

Tactile Temporal Processing in the Auditory Cortex

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Abstract

■ Perception of the outside world results from integration of information simultaneously derived via multiple senses. Increasing evidence suggests that the neural underpinnings of multisensory integration extend into the early stages of sensory processing. In the present study, we investigated whether the superior temporal gyrus (STG), an auditory modality-specific area, is critical for processing tactile events. Transcranial magnetic stimulation (TMS) was applied over the left STG and the left primary somatosensory cortex (SI) at different time intervals (60, 120, and 180 msec) during a tactile temporal discrimination task (Experiment 1) and a tactile spatial discrimination task (Experiment 2). Tactile temporal processing was disrupted when TMS was applied

to SI at 60 msec after tactile presentation, confirming the modality specificity of this region. Crucially, TMS over STG also affected tactile temporal processing but at 180 msec delay. In both cases, the impairment was limited to the contralateral touches and was due to reduced perceptual sensitivity. In contrast, tactile spatial processing was impaired only by TMS over SI at 60–120 msec. These findings demonstrate the causal involvement of auditory areas in processing the duration of somatosensory events, suggesting that STG might play a supramodal role in temporal perception. Furthermore, the involvement of auditory cortex in somatosensory processing supports the view that multisensory integration occurs at an early stage of cortical processing. ■

INTRODUCTION

Perception is inherently multisensory and is therefore supported by a complex network involving not only specialized modality-specific but also heteromodal brain regions. The advantages of having multiple senses are obvious: Although each sense is specialized for capturing specific sensory stimulations, their cooperation increases the likelihood of encoding and interpreting information about biologically relevant events. More specifically, audio–tactile interactions are of particular relevance for the present experiment.

The impact of audio–tactile integration in behavioral tasks has been largely documented in humans. For instance, sounds can dramatically affect touch as it is evident from the “parchment skin illusion” (Guest, Catmur, Lloyd, & Spence, 2002; Jousmaki & Hari, 1998) in which the sensation coming from rubbing the hands together or touching abrasive surfaces can be modified by manipulating the frequency of sounds associated with the tactile stimuli. Furthermore, robust spatially modulated audio–tactile interactions in the part of space immediately surrounding one’s head have been shown through a temporal order judgment paradigm (Kitagawa, Zampini, & Spence, 2005).

Cross-modal audio–tactile effects are particularly relevant for individuals deprived of a given sensory modality. For instance, vibrotactile stimuli can improve the audi-

tory processing of hearing-impaired persons, who can perceive sounds, and even speech, using their sense of touch (Schurmann, Caetano, Jousmaki, & Hari, 2004; Levanen & Hamdorf, 2001; Sherrick, 1984; Gault, 1926). Similarly, auditory feedback during tactile exploration is informative about the touched textures, especially in patients using a hand prosthesis (Lundborg & Rosen, 2001).

The neurophysiological correlates of these audio–tactile interactions involve higher order multisensory association areas, that is, intraparietal sulcus, superior temporal polysensory area, and pFC (Beauchamp, Yasar, Frye, & Ro, 2008; Calvert, 2001), and even areas classically viewed as unisensory, such as primary visual (VI), auditory (AI), and somatosensory (SI) cortices (Ghazanfar & Schroeder, 2006; Schroeder & Foxe, 2005). With respect to audio–tactile interactions, intracranial recordings in macaques have shown direct somatosensory input to the caudomedial (CM) auditory belt area. CM is adjacent to AI and receives direct projections from it. Cutaneous stimulation, proprioceptive stimulation at the elbow, and vibrotactile stimulation activated the CM belt area (Fu et al., 2003; Schroeder et al., 2001). In addition, isolation of single multisensory neurons showed that responses occurred at a slightly longer latency for cutaneous compared with auditory input (Fu et al., 2003).

In humans, brain imaging studies have revealed possible correlates of audio–tactile interactions in the secondary somatosensory cortex (SII), in the auditory areas, and in the posterior parietal cortex (Iguchi, Hoshi, Nemoto, Taira, & Hashimoto, 2007; Gobbele et al., 2003; Foxe et al., 2000,

2002; Lutkenhoner, Lammertmann, Simoes, & Hari, 2002; Calvert, 2001). A recent magneto-encephalographic (MEG) study in normal-hearing adults (Caetano & Jousmaki, 2006) has shown that vibrotactile stimuli elicit activations not only in the SI and SII but also in the auditory cortices. More specifically, initial responses to vibrotactile stimuli, peaking around 60 msec, were observed in SI, followed by transient responses at 100–200 msec in SII and auditory cortices. Additional auditory-sustained activation was identified at 200–700 msec. These results are in line with the findings obtained in a congenitally deaf adult (Levanen, Jousmaki, & Hari, 1998). In addition, functional brain imaging recording (fMRI; Schurmann, Caetano, Hlushchuk, Jousmaki, & Hari, 2006) showed that right vibratory stimuli and even tactile pulses (without vibratory features) have access to the left superior temporal gyrus (STG), corresponding to Brodmann's area (BA) 22, a subregion of the human auditory cortex along the STG and the human homologue of the macaque monkey CM belt region (Kaas, Hackett, & Tramo, 1999). This area is known to receive somatosensory input in the monkey and exactly corresponds to BA 22/39 (see also above Schroeder et al., 2001).

The involvement of auditory areas in tactile functions is not completely unexpected if one considers the similarities existing between skin sensation and hearing (von Bekesy, 1960); for instance, vibrotactile and auditory stimuli share essentially similar temporal patterns, and both senses can detect low-frequency vibrations. Thus, the auditory cortices may play a key role in the analysis of some properties of tactile information, accompanying and complementing the modality-specific processing within the somatosensory cortex. Above all, given that the auditory cortex is highly sensitive to temporal stimulus attributes (Boemio, Fromm, Braun, & Poeppel, 2005; Tervaniemi & Hugdahl, 2003), it is plausible that auditory cortex could be involved even in the processing of the temporal features of tactile stimuli.

On the basis of these considerations, in the present experiment, we sought to prove the pivotal involvement of the auditory cortex in the processing of tactile stimuli by using transcranial magnetic stimulation (TMS). Previous brain imaging studies (Caetano & Jousmaki, 2006; Foxe et al., 2002) have suggested that the processing of tactile stimuli in humans involves associative auditory areas in addition to the somatosensory cortex.

TMS can provide insight into the causal role of particular regions of the cerebral cortex in specific behaviors (Pascual-Leone, Walsh, & Rothwell, 2000). This technique is used to disrupt ongoing neuronal activity in a localized cortical area by briefly inducing an electrical field in the tissue below the magnetic coil. Besides a better spatial resolution than PET and fMRI (Walsh & Cowey, 2000), TMS also has a higher temporal resolution than fMRI, MEG, or electroencephalography (Cowey, 2005): By varying the timing of TMS stimulation during the execution of a task, it is possible to demonstrate the time course

of cortical activity in a given cognitive process (Fogliata et al., 2007; Pascual-Leone et al., 2000).

First, we were interested in addressing the causal role and the temporal course of somatosensory processing in the left STG in addition to SI of the same hemisphere during a tactile temporal discrimination task. Both these areas have been shown to respond to right-sided tactile stimuli (Schurmann et al., 2006). For this purpose, TMS was applied over the left STG and SI at different time intervals in accordance with the time course reported in previous MEG studies (Caetano & Jousmaki, 2006; Levanen et al., 1998). Because hemispheric asymmetry for temporal processing depends on the stimulus duration, here we used tactile stimuli of short duration (25–50 msec), which are expected to be processed essentially in the left hemisphere (Boemio et al., 2005).

A second experiment was then conducted to assess the specificity of the STG involvement with respect to temporal processing. To this aim, we applied TMS over the left STG and SI at different time delays during a tactile spatial discrimination task.

In both experiments, using analyses based on the signal detection theory (Green & Swets, 1966), we verified whether interfering with STG and SI activity by TMS directly affects perceptual sensitivity and/or the response criterion during the experimental tasks.

METHODS

Participants

Thirteen healthy participants took part in Experiment 1 (11 right-handed subjects; 6 women and 7 men; mean age = 35 years). Eight of the same subjects were subsequently tested also in Experiment 2 (6 women and 2 men, all right-handed subjects; mean age = 29 years). All participants gave written informed consent. They were naive to the experimental procedure and to the purpose of the study. All the accepted recommendations for the use and safety of TMS (Wassermann, 1998) were applied. None of the participants had neurological, psychiatric, or other relevant medical problems or had any contraindication to TMS (Wassermann, 1998). The protocol was carried out in accordance with the ethical standards of the Declaration of Helsinki (*British Medical Journal*, 1991, Vol. 302, p. 1194) and was approved by the ethical committee of the University of Milano-Bicocca.

Tactile Temporal Discrimination Task

Custom-made electromagnetic solenoids (Heijo Electronics, Beckenham, UK; www.heijo.com), attached to the participants' index fingers, were used to deliver the tactile stimulations. Two types of stimuli were randomly delivered to either hand, and they differed with respect of their temporal duration: The target stimulus consisted of a long vibration of 25 msec (three 5-msec on phases, with two

5-msec off intervals), and the control stimuli consisted of a short vibration of 15 msec (two 5-msec on phases, with one 5-msec off interval). White noise delivered from two external loudspeakers throughout was used to mask any auditory cues from the tactile stimulators, which were, however, extremely silent. Stimulus types were randomly presented (see below for randomization details); the intertrial interval varied between 6 and 8 sec to prevent carryover effects of TMS on cortical excitability (Walsh & Pascual-Leone, 2003). During the temporal discrimination task, subjects attempted to discriminate the target stimulus from the control stimulus. More specifically, on each trial, the participant was requested to report the long vibration (target) by saying “yes” when the target was presented and to refrain from responding to the short vibration (control stimulus). Verbal “yes” responses were recorded and analyzed off-line. Sequence and timing of both the tactile and the TMS stimuli were under computer control (E-prime software; Psychology Software Tools, Inc., Pittsburgh, PA, www.psychtoolbox.org; see Figure 1A).

Tactile Spatial Discrimination Task

The stimuli and the procedure were identical to those used in Experiment 1. The only difference was in the stimulus type: now subjects were asked to discriminate the spatial length of touches. Three vibrotactile stimulators

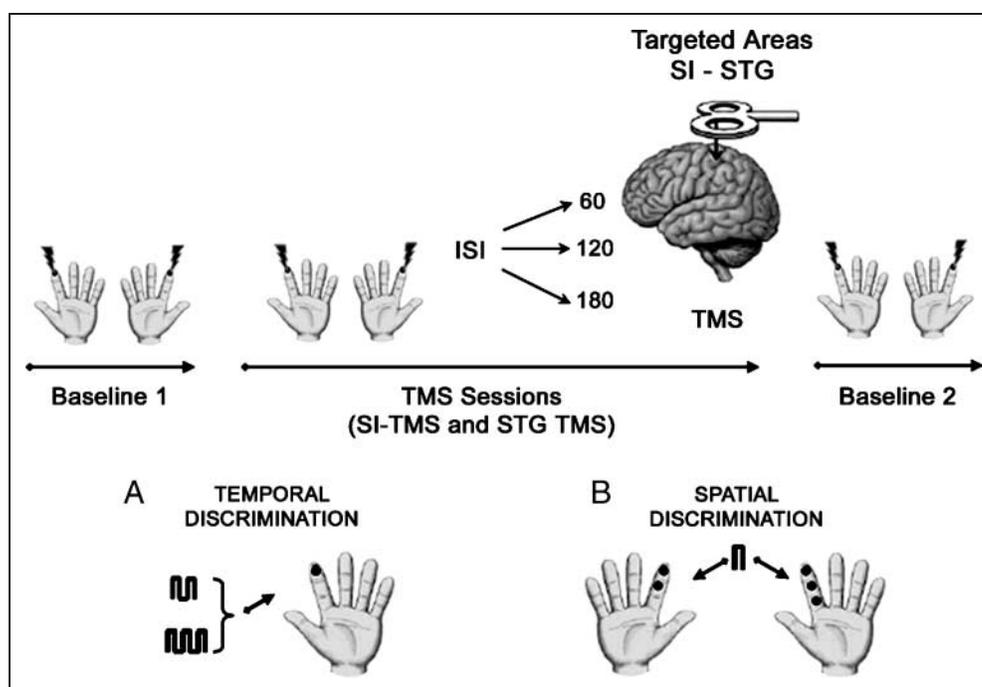
(diameter = 0.8 cm) were strapped to the participant’s index finger. Two types of stimuli were randomly delivered to either hand: The target stimulus consisted of a spatially long vibration produced by the simultaneous switch on of the three vibrotactile stimulators. The control stimulus consisted of a spatially short vibration produced by switching on only two of the three vibrotactile stimulators (the first plus the second stimulator or the second plus the third stimulator). Both the target and the control stimuli had the same duration of 10 msec (one 5-msec on phases, with one 5-msec off interval).

During the spatial discrimination task, subjects had to discriminate the target stimulus from the control stimulus by verbally reporting the spatially long vibration (target; saying “yes” when this was presented) and by refraining from responding to the spatially short vibration (control stimulus). Verbal “yes” responses were recorded and analyzed off-line. Sequence and timing of both the tactile and the TMS stimuli were under computer control (E-prime software; Psychology Software Tools, Inc., www.psychtoolbox.org; see Figure 1B).

TMS Protocol

In both experiments, single-pulse TMS was delivered using a Magstim super rapid transcranial magnetic stimulator (Magstim, Whitland, UK) connected with a figure-of-eight

Figure 1. Overview of the experimental procedure. Subjects attempted to discriminate the duration of the target stimulus from the control stimulus. In the temporal task (A), the target stimuli consisted of a long vibration of 25 msec (three 5-msec on phases, with two 5-msec off interval) and the control stimuli consisted of a short vibration of 15 msec (two 5-msec on phases, with one 5-msec off interval). In the spatial task (B), three vibrotactile stimulators (diameter = 0.8 cm) were strapped to the participant’s index finger. The target stimulus consisted of a spatially long vibration produced by the simultaneous switch on of all the three vibrotactile stimulators. The control stimuli consisted of a spatially short vibration produced by switching on just two stimulators (the first plus the second stimulator or the second plus the third stimulator). Both the target and the control stimuli lasted 10 msec (one 5-msec on phases, with one 5-msec off interval). In both tasks, stimuli were randomly delivered to the left or to the right index finger. In the TMS sessions, TMS single-pulses were delivered to the targeted areas (i.e., left SI or left STG) at different ISI (i.e., 60, 120, and 180 msec, given in a random order) after the tactile delivery. Subjects underwent two baseline sessions, one preceding (Baseline 1) and one following (Baseline 2) the two TMS sessions (SI-TMS and STG-TMS). The order of the TMS sessions was counterbalanced across participants (figure adapted from Harris et al. 2002).



coil (70-mm diameter), allowing focal cortical stimulation (Pascual-Leone et al., 2000). Before the experiment, the motor threshold (MT) at rest was determined for each participant. MT was defined as the minimum intensity that induced a visible contraction in the contralateral first interosseus dorsalis muscle on at least three of six consecutive single TMS pulses. The mean \pm SD MT was $65\% \pm 7\%$ of the maximal output of the stimulator, which is within the safety limits according to the guidelines for rTMS (Wassermann, 1998). The stimulus intensity used during the experiment was set at 120% of the individual MT. Participants tolerated TMS well and did not report any adverse effects.

In both Experiments 1 and 2, TMS was applied over the left SI or the left STG. To appropriately localize these sites on the subject's scalp, we estimated Talairach coordinates underlying coil locations for each participant by using the SofTatic Navigator system (EMS, Bologna, Italy, www.emsmedical.net). This is a frameless stereotaxic image guidance system that allows reconstructing the cerebral cortex in Talairach coordinates based on an MRI-constructed stereotaxic template (accuracy of ± 1 cm, Talairach space; Talairach & Tournoux, 1988). The SofTatic Navigator system therefore permits the computation of an estimated MRI of each participant to guide the TMS coil positioning. In particular, this frameless stereotaxic neuro-navigational system consists of a graphic user interface and a three-dimensional Fastrak digitizer (Polhemus Inc., Colchester, VT) having four receivers and one stylus. Three of these receivers were placed stably on the subject's head. The fourth receiver was accurately positioned on the TMS coil to monitor its position (x , y , and z Cartesian coordinates) and orientation. The stylus was used to register craniometric landmarks on the subject's head. With this system, the estimated MRI images are automatically calculated by means of a warping procedure by operating on a generic MRI volume (template) based on a set of points digitized from the subject's scalp. With respect to using the individual subject's MRIs for the coil localization, the mean \pm SD accuracy of the estimated MRI images obtained with the above procedure is 4.06 ± 1.54 mm; that is, this error is comparable to the spatial accuracy of TMS at MT intensity using the individual subject's MRIs (Herwig et al., 2001). This localization system has been successfully used in several previous TMS studies (Bolognini & Maravita, 2007; Urgesi, Candidi, Ionta, & Aglioti, 2007; Urgesi, Berlucchi, & Aglioti, 2004; Harris & Miniussi, 2003).

In our experiments, the stimulation sites within the left SI and the left STG were chosen according to the coordinates reported by a previous fMRI study (Schurmann et al., 2006): SI (BA 1), $x = -45$, $y = -23$, $z = 53$; and STG (BA 22), $x = -44$, $y = -31$, $z = 12$. Participants wore a tightly fitting Lycra bathing cap used to mark these stimulation sites throughout while the coil was supported and held in place by a mechanical device.

The coil was positioned over SI (i.e., SI-TMS) or STG (i.e., STG-TMS) in separate sessions. In both Experiments

1 and 2, on each trial of all TMS sessions, a tactile vibration (long or short) was followed by a TMS pulse after an ISI of 60, 120, or 180 msec selected randomly.

Experimental Procedure

Throughout Experiments 1 and 2, subjects were comfortably seated in an armchair, in a quiet, dimly illuminated room. Each experiment consisted of five sessions: a training session and four experimental sessions. Between the sessions, subjects were allowed to rest and to have refreshments. The whole procedure lasted about 2 hr.

The training session preceded the experimental ones and allowed participants to familiarize with the temporal discrimination task. Verbal feedback was given concerning the subject's performance after each trial during the training phase only.

In both Experiments 1 and 2, the experimental sessions consisted of two baseline sessions: one preceding (Baseline 1) and one following (Baseline 2) the two TMS sessions. In each baseline session, 16 target stimuli and 16 distractors to either the left or the right index finger were delivered, for a total of 64 trials. During each TMS session (SI-TMS and STG-TMS), the same number of targets as the baseline was delivered for each different ISI (i.e., the interval between the onset of the stimuli and the onset of the TMS pulse could be of 60, 120, or 180 msec). This yielded a total number of 192 trials for each TMS session, given in four different blocks (i.e., 48 trials in each block), separated by short pauses. The order of the TMS sessions was counterbalanced across participants (see Figure 1).

RESULTS

Statistical analysis was performed using Statistica for Windows, release 6.0 (StatSoft Italia SRL). In both Experiments 1 and 2, we first analyzed the mean percentages of errors (target omissions plus incorrect responses to the control stimulus, that is, false alarms), via a repeated measures ANOVA with Side (right hand vs. left hand) and Condition (baseline, SI-TMS at ISI 60 msec, SI-TMS at ISI 120 msec, SI-TMS at ISI 180 msec, STG-TMS at ISI 60 msec, STG-TMS at ISI 120 msec, and STG-TMS at ISI 180 msec) as main factors.

In addition, to determine whether TMS stimulation over STG and SI directly disrupted tactile perceptual sensitivity or simply biased subjects' response criterion, we further analyzed the data following the signal detection theory (Green & Swets, 1966). Such analyses allow assessing the contribution of stimulus-related (i.e., perceptual sensitivity, d') and subject-related (i.e., response bias, c) influences on performance (Green & Swets, 1966). Changes in sensitivity (d') and in response criterion (c) were quantified for each experimental condition.

Analyses of sensitivity and response bias were also run via a 2 (Side) \times 7 (Condition) ANOVA.

When appropriate, pairwise comparisons were run using the Newman-Keuls test.

Because there was no difference between the two baseline conditions (as assessed by *t* tests: Experiment 1—errors, Baseline 1 = 13% versus Baseline 2 = 9%, $p = .3$; d' , Baseline 1 = 3.27 versus Baseline 2 = 3.22, $p = .6$; c , Baseline 1 = 0 versus Baseline 2 = -0.05 , $p = .8$. Experiment 2—errors, Baseline 1 = 12% versus Baseline 2 = 9%, $p = .4$; d' , Baseline 1 = 3.59 versus Baseline 2 = 3.46, $p = .8$; c , Baseline 1 = 0.44 versus Baseline 2 = 0.74, $p = .3$, data from the two baseline sessions were collapsed.

Experiment 1

Accuracy

The ANOVA revealed a significant main effect of the factor Side, $F(1,12) = 10.07$, $p < .008$, $p\eta^2 = .46$, because errors increased when responding to right-sided stimuli as compared with left-sided ones (13% vs. 10%). The significant factor Condition, $F(6,72) = 4.64$, $p < .0004$, $p\eta^2 = .28$, was witnessed by an increase of errors in two conditions: SI-TMS with an ISI of 60 msec (15%) and STG-TMS with an ISI of 180 msec (13.8%). Although these two conditions did not differ between each other ($p = .4$), SI-TMS at ISI 60 differed from all the other conditions (baseline = 11%, SI-TMS at ISI of 120 msec = 8.8%, SI-TMS at ISI of 180 msec = 9%, STG-TMS at ISI of 60 msec = 10.3%, SI-TMS at ISI of 120 msec = 10.7%, $p < .02$ for all comparisons); finally, STG-TMS at ISI of 180 msec significantly differed from SI-TMS at ISI of 120 msec (8.8%, $p < .02$) and SI-TMS at ISI of 180 msec (9%, $p < .02$).

Even more interestingly, the Side \times Condition interaction, $F(6,72) = 4.36$, $p < .0008$, $p\eta^2 = .26$, showed that errors increased specifically for right-sided stimuli, contralateral to TMS but only with SI-TMS at 60 msec of ISI (19%) and with STG-TMS at 180 msec of ISI (18%), with these two conditions differing from all the other conditions ($p < .001$ for all comparisons). There was no difference between SI-TMS at ISI of 60 msec and STG-TMS at ISI of 180 msec ($p = .7$). Finally, no significant difference was found among the experimental conditions for the left-sided, ipsilateral stimuli (see Figure 2A).

Signal Detection Measures (d' and c Values)

The analysis of sensitivity (d') showed a significant main effect of Side, $F(1,12) = 29.49$, $p < .0001$, $p\eta^2 = .71$, with a significant difference between right-sided stimuli (2.89) and left-sided stimuli (3.44). The main effect of Condition, $F(6,72) = 2.36$, $p < .04$, $p\eta^2 = .16$, showed a significant difference in sensitivity between ISIs of 60 and 120 msec during the TMS stimulation of SI (2.65 vs. 3.48, $p < .03$).

Of major interest was the significant Side \times Condition interaction, $F(6,72) = 3.78$, $p < .003$, $p\eta^2 = .24$, which highlighted the specific perceptual basis of the TMS interference over the targeted areas. Indeed, only SI-TMS at ISI of 60 msec (2.04) and STG-TMS at ISI of 180 msec (2.35) selectively reduced perceptual sensitivity for the process-

ing of contralateral, right-sided tactile stimuli ($p < .03$ for all comparisons); this effect was similar in the two conditions, namely, SI-TMS at ISI of 60 msec and STG-TMS at ISI of 180 msec ($p = .3$; see Figure 2B).

The analysis of response bias showed a main effect of Condition, $F(6,72) = 4.11$, $p < .001$, $p\eta^2 = .25$, with significantly lower c values for ISI of 60 msec during either SI (-0.29) and STG (-0.3) stimulations, as compared with SI-TMS at ISI of 180 msec (0.13, $p < .03$) and STG-TMS at ISI of 120 msec (0.15, $p < .04$) or of 180 msec (0.15, $p < .03$). This decrease in criterion value reflects a more liberal response criterion, with subjects more likely to report the target stimulus; given that this response bias occurred independently of the stimulated area and side of the tactile stimulus, it might represent an aspecific alertness effect induced by the early onset (i.e., 60 msec) of the TMS pulse. The main effect of Side, $F(1,12) = 1.02$, $p = .3$, $p\eta^2 = .08$, and Side \times Condition interaction, $F(6,72) = 1.53$, $p = .2$, $p\eta^2 = .11$, did not reach significance (see Figure 2B).

Experiment 2

Accuracy

The ANOVA revealed a significant main effect of the factor Side, $F(1,7) = 9.56$, $p < .02$, $p\eta^2 = .56$: Subjects were less accurate when responding to right-sided stimuli as compared with left-sided ones (14% vs. 11%). The significant factor Condition, $F(6,42) = 3.70$, $p < .005$, $p\eta^2 = .35$, showed a significant difference only between STG-TMS with an ISI of 60 msec (9%) and both SI-TMS with an ISI of 60 msec (15%, $p < .02$) and 180 msec (15%, $p < .02$).

Crucially, there was a significant Side \times Condition interaction, $F(6,42) = 4.75$, $p < .0009$, $p\eta^2 = .39$: Errors increased specifically for right-sided stimuli, contralateral to TMS but only with SI-TMS at 60 msec of ISI (20%) and with SI-TMS at 120 msec of ISI (19%), with these two conditions differing from all the other conditions ($p < .01$ for all comparisons), except for SI-TMS at 180 msec of ISI when responding to right touches (17%, $p = .3$). There was no difference between SI-TMS at ISI of 60 msec and SI-TMS at ISI of 120 msec ($p = .9$). No significant difference was found among the experimental conditions for the left-sided stimuli (see Figure 3A).

Signal Detection Measures (d' and c Values)

Changes in sensitivity (d') and in response criterion (c) were then quantified for each experimental condition and analyzed via a two-way ANOVA.

The analysis of d' showed a significant main effect of Side, $F(1,7) = 7.68$, $p < .03$, $p\eta^2 = .52$, with a significant difference between right-sided stimuli (2.92) and left-sided stimuli (3.17). The main effect of Condition, $F(6,42) = 6.03$, $p < .0001$, $p\eta^2 = .46$, showed a significant difference between the baseline (3.51) and the TMS stimulation of SI

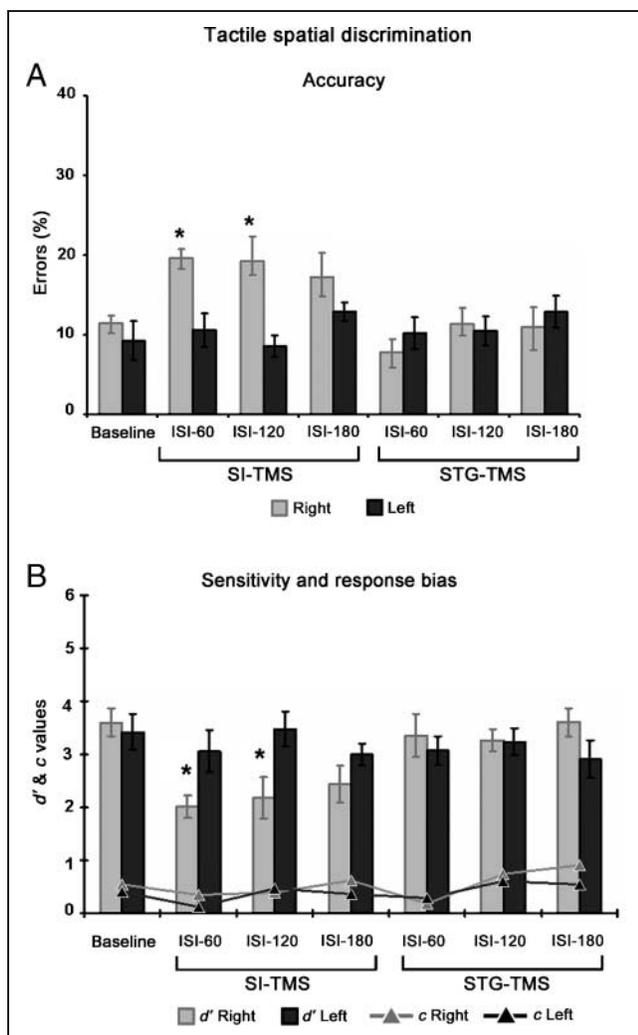


Figure 3. Effects of TMS on tactile spatial discrimination. (A) Accuracy. Mean percentages of errors in spatial discrimination are presented for each experimental condition (baseline; SI-TMS and STG-TMS sessions with ISI of 60, 120, and 180 msec). Gray bars represent the accuracy for right-sided stimuli; black bars represent the accuracy for left-sided stimuli. Asterisks indicate a significant decrease of accuracy for the contralateral tactile stimuli induced by SI-TMS at ISI of 60 and 120 msec. Error bars denote standard errors. (B) Perceptual sensitivity and response criterion. d' (bars) and c (lines) values in spatial discrimination are presented for each experimental condition. Gray bars represent the sensitivity (d') for the right-sided stimuli; black bars represent the sensitivity for the left-sided stimuli. Response criteria (c) are represented by gray triangles for the right-sided stimuli and by black triangles for the left-sided stimuli. Asterisks indicate a significant decrease of sensitivity for the contralateral tactile stimuli induced by SI-TMS at ISI of 60 and 120 msec. Error bars denote standard errors.

significantly higher c values with STG-TMS with ISI of 180 msec (0.73), as compared only to SI-TMS at ISI of 60 msec (0.23, $p < .05$) and STG-TMS at ISI of 60 msec (0.24, $p < .04$). The main effect of Side, $F(1,7) = 1.12$, $p = .3$, $p\eta^2 = .14$, and Side \times Condition interaction, $F(6,42) = 0.86$, $p = .5$, $p\eta^2 = .11$, did not reach significance (see Figure 3B).¹

Control Experiment

Because in the previous experiments we have used a 70-mm figure-of-eight coil, it might be argued that spatial resolution was not sufficiently high and that somatosensory associative areas (SII) or part of it were stimulated rather than the STG. Thus, we run a control experiment with a smaller coil (50 mm) to increase the spatial resolution of our TMS. We tested seven new subjects by using the same experimental procedure of Experiment 1. Mean percentages of error, d' , and c values were then separately analyzed via a 2 (Side) \times 7 (Condition) ANOVA (for details, see Experiment 1). Data from the two baseline sessions were collapsed as in the previous analysis, given that there was no difference between them (as assessed by t tests: errors, Baseline 1 = 10% vs. Baseline 2 = 12%, $p = .7$; d' , Baseline 1 = 3.04 vs. Baseline 2 = 3.19, $p = .5$; c , Baseline 1 = 0.35 vs. Baseline 2 = 0.12, $p = .2$). Overall, the experiment confirmed previous results of Experiment 1.

Accuracy

The ANOVA revealed a significant main effect of the factor Side, $F(1,6) = 8.97$, $p < .02$, $p\eta^2 = .45$, showing a significant difference between right-sided (18%) and left-sided stimuli (12%). The factor Condition, $F(6,36) = 4.89$, $p < .001$, $p\eta^2 = .32$, showed a significant difference only between STG-TMS with an ISI of 180 msec (20%) and the other conditions ($p < .02$ for all comparisons), except for SI-TMS with an ISI of 60 msec (18%, $p = .2$), the last differing only from baseline (11%, $p < .05$).

Crucially, there was a significant Side \times Condition interaction, $F(6,36) = 4.33$, $p < .003$, $p\eta^2 = .28$, showing again the disrupting effects of SI-TMS at ISI of 60 msec (23%) and of STG at ISI of 180 msec (27%) over response to contralateral touches as compared with the baseline (11%) and the other conditions ($p < .01$ for all comparisons; see Figure 2C).

Signal Detection Measures (d' and c Values)

The analysis of sensitivity showed a significant main effect of the factor Side, $F(1,6) = 8.12$, $p < .03$, $p\eta^2 = .64$, highlighting the reduced sensitivity for contralateral tactile stimuli (right-sided = 2.44 vs. left-sided = 3.01), and of the factor Condition, $F(6,36) = 4.1$, $p < .003$, $p\eta^2 = .21$, showing a significant difference only between the baseline (2.22) and the SI-TMS at ISI of 60 msec (2.22, $p < .03$) and of STG at ISI of 180 msec (2.29, $p < .04$). The significant Side \times Condition interaction, $F(6,36) = 2.85$, $p < .02$, $p\eta^2 = .26$, showed a decrease of sensitivity for only contralateral, right-sided tactile stimuli induced only by SI-TMS at ISI of 60 msec (1.65) and STG-TMS at ISI of 180 msec (1.74) as compared with all other conditions ($p < .02$ for all comparisons; see Figure 2D).

Finally, the analysis of response bias showed a main effect of Condition, $F(6,36) = 2.63$, $p < .03$, $p\eta^2 = .28$: SI-TMS at

ISI of 60 msec (-0.16) significantly differed from SI-TMS at ISI of 180 msec (0.35 , $p < .05$) and STG-TMS at ISI of 180 msec (0.33 , $p < .05$). A significant Side \times Condition interaction, $F(6,36) = 2.66$, $p = .04$, $p\eta^2 = .58$, was also found, showing a change in the response criterion (i.e., more liberal) in response to left-sided stimuli with SI-TMS at ISI of 180 msec (-0.28 , $p < .05$) as compared with responses to right-sided touches with SI-TMS at 180 msec (0.4) and STG-TMS at ISI 120 msec (0.47) and to responses to left-sided touches with STG-TMS at ISI 180 msec (0.35 ; see Figure 2D).

DISCUSSION

The present study investigated the causal involvement of the human STG and SI in tactile processing in the temporal and spatial domains. The main finding is that the left STG (BA 22 or Wernicke area in humans, akin to the posterior auditory belt area in the monkey) plays a key role in temporal processing of contralateral tactile stimuli, although being not involved in tactile spatial processing. Instead, the contribution of left SI (BA 1) is not specific for timing tactile events because TMS over SI impaired subjects' performance also in the spatial discrimination task, being therefore involved in processing both spatial and temporal aspects of tactile information. In addition, the time-dependent specificity of the involvement of STG and SI gives insight into the chronometry of tactile stimulus processing in these areas: SI would be implied in an early analysis of temporal (around 60 msec) and spatial (60–120 msec) features of tactile information, whereas STG seems to be involved in a later stage of tactile temporal processing (around 180 msec).

The more critical and original result of this study is thus the effect of TMS stimulation over STG during the temporal task. To our knowledge, this study provides the first causal demonstration of the recruitment of the contralateral associative auditory cortex during temporal discrimination of tactile stimuli. Crucially, the TMS-induced impairment of temporal discrimination was due to a true decrement of tactile sensitivity (d'), without any specific change in the response criterion (c) adopted by participants, ruling out the hypothesis of a mere postperceptual effect due to the additional presence of the TMS pulse. Critically, the STG involvement in tactile processing was specific for the temporal task, whereas the STG effects disappeared during the spatial task.

As we used a 70-mm figure-of-eight coil, one might wonder whether this size of coil also disrupted processing in SII. However, we can rule out this possibility for two reasons: First, we replicated the results of Experiment 1 even by using a smaller, 50-mm figure-of-eight coil (see Results); and second, from an anatomical point of view, SII stimulation should induce a bilateral impairment in tactile processing (Lin & Forss, 2002), which was not observed here.

In the auditory domain, timing is a prominent feature, owing to its relevance in vocalization and speech recog-

nition (Mauk & Buonomano, 2004). Many areas are involved in temporal processing. In addition to the well-known role played by both subcortical structures and higher order cortical areas (Mauk & Buonomano, 2004), a lesion study (Robin, Tranel, & Damasio, 1990) showed that patients with left auditory cortex lesions were impaired on tasks involving the perception of temporal information in speech. Moreover, recent neuroimaging and TMS studies have highlighted the critical involvement of modality-specific cortices in the processing of temporal events. In particular, TMS studies have shown that STG would be necessary for the processing of the temporal features of auditory events, whereas the extrastriate visual area V5/MT would only be involved for visual events (Bueti, Bahrami, & Walsh, 2008; Bueti, van Dongen, & Walsh, 2008). These findings have been interpreted as a demonstration of modality-specific temporal processing.

Although activations of the STG have been typically associated with modality-specific temporal discrimination and reproduction of auditory stimuli (Recanzone & Sutter, 2008; Rao, Mayer, & Harrington, 2001), recent fMRI studies have reported the activation of this cortical region even during temporal processing of visual stimuli (Coull, Vidal, Nazarian, & Macar, 2004; Ferrandez et al., 2003), more specifically, of the left STG for visual discrimination of short, subsecond intervals (Lewis & Miall, 2003). On the contrary, to our knowledge, there is no evidence supporting the role of STG in processing temporal attributes of somatosensory stimuli. Yet, we found that STG is involved also in temporal discrimination of touch, suggesting that STG might play a truly supramodal role in temporal processing, being recruited in both auditory (Bueti, van Dongen, et al., 2008) and tactile timing. The proposal of a specific contribution of associative auditory areas in somatosensory processing would be largely consistent with two types of evidence: First, studies on monkeys have shown that in the auditory association cortex, there are neurons responding to somatosensory inputs (Ghazanfar & Schroeder, 2006; Schroeder & Foxe, 2005; Fu et al., 2003; Schroeder et al., 2001); second, brain imaging studies have demonstrated a cross-modal convergence in the contralateral auditory association cortex when tactile stimuli with frequency properties are used (Schurmann et al., 2006; Foxe et al., 2002).

Our second finding was that interfering with SI activity-impaired tactile discrimination during either the temporal task and the spatial task; in both cases, the SI effect was that of reducing perceptual sensitivity, without affecting the decision-related components of sensory processing (i.e., response bias). These findings suggest that the integrity of the tactile system is essential to process any aspect (spatial and temporal) of the tactile information.

These observations are in general agreement with earlier TMS evidence demonstrating the involvement of SI in vibrotactile frequency discrimination tasks. For instance, TMS applied to SI during the retention period in a working

memory task (Harris, Miniussi, Harris, & Diamond, 2002) or immediately before and after the comparison stimulus in a two-alternative forced-choice paradigm (Morley, Vickery, Stuart, & Turman, 2007) impaired vibrotactile frequency discrimination. With respect to spatial and temporal processing, our results are in line with evidence showing that SI interference can affect both spatial discriminative aspects of touch (Porro et al., 2007; Seyal, Siddiqui, & Hundal, 1997) and temporal vibrotactile discrimination (Hannula et al., 2005). In this respect, our experiment represents an advance from these TMS studies because we used a rigorous psychophysical approach to assess the role of any perceptual basis in the tactile temporal impairment induced by TMS.

Moreover, we underline a differential chronometry of the involvement of STG and SI. In the temporal task, the impairment of tactile discrimination occurred at 60 msec only when SI was stimulated by TMS, whereas it occurred at a delay of 180 msec after STG stimulation. This time course of the SI-STG involvement is broadly consistent with high-density EEG recordings and MEG studies in timing areas activated by vibrotactile stimuli (Auer, Bernstein, Sungkarat, & Singh, 2007; Iguchi et al., 2007; Caetano & Jousmaki, 2006). For instance, a first response to the right vibrotactile stimuli in the left hemisphere is reported, peaking around 60 msec in SI, followed by a further response peaking at about 100–200 msec in Wernicke area (Caetano & Jousmaki, 2006).

These differences in the time course might reflect a differential functional role played by somatosensory and associative auditory areas in tactile temporal processing. Indeed, processing tactile input depends on serially organized hierarchical processes, with more complex encoding of stimulus properties from SI to higher order areas. On the basis of latency differences, it is assumed that the higher order areas receive signals from SI through serial feed-forward projections (Iwamura, 1998). Somatosensory inputs to the associative auditory cortex meet the criteria for feed-forward connections (targeting layer IV; Schroeder & Foxe, 2005).

With respect to tactile spatial processing, the disrupting effects of TMS over SI were maximal at 60–120 msec, and after that performance returned to control levels. This time course of tactile spatial processing within the postcentral gyrus is broadly consistent with previous TMS studies (Porro et al., 2007; Seyal et al., 1997).

Given the evidence above, we propose that SI is not specific for timing tactile events, whereas STG is selectively implicated in tactile temporal processing. The involvement of STG at a later stage of somatosensory temporal processing, following SI processing, suggests that this area may be important to accomplish and optimize the elaboration of the temporal properties of tactile sensations; indeed, this cortical area would be mostly efficient in the processing of temporal information, but not of spatial one, regardless of the auditory or somatosensory modality.

In conclusion, our findings show that STG, commonly associated with auditory temporal processing, is necessary

for the perception of tactile duration, in conjunction with the modality-specific processing occurring within SI. These findings implicate that associative auditory areas are critical for the temporal processing of stimuli belonging to more than one sensory modality. Given that somatosensory (e.g., vibration) and auditory modalities share similar temporal features and may be associated in common cross-modal events, it is functionally relevant that the brain is equipped, within the auditory cortex, for processing temporal information derived from both audition and touch.

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Note

1. Given that only 8 of 13 subjects performed Experiment 2, data from Experiment 1 were reanalyzed by considering only the same eight participants that took part in both experiments. The results confirmed previous findings: Only SI-TMS at ISI of 60 msec and STG-TMS at ISI of 180 msec significantly impaired temporal processing of contralateral touches, either by increasing errors, Side \times Condition, $F(6, 42) = 3.66, p < .005, p\eta^2 = .34$, SI-TMS at ISI of 60 msec = 16%, STG-TMS at ISI of 180 msec = 18% as compared with baseline = 8% and the other conditions, $p < .01$ for all comparisons, or by decreasing perceptual sensitivity errors, Side \times Condition, $F(6, 42) = 2.72, p < .03, p\eta^2 = .28$, SI-TMS at ISI of 60 msec = 2.17, STG-TMS at ISI of 180 msec = 2.46, $p < .01$ for all comparisons, as compared with baseline = 3.73 and the other conditions, $p < .01$ for all comparisons, without inducing changes of the response criterion errors, Side \times Condition, $F(6, 42) = 0.55, p = .8, p\eta^2 = .07$.

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