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Short Communication

ARE ANGRY MALE AND FEMALE FACES REPRESENTED IN OPPOSITE HEMISPHERES OF THE FEMALE BRAIN? A STUDY USING REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (rTMS)

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The universality across cultures for recognizing the facial expression of anger suggests an evolved mechanism for dealing with threat. Using low frequency repetitive transcranial magnetic stimulation (rTMS) and a paradigm involving color-naming latencies for angry, fearful and neutral faces, and for emotional and neutral words respectively, we found evidence for a hemispheric specialization according to the sex and emotional content of faces in female subjects. Participants showed increased attention specifically to male angry faces after stimulation of the right superior temporal lobe, whereas they showed increased attention to angry female faces after left temporal stimulation. No effect was detected regarding the processing of fearful faces or emotional words. This result suggests differential processing of sex-specific threat-related stimuli specifically involving both hemispheres, i.e., that male and female faces are processed in opposite hemispheres, which might reflect the divergent adaptive significance of male and female threat for young females.

Keywords: Threat recognition; facial expressions of emotions; repetitive transcranial magnetic stimulation; superior temporal sulcus; sex differences; hemispheric specialization.

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1. Introduction

Darwin noted the universality across cultures for the facial expression of anger. It is then plausible that a mechanism for the rapid recognition of angry faces has evolved for dealing with threat [11, 12]. Evidence demonstrates that different neural networks process distinct negative emotions such as sadness, disgust, fear and anger [1, 5, 28, 34]. The superior temporal sulcus region (STS) is believed to constitute a multimodal interface specifically involving the detection of gaze direction, emotion recognition from facial expressions including anger, movement and intentions of biological agents, and "implied" motion [3, 4, 9, 16, 17, 20, 21, 22, 24, 27]. Candidate structures for the detection of fearful facial expressions primarily comprise the amygdala, the left inferior frontal lobe and right fusiform gyrus [34].

With respect to laterality in emotion recognition research, there is limited evidence from neuropsychological [42], psychophysiological [25, 36] and functional brain imaging studies [34], for structures in both hemispheres to play a part in the mediation of anger. Previous work using repetitive transcranial magnetic stimulation (rTMS) has shown that low-frequency stimulation over the right prefrontal cortex increases the attention to angry facial expressions [38], and reduces attention to fearful faces [39]. Since the STS has extensive reciprocal connections with the amygdala, which in turn is connected to the orbitofrontal cortex [3], we hypothesized that rTMS applied to the STS region would reveal lateralization effects in the detection of threat in facial expressions.

We used rTMS on the temporal lobe over the STS region (see Fig. 1) in conjunction with a color-naming latency paradigm for male and female faces with angry, fearful and neutral expressions of emotion [38, 39]. To test whether latency differences were specific for faces, we applied a color-naming latency test involving emotional and neutral words [6, 15]. For such color-naming latency tests, the term "emotional stroop task" has been widely used (e.g., Ref. 33). In these tests, the faces serve as an implicit or unconscious distraction from the task of identifying the color of the face. rTMS provides a powerful tool in exploring whether a certain brain area is not only involved but necessary for performing a particular task [26]. Low-frequency rTMS is known to produce temporary disruption of neural activity in a circumscribed area of the cerebral cortex under or near to the center of the stimulation coil, and to induce contralateral excitation due to a reduction in transcallosal inhibition, depending on stimulus intensities [23, 32]. Cortical rTMS may also influence the neurotransmitter activity of subcortical brain areas [35]. In this single-blind study, we compared the responses of healthy individuals during two color-naming latency tasks, depicting facial expressions of emotion and emotional words before and after rTMS, over the right and left STS structures of the temporal lobes. In this study which lacked the opportunity to control the exact stimulation site by magnetic resonance imaging (MRI), we decided to include only female subjects, because their temporal lobes are less asymmetric compared with males [14]. Thus, the likelihood of hitting equivalent spots of the cortex surface on both sides was greater in female subjects than in male subjects.

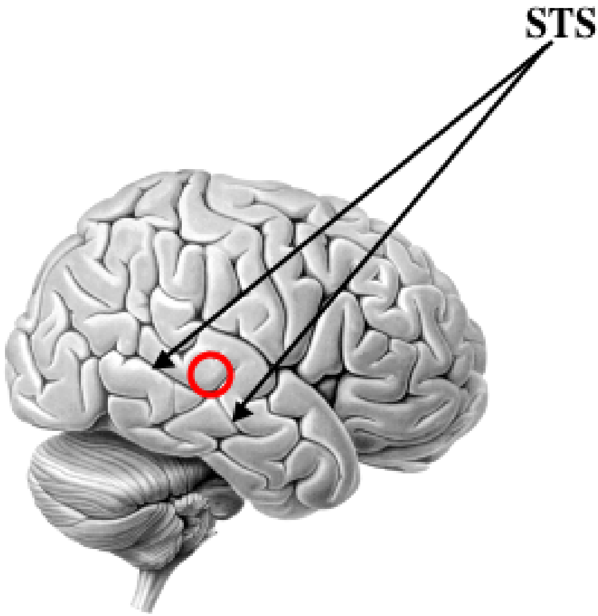

Fig. 1. Approximate rTMS site (shown in circle) over the right superior temporal sulcus (STS) (mirrored over the left STS).

2. Methods

2.1. *Participants*

Seven right-handed female subjects aged 18 to 27 participated in this study after giving written consent. Persons with neurological or psychiatric disorders or other contraindications to rTMS were excluded in accordance with the International Safety Guidelines for the application of rTMS [41]. All participants had normal or corrected to normal vision. Subjects were nave of rTMS and unaware of the aim of the study. The study was approved by the University of Sydney's ethics committee.

2.2. *Apparatus*

1 Hz rTMS was applied for 15 minutes at 90% of the individual motor threshold (MT) on the right or left STS region (see Fig. 1), using a figure-of-eight configurated water-cooled coil (coil diameter 5 cm; MagPro X 100/Medtronic, Denmark). Although it would have been desirable to apply suprathreshold stimulus intensities (e.g., 110% of MT or higher), we used 90% of the individuals' MT as the maximum tolerable stimulus intensity in this location, where direct (and potentially painful) stimulation of the superficial temporal muscle was unavoidable. Each train consisted of 900 impulses. 1 Hz-stimulation was chosen. It has been demonstrated to result in a depression of the excitability of the cortical area beneath the center of the coil for several minutes after stimulation [10] and excitation (disinhibition) of the contralateral cortical areas [18, 23, 26]. MT was determined over the dominant hemisphere by induction of an involuntary reflex twitch in the right-hand digits in at least six

out of ten consecutive trials using a single TMS pulse. The scalp coordinates for the STS region on both sides were located stereotaxically (marked on a tightly fitted swimming cap), as 50% of the distance between the standard EEG positions of T3/T4 and T5/T6 electrodes according to the International 10–20 system and a 25% of the distance between T3/T4 and T5/T6 perpendicular towards vertex (Cz). During determination of MT, the stimulation coil was held tangentially to the stimulus point with the handle of the coil pointing posterior. During STS stimulation, the handle of the coil was held in a vertical position pointing upwards. In the control condition, the exact set-up procedure was followed, but rTMS was not applied as the coil placed over Pz was tilted 180° with the non-stimulating plane of the coil facing the scalp, leaving the potentially distracting sound of the TMS-machine unchanged. In order to ensure credibility of the control condition, participants were instructed that, in contrast to right or left side stimulation, no subjective experience of direct muscle stimulation was to be expected over Pz, due to an absence of any muscles in this location. The three experimental sessions were conducted in random order on separate days, that are at least 2 days apart.

2.3. *Task and procedure*

All subjects had a practice run using the standard Stroop Test before rTMS. In the color-naming tasks, which were carried out before and immediately after stimulation, subjects were asked to respond as quickly as possible to the color (red, green, blue, and yellow) of pictures of 10 male and 10 female angry, fearful or neutral faces (60 stimuli in total; [13, 38, 39]), and to the color of 48 emotionally salient and 48 neutral words [33]. Colors and faces or words were randomly combined. Participants were explicitly told to focus on the face or word, and to specify its color (not its emotion) by pressing buttons with their left and right index and middle fingers on a computer keyboard with matching colored stickers. Pushing the keys terminated, the presentation of the stimuli and the next stimulus appeared on the screen without delay. This procedure creates time pressure on the test subjects, such that the negative aspects of the stimuli have more weight [33]. The stimuli were presented in random order on a 17-inch 60-Hz computer screen at an approximate distance of 70 cm (Fig. 2). Overall, it took less than five minutes for subjects to complete the tasks. Thus, stimulus application was ensured to lie within the critical period of functional suppression of the targeted cortex area beneath the coil.

2.4. *Analysis*

The data were analyzed and processed with the Statistical Product and Service Solutions (SPSS) version 11.0 for Macintosh. The dependent variables in both the face and the word color-naming tasks were Attentional Bias Scores (i.e., mean individual color-naming latencies of emotional stimuli divided by the mean individual color-naming latencies of neutral stimuli). We calculated the difference between the

Fig. 2. Illustration of the color-naming task and the location of application of rTMS. Participants were asked to identify the color of standard Ekman faces and not their emotional state in our paradigm. This was done before and after the application of rTMS to the superior temporal sulcus region (STS) as indicated by the gray kidney-shaped magnetic coil in the lower figure. Artificially colored still photographs of males and females displaying anger, fear or a neutral facial expression, and of emotional and neutral words were randomly presented to the subjects on a computer screen. When the subject pushed the respective colored button the next face occurred on the screen without delay. This situation creates time pressure on the subjects and picks up subtle differences in attention to specific stimuli (i.e., emotions) as measured by an "attentional bias" score where longer reaction time indicates greater attention.

baseline quotient (before rTMS) and the quotient after rTMS. A positive value indicated increased attention towards the emotional stimuli, whereas a negative value indicated a decrease of attention compared with baseline. The greater the latency of the participant's response time, the greater the implicit or nonconscious distraction caused by the particular facial emotion. The effects of the color-naming stimuli (female and male faces, emotional words), and brain region of rTMS stimulation (left, right, Pz) were assessed with analyses of variance (ANOVA) for all conditions. When significant effects were indicated, post-hoc comparisons used paired samples t-tests. The significance level was set at $p < 0.05$.

3. Results

An ANOVA for the face conditions showed no significant interaction between brain region and all angry faces of both male and female faces taken together

(F = 2.618, p = 0.141, Greenhouse–Geisser corrected, n.s.), or between brain region and all the fearful faces (F = 0.27, p = 0.724, Greenhouse–Geisser corrected, n.s.), nor did the analysis reveal a significant effect in the emotional word condition ($F = 0.053$, $p = 0.92$, Greenhouse–Geisser corrected, n.s.). When differentiating between male and female faces, however, the ANOVA revealed a significant interaction between gender and brain region for angry faces ($F = 7.909$, $p = 0.007$, Greenhouse–Geisser corrected). The participants selectively increased their attention toward male angry faces after right temporal rTMS by 19.3% ($sd = 13.07$), with no significant change occurring between left rTMS and control conditions. The participant's attention toward female angry faces increased after left temporal rTMS by 10.3% ($sd = 12.2$), with no significant change for right rTMS and control conditions. Paired samples t-test were significant for attentional bias scores for male angry faces after right rTMS, compared with the other stimulus locations (t = 2.3, p = 0.05), and for attentional bias scores for female angry faces after left rTMS, compared with right-side stimulation (t = 2.6, p = 0.043) and sham (t = 2.8, p = 0.031). No such differential response patterns emerged when showing fearful male or female faces (ANOVA: F = 2.178, p = 0.167, Greenhouse–Geisser corrected, n.s.). Effects of rTMS stimulation on the processing of angry [Fig. 3(a)] and fearful [Fig. 3(b)] faces, and on the processing of emotional words [Fig. 3(c)]. Figure 3 depicts the main results of the study comparing task performance for male and female faces,

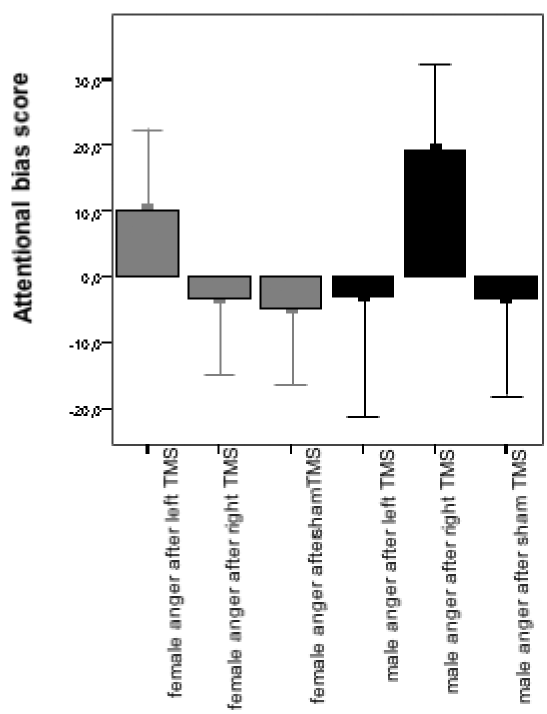

Fig. 3(a). Effects of rTMS-stimulation on the processing of angry faces.

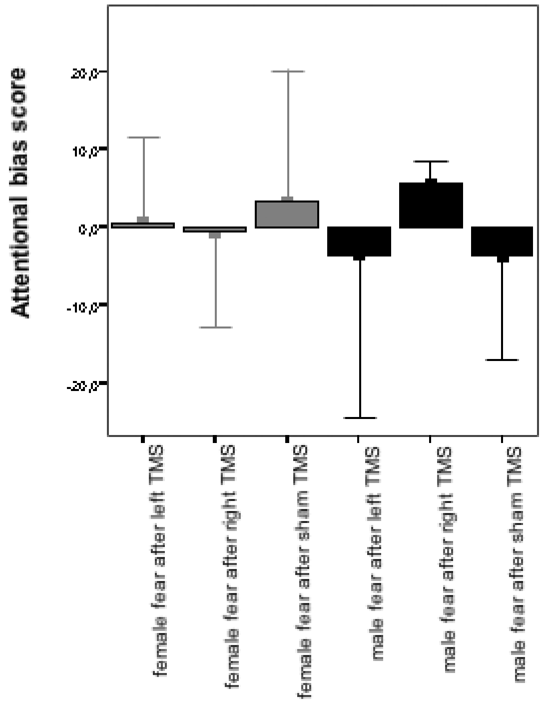

Fig. 3(b). Effects of rTMS-stimulation on the processing of fearful faces.

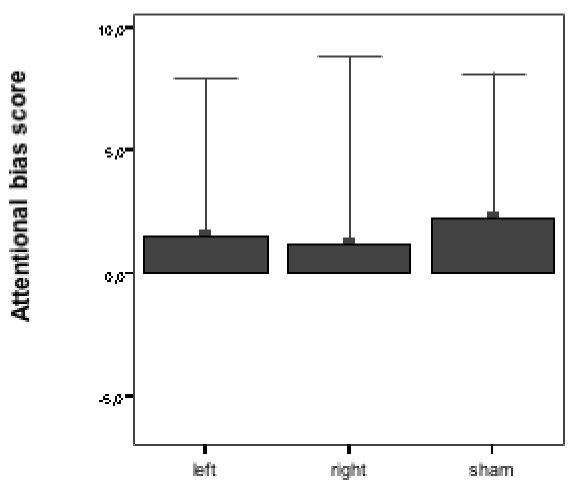

Fig. 3(c). Effects of rTMS-stimulation on the processing of emotional words.

and for emotional words, respectively, after right, left and sham rTMS. The columns indicate the differences of the attentional bias scores in percent after rTMS, relative to before rTMS. A value of +10, e.g., would mean an increase of the subjects' attention by 10%.

4. Discussion

A wealth of research has unveiled the existence of a dedicated domain-specific neural network for social interaction, where rapid threat detection presumably evolved in response to the demands of the social environment [2, 8]. In contrast to previous studies using low-frequency rTMS over the prefrontal cortex [38, 39], our study did not reveal general differences in anger and fear recognition, after stimulation of the superior temporal lobe structures on both sides. Most interesting and quite unexpectedly, however, we discovered that the STS region, at least in young females, is critically involved in the recognition of sex-dependent anger, and that angry male and female faces are processed in opposite hemispheres. It is unlikely that such a response pattern could have occurred by chance, since we found the representation in opposite hemispheres in 6 out of 7 female participants. No such sex-specific hemispheric specialization of emotion processing has been previously reported. Our present study could therefore add a new dimension to contemporary views on the processing of facial emotions including the left-right, valence and approach-withdrawal theories. For example, in contrast to previous research [19], we found that it may also be the sex of the angry face that determines the hemisphere involved in processing. There is evidence for sex-differences in the decoding of facial expression, with females generally being superior to males at the identification of affect from nonverbal cues of face, body and voice. This sex-difference is invariant across the sex or age of the stimulus person, tasks, and cultures [7]. However, females have been found to read negative emotions less accurately than males, particularly in male faces [31, 40]. Our result that angry male and female faces are selectively processed in opposite hemispheres in young female subjects suggests that the decoding of threat stimuli, as presented in male and female angry faces, may require different computational resources. From an evolutionary perspective, for females, a female angry face may be perceived as less threatening and subjected to holistic facial processing associated with the right hemisphere [29, 30]. In contrast, threat to survival may be more associated with a male angry face. Hence, the threat analysis of male faces may require additional decoding and feature analysis of the face [29, 30, 37], and perhaps recognition of the "implied motion" conveyed by male angry faces, which could be associated with left hemisphere activation.

We found that the attention to female angry faces increased on average by 10% after rTMS over the left STS, whereas the attention to male angry faces increased by $\sim$20% after rTMS over the right STS. Our results for angry male faces are consistent with those of Van Honk *et al.*, [38, 39], who argued persuasively that the processing takes place in the left hemisphere. In other words, under our stimulation conditions, rTMS primarily has an excitatory influence on the contralateral cortex as is supported by other studies [18, 23]. Consequently, our results for angry female faces point to processing in the right hemisphere, i.e., the hemisphere opposite to that for angry male faces.

Our result suggests differential processing of sex-specific threat-related stimuli specifically involving both hemispheres, i.e., that male and female faces are processed in opposite hemispheres, which might reflect the divergent adaptive significance of male and female threat for young females.

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