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**Role of the right inferior parietal cortex in auditory selective attention: an rTMS
study**

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Abstract

Selective attention is the process of directing limited capacity resources to behaviourally relevant stimuli while ignoring competing stimuli that are currently irrelevant. Studies in healthy human participants and in individuals with focal brain lesions have suggested that the right parietal cortex is crucial for resolving competition for attention. Following right-hemisphere damage, for example, patients may have difficulty reporting a brief, left-sided stimulus if it occurs with a competitor on the right, even though the same left stimulus is reported normally when it occurs alone. Such “extinction” of contralesional stimuli has been documented for all the major sense modalities, but it remains unclear whether its occurrence reflects involvement of one or more specific subregions of the temporo-parietal cortex. Here we employed repetitive transcranial magnetic stimulation (TMS) over the right hemisphere to examine the effect of disruption of two candidate regions – the supramarginal gyrus (SMG) and the superior temporal gyrus (STG) – on auditory selective attention. Eighteen neurologically normal, right-handed participants performed an auditory task, in which they had to detect target digits presented within simultaneous dichotic streams of spoken distractor letters in the left and right channels, both before and after 20 minutes of 1Hz rTMS over the SMG, STG or a somatosensory control site (S1). Across blocks, participants were asked to report on auditory streams in the left, right, or both channels, which yielded focused and divided attention conditions. Performance was unchanged for the two focused attention conditions, regardless of stimulation site, but was selectively impaired for contralateral left-sided targets in the divided attention condition following stimulation of the right SMG, but not the STG or S1. Our findings suggest a causal role for the right inferior parietal cortex in auditory selective attention.

Introduction

In a noisy and dynamic auditory environment, we must selectively attend to the most relevant signal amongst several competing stimuli. Because conscious perception is capacity limited, we cannot attend to all signals concurrently. Instead, we must shift our attention from moment-to-moment, location-to-location or even from ear-to-ear. For example, we may need to pick out of several ongoing conversations the one most relevant to us, or shift attention from a speaker on the left to another on the right or from a conversation in the left ear to another on the phone in our right ear.

Investigations of the mechanisms underlying how the brain resolves this ongoing competition have focused primarily on vision, with little research on the auditory system. Here, we aimed to determine the causal role of two cortical regions, the supramarginal gyrus (SMG) and the superior temporal gyrus (STG), in the voluntary control of auditory attention.

The brain's ability to resolve competition between auditory signals has been formally described in behavioural studies. For example, Duncan, Martens and Ward [1] presented neurologically normal participants with strings of spoken syllables to each ear simultaneously, with target words embedded within the strings. Participants were asked to attend to just one ear (focused attention) or both ears (divided attention) and report the target words. Performance was high in the focused attention (one ear) condition, indicating successful suppression of the information in the unattended ear. Performance was poorer in the divided attention condition, however, suggesting that dividing attention renders listeners more susceptible to interference from competing auditory inputs.

These limits on attentional capacity have also been demonstrated in clinical populations. Of note is the clinical condition of spatial neglect following unilateral (usually right) hemisphere damage. Neglect patients often miss sensory events arising from the contralesional side of space due to a strong attentional bias to the ipsilesional side and a deficit in shifting attention to the contralesional side when required to do so. Many such patients also demonstrate a difficulty with stimuli on the left (following right hemisphere damage) when competing stimuli occur simultaneously on the right – an effect called *spatial extinction* [2-4]. In the laboratory, the phenomenon of extinction has been shown for auditory stimuli using dichotic listening tasks. Patients have greater difficulty reporting events presented to the left ear when instructed to divide their attention and report on two different auditory streams in each ear simultaneously [5, 6], or show spatial extinction for brief, concurrent auditory events [2-4].

Neuroimaging studies have implicated the right parietal lobule [7], in particular the SMG (BA 40; [8]) in auditory spatial orienting and control. A study by Pugh et al. [9] investigated differences in fMRI activation between binaural and dichotic listening conditions. In the binaural condition, participants received one stream of information to both ears, whereas in the dichotic condition they received two different streams - one to each ear - simultaneously. Participants were instructed to attend to one ear or the other. Under dichotic listening conditions, in which attentional demands were greater, there was an increase in activation in the inferior parietal lobe (IPL) and superior temporal gyri (with stronger effects in the right parietal cortex) relative to the binaural condition. Similarly, Westerhausen et al. [10] presented a group of healthy participants with a dichotic listening task that varied the relative salience of stimuli in

the left or right ears. Participants were instructed to attend to either the louder or the softer stream, and thus had to hold their attention to stimuli in one ear or the other.

Neural activation reflected an interaction between the salience of the stimuli and top-down attentional instructions, and included the right IPL and SMG in particular.

Specifically, increases in activity within the SMG depended on the extent to which stimulus salience had to be compensated for by top-down attentional control [10].

Evidence from neuropsychological studies have shed further light on the neural substrates of auditory selective attention. As mentioned above, neglect patients typically have lesions centered around the right IPL and temporoparietal junction [11-13]. In terms of spatial extinction, a recent meta-analysis has implicated the right angular gyrus and temporoparietal junction as critical lesion sites [14]. However, lesion sites may vary widely between patients and are often large, spreading across multiple neighbouring regions. Moreover, as stroke is more common in older individuals, patients often have peripheral sensory loss that can contribute to any attentional deficit [15].

Brain stimulation techniques such as repetitive transcranial magnetic stimulation (rTMS) can be used to produce temporary and reversible disruption of focal regions of the cortex [16, 17]. This allows testing of multiple sites within healthy individuals to determine regions of cortex that are causally involved in a specific perceptual, cognitive or motor task. Previous TMS studies have implicated the inferior parietal lobe as important for auditory processing and attention [18, 19], and TMS studies in vision and touch have identified critical brain regions for selective attention. For example, rTMS of the right parietal region has been shown to impair detection of

contralateral visual stimuli when an ipsilateral stimulus is also presented – producing an extinction-like effect in normal participants [20-22]. In particular, regions in the right ventral attention network, such as the right SMG and STG, have been implicated in visual and tactile attention [20, 23, 24] and in attentional deployment during visual search [25].

Here we utilised low frequency rTMS to assess the causal roles of two key regions within the right hemisphere in auditory selective attention. Our choice of right hemisphere sites was informed by relevant neuroimaging and neuropsychological data reviewed above. Both the SMG and STG have been implicated in auditory spatial attention [8] and in the voluntary allocation of auditory attention [9, 26]. Moreover, both the SMG and STG have been implicated in the clinical conditions of neglect and spatial extinction [12, 14, 27]. Any effects of rTMS over these two sites were compared with those following stimulation of a control site, the right primary somatosensory cortex (S1), which is located in close proximity to the two experimental sites but should have no role in auditory attention. Area S1 has also been used as a control site in previous studies of auditory perception and spatial attention [28, 29].

In the experiment, participants were presented with two different streams of spoken auditory targets (digits) amongst competing distractors (letters), one stream to each ear (Figure 1A). They were asked to monitor one channel (left or right, in separate blocks) and to report targets on that side only (focused attention), or both channels to report targets on either side (divided attention). We focused our analysis on the divided attention condition, in which concurrent auditory inputs competed for

selection, and compared performance in each ear under divided attention with performance for the respective ear in the focused attention condition. Any cost for the divided attention condition was compared separately for the left and right ears, both before and after rTMS of each of the three right hemisphere sites.

Method

Participants

Eighteen right-handed individuals participated in the study (11 female; age range 19 to 28 years; $M = 24.3$, $SD = 2.9$). Participants reported no history of hearing impairment or hearing injury. All participants were screened for contraindications to TMS [30, 31] and none reported a history of seizure, epilepsy or other brain injury, nor were any taking neuroactive medications. All procedures were approved by The University of Queensland Medical Research Ethics Committee, and written informed consent was obtained from each participant before the start of the experiment.

Auditory attention task

For the auditory attention task, participants listened to two different streams of spoken letters presented dichotically via headphones, and were asked to make a speeded key press using the index finger of their right hand when a target number occurred. Stimuli consisted of the letters A to Z (excluding O and H to avoid confusion with numbers “0” and “8”) presented with equal likelihood, and the digits were the numbers 1-9 (excluding 5 and 7 due to longer spoken duration/two-syllable length) presented with equal likelihood. Across separate blocks of trials, participants were instructed to report target numbers in the left ear only (Attend Left), the right ear only

(Attend Right), or in either ear (Attend Both). All aspects of stimulus presentation and timing were controlled via custom software running in Matlab on a Dell T1600 PC under Windows 7 with integrated high-definition audio and NVIDIA Quadro 2000 Video Card. Stimuli were all one-syllable, p-centred [32], matched for volume and frequency with duration of 500 ms, and recorded in a male voice. Stimuli were presented through Sennheiser HD 280 PRO noise cancellation headphones with 64 ohm nominal impedance.

Each trial consisted of 20 spoken items presented at a rate of 2 Hz. Items were pseudo-randomised to ensure that no letters were repeated within a trial or occurred concurrently in the left and right channels. The streams in each channel commenced simultaneously at the beginning of each trial. Target numbers appeared either 0, 1 or 2 times within each trial with targets never occurring in the first 2 positions of the stream. In 1-target trials, the target number could occur in any randomised position between 13-18 of the 20 items. In 2-target trials, the first target appeared between positions 3 – 12, and the second appeared in positions 16 – 18, with a minimum of six items between the two (to avoid response overlaps between the first and second targets). For the Attend Both trials, targets could appear in either channel, requiring participants to monitor both streams (see Figure 1A). For Attend Left and Attend Right trials, targets only occurred in the attended stream and the number of targets was matched for left and right trials. At the end of each trial there was a 2 s delay before commencement of the next trial.

The task was delivered in eight blocks of 13 trials each, or 14 in the Attend Both condition: two Attend Left blocks, two Attend Right blocks, and four Attend Both

blocks. We included twice the number of Attend Both trials as these were central to our question of the effects of parietal rTMS on divided auditory attention. The order of blocks was randomised each session. At the completion of each block, participants were given the opportunity to rest with a self-paced protocol. The eight blocks were completed in approximately 20 minutes. Participants were given one block of practice trials prior to starting the main task in the first session, and in the subsequent sessions only if the participant required additional practice. The auditory attention task was undertaken once immediately prior to the rTMS protocol, and then again immediately afterward.

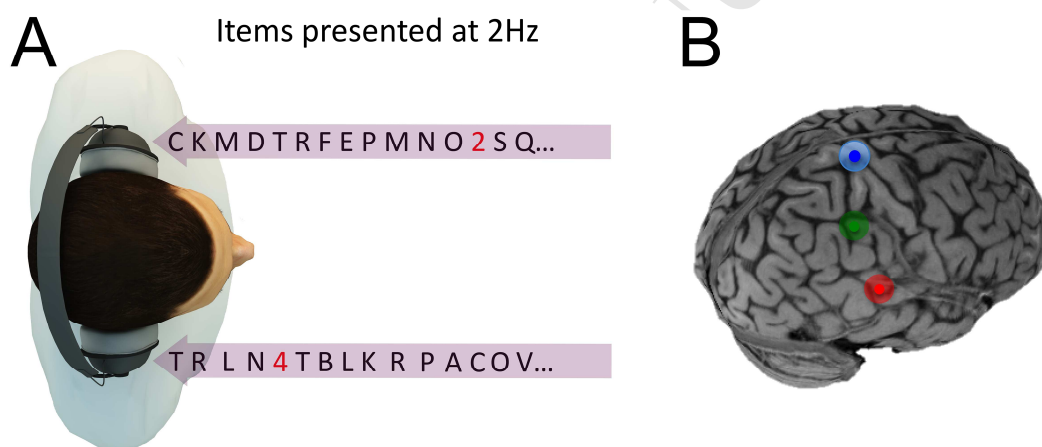


Figure 1. Schematic of auditory attention task and right hemisphere rTMS stimulation sites. A. Illustration of the auditory selective attention task. Target digits (depicted in red) appeared in a stream of distractor letters. The schematic shows a trial of the Attend Both condition in which targets could occur in either ear and attention had to be divided across both channels. B. Locations of the three sites of stimulation: blue marks S1, green is SMG and red is the STG.

Determination of rTMS stimulation sites

Before participants' first session, a T1-weighted high resolution (0.9 mm isotropic) structural MRI scan was acquired using a Siemens 3T Magnetom Trio (Centre for Advanced Imaging, The University of Queensland). Some volunteers provided a scan from previous research participation. Scans were processed using Visor1 neuro-

navigation software and ASA-Lab (ANT, The Netherlands). The structural scans were used to locate and target with TMS the three sites of interest in the right hemisphere, as shown in Figure 1B. The S1 (control) site was defined as lying between the central and post-central sulcus, posterior to, but approximately along the midline of, the superior frontal sulcus [28]. The SMG was defined as the region adjacent to the dorsolateral projection of the lateral sulcus, posterior to the post-central sulcus and anterior to the superior temporal sulcus [28]. For the STG site, the most posterior segment was chosen as the stimulation site to avoid the TMS coil overlapping the ear during stimulation (see Figure 1B). This was defined as the region lying between the central and superior temporal sulcus, adjacent and posterior to the inferior branch of the central sulcus. Each site was targeted using a Polaris-based infrared frameless stereotaxic system and Visor1 software. Talairach coordinates for the three sites were generated using ASA-Lab. The mean (*SD*) coordinates (*x*, *y*, *z*) for the group were **S1** = 21.6 (5.7), -37.5 (6.5), 69.3 (3.4); **SMG** = 55.4 (7.8), -44.5 (9.3), 44.2 (5.0); **STG** = 65.1 (3.6), -39.2 (6.5), 13.4 (7.9). All participants received rTMS over one of the three sites at the same time of day in sessions separated by at least 24 hours. The order of stimulation site was counterbalanced across participants.

rTMS protocol

A Magstim SuperRapid bi-phasic TMS system and figure-of-eight coil (p/n 9925-00, outer diameter 9 cm) were used for the stimulation protocol. For all participants, rTMS was delivered at 1 Hz for 20 minutes (1200 pulses) at a stimulus intensity of 100% resting motor threshold (rMT). To establish the intensity of stimulation for each individual for the rTMS, the rMT was determined using a visual detection method. Specifically, the hotspot for the left thumb representation was located by

systematically moving the TMS coil over the scalp of the right hemisphere (stimulating at a slightly suprathreshold intensity) until a location was found that resulted in the most consistent and largest evoked thumb movements. This hotspot was marked using the neuro-navigation system and the rMT was established prior to each session, defined as the lowest intensity that produced visible movements of the left thumb on at least 50% of trials [33]. A two-down, one-up procedure was used, starting at a suprathreshold level. Specifically, machine output was dropped by 2% until fewer than 5/10 twitches were observed, and then increased by 1% until at least 5/10 pulses induced a visible thumb movement. Two operators were used for this procedure. Across the three sessions, average rMT varied by an average of just 3.61% ($SD = 2.23\%$). The mean stimulus intensity was 57% of machine output (range 44-71%).

For all sites the TMS coil was held with the handle oriented backwards toward the operator standing directly behind the seated participant. Participants wore earplugs throughout delivery of rTMS. The neuro-navigation system was used online to maintain coil position and orientation over the stimulation site. Two TMS coils were used in each session to avoid overheating, with the change made half way through the 1200 pulses. None of the participants experienced any adverse reactions to the TMS.

Data analysis and statistics

Our central question was whether right hemisphere rTMS would affect performance in the critical divided attention trials, in which participants monitored left and right auditory streams concurrently, compared with their performance under focused attention (Attend Left or Attend Right). To assess this directly, we derived a metric of

the cost of dividing attention. For left targets, for example, we took mean accuracy in the Attend Both condition and the Attend Left condition and calculated a difference score as follows:

$$(\textit{Attend Both accuracy} - \textit{Attend Left accuracy}) / \textit{Attend Left accuracy}$$

The same procedure was used to calculate differences between Attend Both and Attend Right conditions for right targets. These individual difference scores reflect the cost of dividing attention, with negative values indicating worse performance when attending to both streams relative to only attending to a single stream. These difference scores were also computed for average reaction times (RTs). However, before any analyses were conducted, all RTs below 200 ms were removed (number of anticipations = 18), as were those 3 SDs or more above the mean (number of outliers = 84) removing a total of only 0.786% of responses. RT analyses were conducted on correct responses only.

To address our main question of whether right hemisphere stimulation altered performance for contralateral (left) targets, we conducted an analysis of variance (ANOVA) involving the fixed factors of TMS site (SMG, STG, S1), phase (pre-, post-stimulation) and target side (left, right). We included both subjects and task blocks (N = 4 in the critical divided attention condition) as random factors. For the random factor of block, we computed individual difference scores for left and right targets for each of the four blocks of the divided attention task, baselined to the average performance for corresponding left and right targets in the focused attention condition. A linear mixed model ANOVA was conducted to account for non-independence of the four observations from the same participant across blocks.

Results

The cost of dividing attention

Our central question was whether rTMS over one or more right hemisphere sites would affect discrimination of contralateral targets in the presence of competing ipsilateral stimuli under conditions of divided attention. Figure 2 displays the effects of divided attention relative to focused attention (mean difference scores) on performance for left and right targets, separately for each site of stimulation.

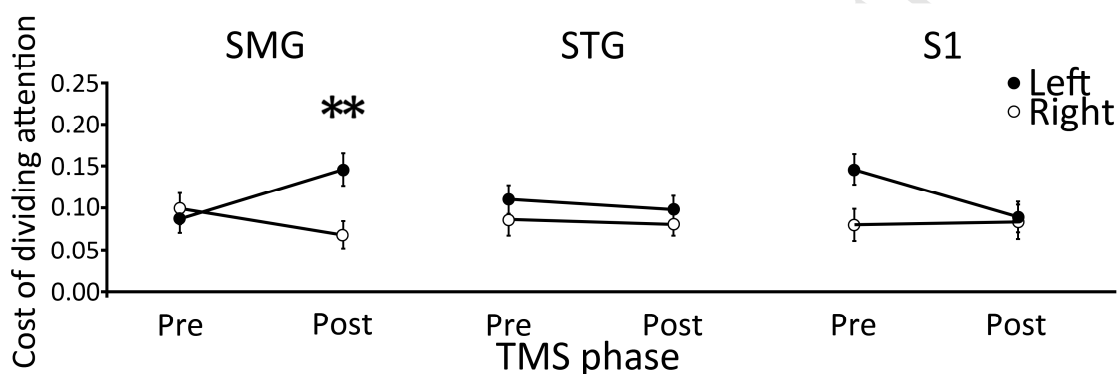


Figure 2. Mean cost of dividing attention shown separately for the three stimulation sites before and after rTMS. The difference scores are plotted here to capture the cost of divided versus focused attention. For plotting purposes, sign is reversed with positive values indicating greater cost of divided versus focused attention. Stimulation of the right SMG led to greater cost on contralateral targets and marginally less cost on ipsilateral targets. There was no significant effect of rTMS over STG or S1 on divided attention. Error bars represent the standard error for the group. ** $p=0.001$.

A linear mixed model ANOVA was conducted with subject and block as random factors, and with fixed factors of TMS site (SMG, STG, S1), phase (pre-, post-stimulation) and target side (left, right). Outliers for each condition at each site and phase were identified using boxplots and replaced using the nearest neighbor approach[34] $M = 3.778$ (5.24%), $SD = 1.986$ (2.758%), range = 0-8. There was a significant three-way interaction of TMS site x phase x target side, $F(2, 832) = 4.814$, $p = .008$.

Separate linear mixed model ANOVAs were then conducted for each TMS site independently, with random factors of subject and block, and fixed factors of phase (pre-, post-stimulation) and target side (left, right). For SMG, there was a significant phase x target side interaction, $F(1, 267) = 7.025, p = .009$. Post-hoc pairwise comparisons showed a significant increase in cost from pre- to post-stimulation for left targets ($t(267) = -.058, p = .015$, Bonferroni corrected), and a significant increase in cost for left versus right targets post-stimulation, ($t(267) = .077, p = .001$, Bonferroni corrected). There was no significant phase x target side interaction for stimulation over STG ($F(1,267) = .042, p = 0.838$) or S1 ($F(1, 267) = 3.188, p = .075$).

Figure 3 shows each individual's bias performance under divided attention conditions. Individual biases pre- and post-stimulation were computed by subtracting the average difference scores for left targets from the difference scores on right targets. Larger difference scores indicate a greater cost of dividing attention relative to focused attention conditions. Thus, positive bias values indicate a larger cost under divided attention conditions for left than for right targets. It is clear from Figure 3 that for most participants, the cost of dividing attention was greater for left targets than right targets following rTMS of the right SMG.

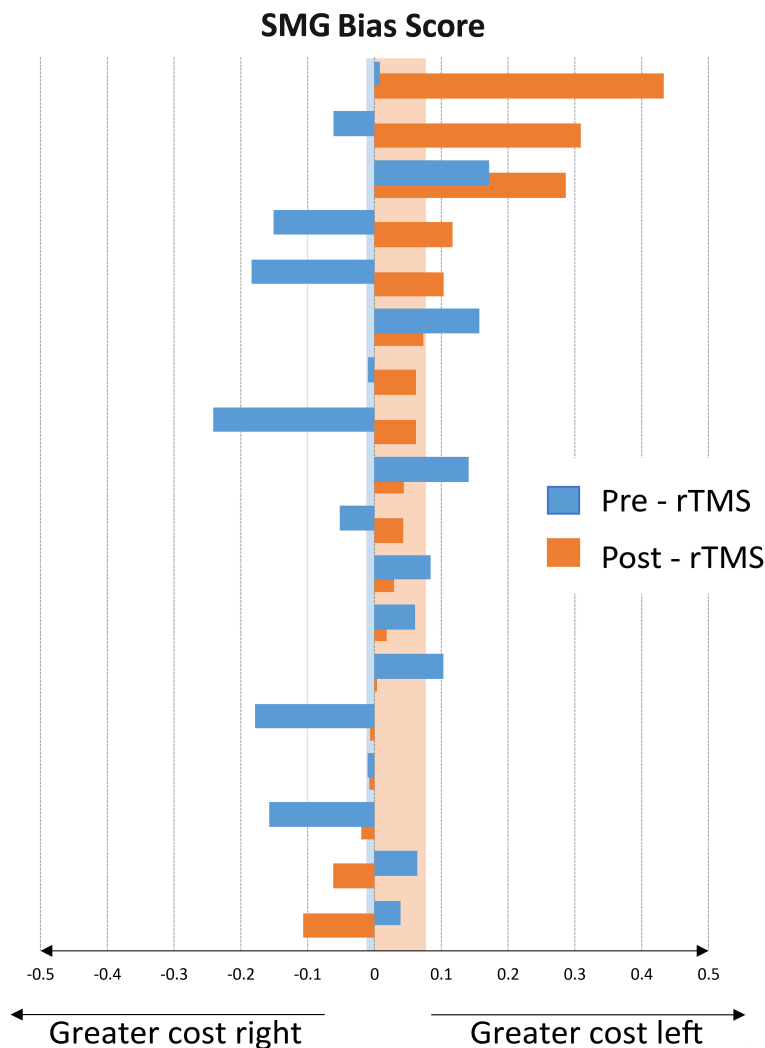


Figure 3. Individual participant's bias scores before and after rTMS in the divided attention condition. Each pair of bars represents one participant's scores at the pre- (blue) and post- (orange) stimulation phases. Bias scores were computed from participants' individual difference scores, which capture the cost of dividing attention relative to the focused attention condition. Positive values (x axis) indicate larger difference scores between focused and divided attention for left targets, indicating relatively greater accuracy for right targets on divided attention conditions. The majority of participants demonstrated a shift in bias score toward the right from pre- to post-stimulation. The blue and orange vertical shaded regions represent the average bias scores for the group.

Accuracy on focused attention trials

To rule out the possibility that the results for the divided attention condition arose from an effect of TMS on perception of left- or right-sided auditory stimuli, rather than on selective attention under competition, we also analysed accuracy for the

focused attention trials. Mean accuracies across pre- and post-stimulation phases for the Attend Left and Attend Right trials are presented in Figure 4. On average, for the focused attention blocks, accuracy was high prior to stimulation and was similar for Attend Left and Attend Right trials ($t(17) = 0.371, p = 0.715$), with several participants performing at ceiling.

A linear mixed model ANOVA was conducted with random factors of subject and block, and fixed factors of site (SMG, STG, S1), phase (pre-, post-stimulation) and target side (left, right). There was no significant three-way interaction of site x phase x target side ($F(2, 402) = 1.318, p = .269$), and no other significant main effects or interactions (all $p > 0.05$). Separate linear mixed model ANOVAs conducted at each site yielded no significant two-way interactions between phase and target side (SMG – $F(1, 123) = 1.687, p = 0.196$; STG – $F(1, 123) = 0.317, p = 0.575$; S1 – ($F(1, 123) = 2.137, p = 0.146$), and no significant main effects (all $p > 0.1$).

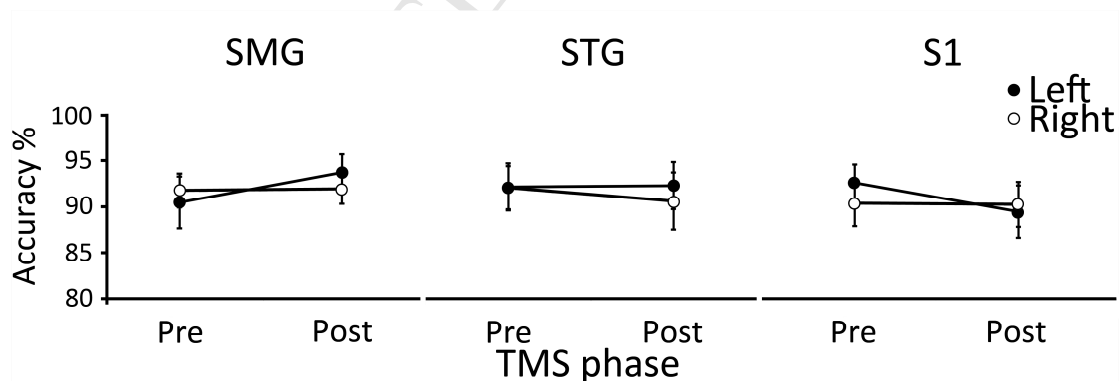


Figure 4. Mean accuracy for the focused attention conditions (Attend Left and Attend Right), shown separately for the three stimulation sites before and after rTMS. There was no significant effect of rTMS over any site. Error bars represent the standard error for the group.

Reaction Times

RTs were also analysed to investigate whether rTMS influenced the speed of responses. The RT data (presented in Table 1) were analysed using repeated measures ANOVAs with factors of phase (pre, post TMS) and target side (left, right) for focused- and divided attention conditions, separately for each stimulation site. There were no significant differences at either stimulation site for either the focused or divided attention conditions (all $p > 0.10$).

Table 1. *Mean reaction times (in milliseconds) for the Attend Both, Attend Left and Attend Right conditions of the auditory attention task. Values are shown separately for pre- and post-stimulation phases. Standard deviations are given in parentheses.*

	Attend Both		Attend Left		Attend Right	
	Pre	Post	Pre	Post	Pre	Post
SMG	815.19 (81.63)	793.33 (74.09)	762.23 (80.36)	740.50 (75.58)	744.47 (68.19)	721.02 (61.93)
STG	817.39 (118.07)	800.15 (102.83)	741.07 (91.20)	742.04 (105.53)	750.14 (103.30)	741.46 (81.20)
S1	823.81 (111.06)	798.79 (110.67)	760.23 (101.21)	745.17 (124.92)	756.61 (79.85)	751.58 (139.23)

False Alarms

We defined false alarms as instances in which a participant responded in the absence of a target. Overall, false alarm rates were very low across all experimental conditions, and thus could not be analysed statistically. Critically, however, the absolute false alarm rates did not vary appreciably between the focused and divided attention conditions, stimulation site or between phases (range: 1.9 – 3.1%).

Discussion

Here we have shown that inhibitory TMS over the right SMG leads to poorer detection of left relative to right auditory targets when attention is divided –

producing an ‘extinction-like’ effect in healthy individuals. There was no such effect following stimulation of the right STG or the control site over S1. By contrast, the same inhibitory TMS protocol did not alter performance in the focused attention conditions, for any of the three stimulation sites, suggesting that the extinction-like effect for the SMG under divided attention conditions was not due to a change in perception for left-sided targets alone. Instead, rTMS affected performance specifically when participants had to report contralateral targets in the presence of competing ipsilateral events. Thus, the right SMG appears to play a causal role in auditory selection under conditions of divided attention.

The SMG’s role in auditory attention

Consistent with our findings, there is evidence from human neuroimaging research linking auditory attentional control with activation of the SMG [7, 8, 10]. For example, a previous study manipulated attentional demands in a dichotic listening task and found a set of fronto-parietal regions, including the right IPL and SMG, that were selectively active [10]. A recent rTMS study also found that the right inferior parietal cortex modulates frontal lobe network activity in auditory spatial attention [18]. In another fMRI study, Kong et al. [35] used multivoxel pattern analysis (MVPA) and an auditory spatial attention task to show that neural activity patterns within the SMG can predict the direction of auditory spatial attention [35]. These findings suggest that the SMG plays a role in the flexible shifting of attention across auditory space, consistent with our findings of a causal role for the right SMG in auditory selective attention.

The SMG’s role in spatial attention

Functional imaging studies have also identified a broad fronto-parietal network involved in a variety of attentionally demanding tasks [36]. In a review of several neuroimaging studies, Corbetta and Shulman [37] proposed two systems within this fronto-parietal network. A dorsal stream, which includes the intraparietal cortex and superior frontal cortex, is thought to be responsible for top-down, goal-directed control. By contrast, a ventral stream, involving the right inferior frontal cortex and temporoparietal cortex, is assumed to act as a bottom-up system for detecting relevant stimuli based on stimulus-driven factors, such as salience. The SMG is located in the ventral stream of this larger network of regions involved in spatial attention more generally. It is thought that the dorsal and ventral systems functionally interact to direct attention effectively [37]. Braga et al. [38] argue that although both dorsal and ventral attention systems are specialized for distinct attentional sub-processes, flexible attentional control can only be implemented by dynamic interactions between the two systems. For example, the dorsal system might hold a target-template 'in mind' whilst the ventral system searches for a target with features that match that template. A deficit in selective attention could thus arise from a failure to maintain the target-template online, or a more local difficulty in detecting relevant features particularly under conditions in which there is a high-level of similarity between the target and other competing stimuli. In the context of the present investigation, it could be that reduced detection of left targets following right SMG stimulation resulted either from disruption of the target-template or a problem distinguishing the contralateral target's (digits) features from those of distractors (letters).

Is the SMG modality specific or multimodal?

Causal evidence from brain stimulation research has linked the right SMG not only to auditory selective attention, but also to cross-modal spatial attention. For example, Chambers et al. [23] reported that stimulation of the right SMG led to performance deficits in selecting behaviourally relevant visual or somatosensory stimuli following an irrelevant somatosensory cue. This suggests that disruption of the right SMG impaired participants' ability to coordinate information between the visual and tactile senses for spatial selection [23]. Westerhausen et al. [10] noted that the set of fronto-parietal regions, including the SMG, activated during auditory attentional control, matches those seen in similar tasks involving the visual [37] and somatosensory [39] modalities, consistent with the suggestion that the IPL is part of a supramodal attention network [40-42]. Evidence from EEG studies has also suggested that attentional control involves a supramodal network encompassing frontal and parietal regions [41, 42].

It is important to note, however, that not all studies have supported the suggestion that the SMG is part of a supramodal network. For example, Chambers, Stokes and Mattingley [43] found that TMS disruption of the SMG impaired the effectiveness of a visual cue when the following target was also visual, but not when the target was somatosensory. They argued that the SMG has a modality-specific role for visual orienting in space, rather than a supramodal role. Similarly, other brain stimulation work has suggested that stimulation of the IPL (BA 40) impairs performance on contralateral modality-specific auditory and visual targets, but not multisensory audiovisual targets [19] and another study implicated the angular gyrus (AG), rather than the SMG, is involved in binding auditory and visual stimuli [28, 44]. Findings

from psychophysical experiments have also revealed dissociations between modalities in the control of spatial attention [45, 46].

SMG and neuropsychological data

It is well known that spatial neglect can occur in several sensory modalities in individual patients [47-49], and can even arise cross-modally in the case of spatial extinction [50-52]. There has been much debate regarding the critical site of damage that leads to extinction and neglect [12, 14, 27] (see also [53-55]). Here we have identified the SMG as a critical site for auditory extinction, albeit in healthy adult participants, and for stimulus identification of concurrent inputs rather than mere detection as in most clinical cases. Neuropsychological studies have suggested that damage to regions of the dorsal stream alone is not sufficient to produce neglect, but that damage to ventral regions, including the SMG, seems to be critical. The model of Corbetta and Shulman proposes that these ventral regions are right hemisphere specialized, and that they interact with the bilateral dorsal system in the control of spatial attention [56]. By contrast, other investigators have proposed that the right hemisphere is exclusively specialized for attention [57-59], and recent connectivity analyses has yielded support for this right hemisphere dominance model [60].

Concluding Remarks

In summary, using rTMS we have identified the right SMG as a crucial region for selective attention across auditory space. Our findings are broadly consistent with the neuroimaging literature that has reported increased activation in the right SMG for auditory spatial orienting [7, 8] and selectively attending to auditory information in dichotic listening tasks [9, 10]. Additionally, and consistent with brain stimulation

studies of vision and touch [20, 23, 24], our results implicate the right SMG in the voluntary allocation of auditory spatial attention. More broadly, our results fit with the neuropsychological literature, which has implicated lesions encompassing the right SMG in spatial neglect and extinction [12, 13, 27]. Future research should investigate the role of the left SMG to determine whether it is also involved in spatial attention, particularly for contralateral (right-sided) auditory events. Such a study could help identify whether the control of auditory attention is predominantly right lateralized [57, 61], or whether each hemisphere controls attentional orienting exclusively to the contralateral space [59, 62, 63].

References

1. Duncan, J., S. Martens, and R. Ward, *Restricted attentional capacity within but not between sensory modalities*. *Nature*, 1997. **387**(6635): p. 808-10.
2. De Renzi, E., M. Gentilini, and C. Barbieri, *Auditory neglect*. *Journal of Neurology, Neurosurgery & Psychiatry*, 1989. **52**(5): p. 613-617.
3. De Renzi, E., M. Gentilini, and F. Pattacini, *Auditory extinction following hemisphere damage*. *Neuropsychologia*, 1984. **22**(6): p. 733-744.
4. Pavani, F., E. Ladavas, and J. Driver, *Auditory and multisensory aspects of visuospatial neglect*. *Trends Cogn Sci*, 2003. **7**(9): p. 407-414.
5. Bellmann, A., R. Meuli, and S. Clarke, *Two types of auditory neglect*. *Brain*, 2001. **124**(Pt 4): p. 676-87.
6. Carlyon, R.P., et al., *Effects of attention and unilateral neglect on auditory stream segregation*. *J Exp Psychol Hum Percept Perform*, 2001. **27**(1): p. 115-27.
7. Wu, C.T., et al., *The neural circuitry underlying the executive control of auditory spatial attention*. *Brain Res*, 2007. **1134**(1): p. 187-98.
8. Bushara, K.O., et al., *Modality-specific frontal and parietal areas for auditory and visual spatial localization in humans*. *Nat Neurosci*, 1999. **2**(8): p. 759-66.
9. Pugh, K.R., et al., *Auditory selective attention: an fMRI investigation*. *Neuroimage*, 1996. **4**(3 Pt 1): p. 159-73.
10. Westerhausen, R., et al., *Identification of attention and cognitive control networks in a parametric auditory fMRI study*. *Neuropsychologia*, 2010. **48**(7): p. 2075-2081.
11. Karnath, H.O. and C. Rorden, *The anatomy of spatial neglect*. *Neuropsychologia*, 2012. **50**(6): p. 1010-7.
12. Mort, D.J., et al., *The anatomy of visual neglect*. *Brain*, 2003. **126**(Pt 9): p. 1986-97.
13. Verdon, V., et al., *Neuroanatomy of hemispatial neglect and its functional components: a study using voxel-based lesion-symptom mapping*. *Brain*, 2010. **133**(Pt 3): p. 880-94.
14. Molenberghs, P., M.V. Sale, and J.B. Mattingley, *Is there a critical lesion site for unilateral spatial neglect? A meta-analysis using activation likelihood estimation*. *Front Hum Neurosci*, 2012. **6**: p. 78.
15. Suetterlin, K.J. and A.A. Sayer, *Proprioception: where are we now? A commentary on clinical assessment, changes across the life course, functional implications and future interventions*. *Age Ageing*, 2013. **43**(3): p. 313-8.
16. Chambers, C.D. and J.B. Mattingley, *Neurodisruption of selective attention: insights and implications*. *Trends in cognitive sciences*, 2005. **9**(11): p. 542-550.
17. Rushworth, M. and P. Taylor, *TMS in the parietal cortex: updating representations for attention and action*. *Neuropsychologia*, 2006. **44**(13): p. 2700-2716.
18. Karhson, D.S., J.R. Mock, and E.J. Golob, *The Role of Right Inferior Parietal Cortex in Auditory Spatial Attention: A Repetitive Transcranial Magnetic Stimulation Study*. *PLoS One*, 2015. **10**(12): p. e0144221.

19. Bolognini, N., et al., *TMS modulation of visual and auditory processing in the posterior parietal cortex*. *Exp Brain Res*, 2009. **195**(4): p. 509-17.
20. Chambers, C.D., et al., *Enhancement of visual selection during transient disruption of parietal cortex*. *Brain Res*, 2006. **1097**(1): p. 149-55.
21. Hilgetag, C.C., H. Theoret, and A. Pascual-Leone, *Enhanced visual spatial attention ipsilateral to rTMS-induced 'virtual lesions' of human parietal cortex*. *Nat Neurosci*, 2001. **4**(9): p. 953-7.
22. Pascual-Leone, A., et al., *Induction of visual extinction by rapid-rate transcranial magnetic stimulation of parietal lobe*. *Neurology*, 1994. **44**(3 Pt 1): p. 494-8.
23. Chambers, C.D., J.M. Payne, and J.B. Mattingley, *Parietal disruption impairs reflexive spatial attention within and between sensory modalities*. *Neuropsychologia*, 2007. **45**(8): p. 1715-24.
24. Schenkluhn, B., et al., *Parietal stimulation decouples spatial and feature-based attention*. *J Neurosci*, 2008. **28**(44): p. 11106-10.
25. Ellison, A., et al., *An exploration of the role of the superior temporal gyrus in visual search and spatial perception using TMS*. *Brain*, 2004. **127**(Pt 10): p. 2307-15.
26. Salmi, J., et al., *Brain networks of bottom-up triggered and top-down controlled shifting of auditory attention*. *Brain Res*, 2009. **1286**: p. 155-64.
27. Karnath, H.O., et al., *The anatomy of spatial neglect based on voxelwise statistical analysis: a study of 140 patients*. *Cereb Cortex*, 2004. **14**(10): p. 1164-72.
28. Kamke, M.R., et al., *Parietal disruption alters audiovisual binding in the sound-induced flash illusion*. *Neuroimage*, 2012. **62**(3): p. 1334-41.
29. Morris, A.P., C.D. Chambers, and J.B. Mattingley, *Parietal stimulation destabilizes spatial updating across saccadic eye movements*. *Proceedings of the National Academy of Sciences*, 2007. **104**(21): p. 9069-9074.
30. Rossi, S., Hallett, M., Rossini, P. M., Pascual-Leone, A. & Safety of TMS Consensus Group. , *Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research*. *Clinical neurophysiology*, 2009. **120**(12): p. 2008-2039.
31. Rossi, S.H., M.; Rossini, P. M. & Pascual-Leone, A., *Screening questionnaire before TMS: an update*. *Clinical neurophysiology*, 2011. **122**(8): p. 1686.
32. Morton, J., S. Marcus, and C. Frankish, *Perceptual centers (P-centers)*. *Psychological Review*, 1976. **83**(5): p. 405.
33. Rossini, P.M., et al., *Non-invasive electrical and magnetic stimulation of the brain, spinal cord and roots: basic principles and procedures for routine clinical application. Report of an IFCN committee*. *Electroencephalogr Clin Neurophysiol*, 1994. **91**(2): p. 79-92.
34. Wike, E.L., *Data analysis: A statistical primer for psychology students*. 2006: Transaction Publishers.
35. Kong, L., et al., *Auditory spatial attention representations in the human cerebral cortex*. *Cerebral Cortex*, 2014. **24**(3): p. 773-784.
36. Duncan, J. and A.M. Owen, *Common regions of the human frontal lobe recruited by diverse cognitive demands*. *Trends Neurosci*, 2000. **23**(10): p. 475-83.

37. Corbetta, M. and G.L. Shulman, *Control of goal-directed and stimulus-driven attention in the brain*. Nat Rev Neurosci, 2002. **3**(3): p. 201-15.
38. Braga, R.M., et al., *Echoes of the brain within default mode, association, and heteromodal cortices*. The Journal of Neuroscience, 2013. **33**(35): p. 14031-14039.
39. Macaluso, E. and J. Driver, *Spatial attention and crossmodal interactions between vision and touch*. Neuropsychologia, 2001. **39**(12): p. 1304-16.
40. Macaluso, E. and J. Driver, *Multimodal spatial representations in the human parietal cortex: evidence from functional imaging*. Advances in neurology, 2002. **93**: p. 219-233.
41. Eimer, M., J. van Velzen, and J. Driver, *Cross-modal interactions between audition, touch, and vision in endogenous spatial attention: ERP evidence on preparatory states and sensory modulations*. J Cogn Neurosci, 2002. **14**(2): p. 254-71.
42. Eimer, M. and J. Van Velzen, *Crossmodal links in spatial attention are mediated by supramodal control processes: evidence from event-related potentials*. Psychophysiology, 2002. **39**(4): p. 437-49.
43. Chambers, C.D., M.G. Stokes, and J.B. Mattingley, *Modality-specific control of strategic spatial attention in parietal cortex*. Neuron, 2004. **44**(6): p. 925-30.
44. Hamilton, R.H., et al., *Gone in a flash: manipulation of audiovisual temporal integration using transcranial magnetic stimulation*. Front Psychol, 2013. **4**: p. 571.
45. Spence, C. and J. Driver, *Audiovisual links in endogenous covert spatial attention*. J Exp Psychol Hum Percept Perform, 1996. **22**(4): p. 1005-30.
46. Spence, C., F. Pavani, and J. Driver, *Crossmodal links between vision and touch in covert endogenous spatial attention*. Journal of Experimental Psychology: Human Perception and Performance, 2000. **26**(4): p. 1298.
47. Pavani, F., et al., *Auditory deficits in visuospatial neglect patients*. Cortex, 2004. **40**(2): p. 347-365.
48. Brozzoli, C., et al., *Neglect and extinction: within and between sensory modalities*. Restorative neurology and neuroscience, 2006. **24**(4-6): p. 217-232.
49. Jacobs, S., C. Brozzoli, and A. Farnè, *Neglect: a multisensory deficit?* Neuropsychologia, 2012. **50**(6): p. 1029-1044.
50. Mattingley, J.B., et al., *Attentional competition between modalities: extinction between touch and vision after right hemisphere damage*. Neuropsychologia, 1997. **35**(6): p. 867-880.
51. Làdavas, E., et al., *Neuropsychological evidence of an integrated visuotactile representation of peripersonal space in humans*. Journal of Cognitive Neuroscience, 1998. **10**(5): p. 581-589.
52. Ladavas, E., F. Pavani, and A. Farne, *Auditory peripersonal space in humans: a case of auditory-tactile extinction*. Neurocase, 2001. **7**(2): p. 97-103.
53. Heilman, K.M., et al., *Localization of lesions in neglect*. Localization in neuropsychology, 1983. **33**: p. 471-92.
54. Vallar, G. and D. Perani, *The anatomy of unilateral neglect after right-hemisphere stroke lesions. A clinical/CT-scan correlation study in man*. Neuropsychologia, 1986. **24**(5): p. 609-22.

55. Marshall, J.C., et al., *Spatial awareness: a function of the posterior parietal lobe?* Cortex, 2002. **38**(2): p. 253-257.
56. Corbetta, M. and G.L. Shulman, *Spatial neglect and attention networks.* Annu Rev Neurosci, 2011. **34**: p. 569-99.
57. Heilman, K.M. and T. Van den Abell, *Right hemispheric dominance for mediating cerebral activation.* Neuropsychologia, 1979. **17**(3): p. 315-321.
58. Mesulam, M.M., *A cortical network for directed attention and unilateral neglect.* Ann Neurol, 1981. **10**(4): p. 309-25.
59. Kinsbourne, M., *The cerebral basis of lateral asymmetries in attention.* Acta Psychol (Amst), 1970. **33**: p. 193-201.
60. Dietz, M.J., et al., *Effective connectivity reveals right-hemisphere dominance in audiospatial perception: implications for models of spatial neglect.* The Journal of Neuroscience, 2014. **34**(14): p. 5003-5011.
61. Mesulam, M.-M., *Spatial attention and neglect: parietal, frontal and cingulate contributions to the mental representation and attentional targeting of salient extrapersonal events.* Philosophical Transactions of the Royal Society B: Biological Sciences, 1999. **354**(1387): p. 1325-1346.
62. Kinsbourne, M., *Hemi-neglect and hemisphere rivalry.* Adv Neurol, 1977. **18**: p. 41-9.
63. Bultitude, J.H. and A.M.A. Davies, *Putting attention on the line: Investigating the activation-orientation hypothesis of pseudoneglect.* Neuropsychologia, 2006. **44**(10): p. 1849-1858.

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Contributions

CAB, TAB, MK and JBM designed the research; CAB, SDG and DL performed the research, CAB analysed the data; and CAB, JBM, SDG and MK wrote the manuscript.

Competing Interests

The authors declare no competing financial interests.

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