exhibited a positive EI value from the detection task (Fig. 2c). Two subjects were excluded from Experiment 1 and 3 subjects were excluded Experiment 2 on this basis.

Frequency and intensity discrimination tasks. Performance accuracy was quantified for each modality condition within the Baseline, Unimodal, and Mixed blocks. Because frequency discrimination performance did not differ significantly across stimulus pairs (Fig. S7), we collapsed over the frequency condition in the main analyses. For instance, performance on auditory-only trials was computed over 42 trials in the Baseline, Unimodal_A, and Mixed blocks. We similarly collapsed over the amplitude condition in analyses of the intensity discrimination task (Fig. S8).

In group-level analysis, to test whether discrimination accuracy on the auditory-only trials differed across blocks (Fig. 3), we performed a one-way repeated-measures ANOVAs with block (Baseline, Unimodal, Mixed) as the within-subjects factor. If the main effect of block was statistically significant ($p<0.05$), we performed post hoc tests which were adjusted for multiple comparisons using the Bonferroni correction. We reported the uncorrected p-values in the text. Performance with TMS over the S1 site and the control site were analyzed separately. We applied the same analysis logic to the tactile-only trials (Figs. 2) and the crossmodal trials (Fig. S5) in Experiment 1. Data from the intensity discrimination task in Experiment 2 (Fig. 3) were similarly analyzed.

EMG trace analysis. EMG data were analyzed for subjects included in the group-level analyses of the discrimination data. (Note that EMG data were available for 12/13 subjects in Experiment 1 due to a technical problem.) Trial-wise EMG traces were sorted according to modality condition (auditory-only, tactile-only trials) and block (Unimodal_A, Unimodal_T, Mixed). EMG traces were visually inspected to identify trials containing MEPs. For each condition and block, we calculated the likelihood that a TMS pulse produced a MEP. In group-level tests, we compared these likelihoods for the unimodal and the Mixed blocks using 2-tailed paired t-tests for each modality condition separately. To calculate MEP amplitudes, we computed the difference between the maximum and minimum voltages recorded in the interval ranging from 19–65msec after each TMS pulse. Restricting our analyses to this interval served to exclude artefactual voltage changes related to TMS discharge. In group-level tests, we compared MEP amplitudes between the unimodal and Mixed blocks for each modality condition using Wilcoxon signed-ranks tests.

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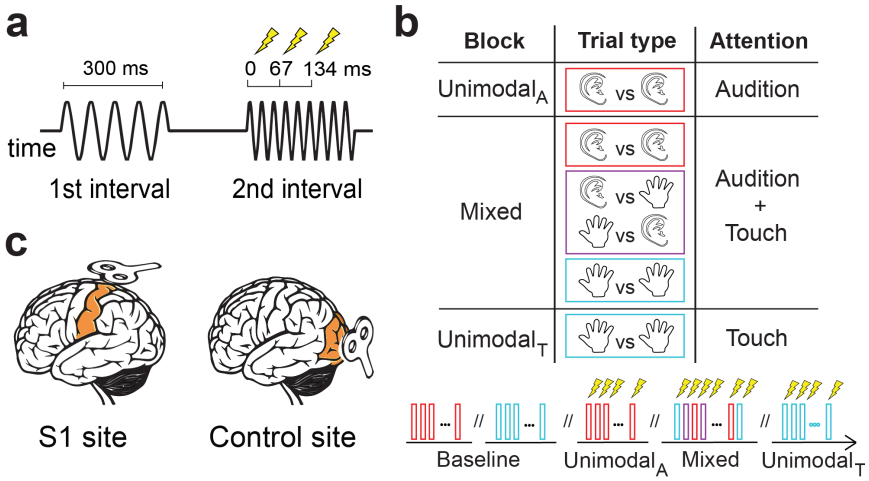

Figure 1 | Experimental design. a, Frequency discrimination task in which the participant judged which stimulus was perceived to be higher in frequency on each trial. In blocks involving TMS, a burst (3 pulses) was delivered on each trial during the 2nd interval. **b**, Separate blocks involving TMS (Unimodal$_A$, Unimodal$_T$, Mixed) comprised auditory-only trials (red), tactile-only trials (cyan), or both unimodal and crossmodal (purple) trials, respectively. With this design, participants were required to direct attention to audition, touch, or both modalities depending on the block. Block order was randomized. Prior to the TMS blocks, separate blocks of auditory and tactile discrimination trials (Baseline) were completed without TMS. **c**, In separate sessions, TMS was delivered over somatosensory cortex (S1 site) or visual cortex (Control site).

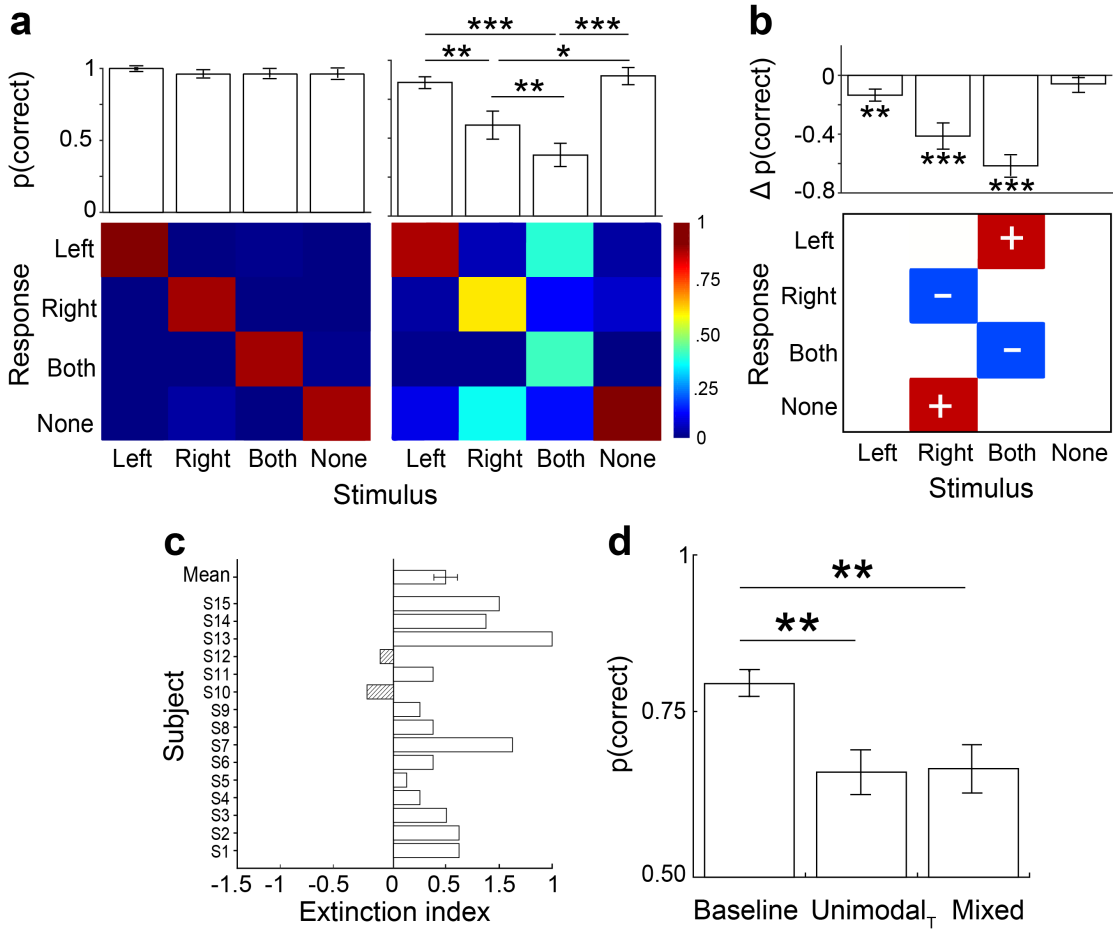

Figure 2 | TMS over S1 selectively impairs contralateral touch. a, Group-averaged (n=15) tactile detection performance and response probabilities (confusion matrix) in participants detecting taps delivered to the index finger on the left hand, right hand, both hands, or no touch without TMS (left) and with TMS over left S1 (right). **b,** Impaired performance with TMS over left S1 is associated with reduced detection of taps on the right hand: Subjects are more likely to report no stimulation on 'Right' trials and touch on the left hand or no touch on 'Both' trials. Red and blue cells are conditions where response probabilities increased or decreased, respectively, by greater than 20% with TMS relative to performance without TMS. **c,** Individual and group-averaged extinction index (EI) values indicating relative TMS effects on detection performance on the left and right hands. Positive EI values indicate that TMS reduced detection performance on the right hand (contralateral to the stimulated cortex) more than the left hand. The two subjects who failed to show positive EI values were excluded from subsequent analyses. **d,** Tactile frequency discrimination performance (n=13) during Baseline, Unimodal$_T$, and Mixed blocks. No TMS was applied during the Baseline block. Error bars indicate s.e.m. *** $p<0.001$, ** $p<0.01$, * $p<0.05$

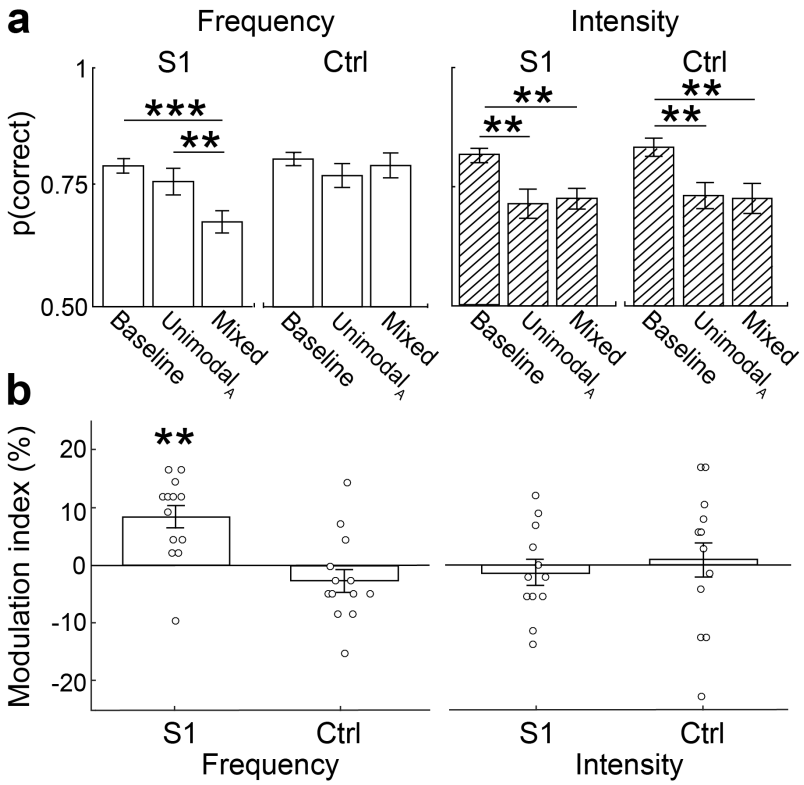

Figure 3 | Crossmodal TMS impairs auditory perception. a, Performance on auditory-only frequency discrimination trials (solid, n=13) and intensity discrimination trials (striped, n=12) for the different blocks (Baseline, Unimodal$_A$, Mixed). No TMS was applied during the Baseline block. Frequency perception is impaired only during the Mixed block by TMS over somatosensory cortex (S1), but not over a control site (Ctrl). In contrast, TMS impaired intensity perception regardless of block or site. **b,** Group-averaged (bar) and individual-subject (dots) modulation index (MI) values for frequency discrimination task (left) and intensity discrimination task (right) with TMS over S1 or over the control site. Positive MI values indicate reduced performance in the Mixed block relative to the Unimodal$_A$ block. Error bars indicate s.e.m. *** $p<0.001$, ** $p<0.01$, * $p<0.05$.