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„Continuous Theta Burst Stimulation of the Right Supramarginal Gyrus and Empathic Evaluation"

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INTRODUCTION

Taken individually, human beings are inferior to many other mammalian species when it comes to physical strength and robustness (Zaki & Ochsner, 2012). Nevertheless, humanity emerged as the dominating species on the terrestrial globe, with the ability to adapt to a broader range of habitats and changing environments than any other animal. How did we manage to get so far, even though our physical prerequisites are not that promising at all?

There may be various potential explanations, but it seems outmost plausible, that our interpersonal predispositions concerning social cognition have great impact on our dominating role as a species (Tomasello, Carpenter, Call, Behne, & Moll, 2005). These interpersonal predispositions, for example the ability to understand feelings and thoughts of other humans and the ability to cooperate, are strongly underpinned by the multifaceted psychological construct of empathy (Zaki & Ochsner, 2012). Even though a wide range of definitions for empathy can be found in psychological literature, there is broad agreement on three fundamental components (Lamm, Batson, & Decety, 2007): Capacities to represent the affective state (e.g. emotions, feelings) of another individual, capacities to represent the cognitive state (e.g. perspective, thoughts) of another person and monitoring mechanisms, which aim to negotiate and distinguish between the inner states of oneself and of others.

1. Theoretical concept of affective empathy

As one result of the distinct but interrelated processes that constitute the phenomenon of empathy, individuals are able to share and understand the affective states of other people (Rameson & Lieberman, 2009). Some psychologists and related scientists (e.g. Adolphs, Damasio, Tranel, Cooper, & Damasio, 2000; Preston & de Waal, 2002) argue that the occurring processes can be described as in the following: The perception of someone else's affective state activates one's own representations of the state, and the activation of these representations automatically elicits the associated affective responses, at least if not inhibited or modulated. So, at a very basic level, people may satisfy their curiosity in understanding the feelings of other persons by simulating how they themselves would feel (Pronin, 2008).

It is worth mentioning, that this theory seems to be tentatively in accordance with results of neuroscientific studies: It frequently has been demonstrated that observing emotions in others partly activates brain regions that are also active during the first hand experience of these emotions (Fan, Duncan, de Greck, & Northoff, 2011). A very popular example stems from a MRI study of Singer et al. (2004): Some parts (e.g. anterior medial cingulate cortex, anterior insula) of the brain's network, which is activated during the direct experience of pain, are also active during the perception of pain in others. Therefore it often is suggested that sharing and understanding other's affective states partly is based on shared emotional representations. Furthermore, this brings up the assumption that self-projection and simulation are some of the processes that account for an important aspect when it comes to interpersonal understanding (Silani, Lamm, Ruff, & Singer, 2013).

As already mentioned, empathic phenomena are not only characterized by shared emotional representations but as well by monitoring and modulating functions, such as processes of self-other distinction. Empathizing with someone else usually is not only the mere taking over and sharing of the affective state of that person, it therefore cannot completely be explained through overlapping co-representations. Imagine a psychiatrist who empathically observes a patient in big emotional pain: A complete co-activation of affective representations would be devastating, in the sense that the psychiatrist also would be in great pain and therefore not able to help. Since usually there is no complete co-activation and processes of self-other distinction are involved, the psychiatrist should automatically be able to keep track of the origins of the experienced pain, identifying the other (the patient) and not the self as source of it. While most likely not experiencing the same affective state as the patient, the psychiatrist should be able to help and react in a prosocial manner, a behavioral response often linked to empathy. Important behavioral evidence for the insufficiency of self-projection to fully explain empathic phenomena comes from Batson, Early and Salvarini (1997): They demonstrated that imaging how one would feel or how another person would feel in a specific situation is likely to entail different affective states. MRI data supporting this finding come from Jackson, Brunet, Meltzoff and Decety (2006): Though imagining oneself in pain as well as imagining another person in pain are both associated with activation in the anterior medial cingulate cortex and the anterior insula, it seems that these two processes selectively activate different parts within these regions.

Processes of self-other distinction distinguish between self- and other-related representations and help us to locate whether an experienced inner state originates in the self or the other (Lamm, Bukowski & Silani, 2016). Moreover, processes of self-other distinction prevent our own inner states from interfering with our understanding of the inner states of other people. Since our own affective states and self-related emotional representations are the most prominent to us, they sometimes can conflict with our representations of other-related emotions, leading to an egocentrically biased understanding of the inner states of others. For example, it has been observed that people tend to give egocentrically biased judgements about the affective states of other persons when experiencing emotions (elicited through touch) of opposing valence to the emotions of the person they have to judge (Silani et al., 2013). However, Silani and colleagues also reported, that healthy adults under natural circumstances appear rather proficient in overcoming such egocentrically biased judgements. Altogether, it seems like inhibition, suppression or devaluation of self-related representations are some of the processes that enable accurate self-other distinction when it comes to the understanding of affective states of others.

2. Right supramarginal gyrus and integration of self- and other-related information

Steinbeis (2016) reviewed recent findings from neuroscientific studies and came to the conclusion that processes of self-other distinction in the affective domain are consistently and specifically associated with elevated activation in the right supramarginal gyrus (rSMG). The rSMG expands over the anterior part of the right tempo-parietal junction (rTPJ) and is located anterior to the right angular gyrus at the inferior parietal lobe (Lamm et al., 2016). The rTPJ frequently is associated with processes of self-other distinction relating to theory of mind and perspective taking (Schurz, Radua, Aichhorn, Richlan, & Perner, 2014), playing an important role in the distinction of self- and other-related cognitive representations and in processes relating to social cognition in general. Notably, the rTPJ is also recruited during processes that are far from exclusive to social cognition, for example during lower-level computational processes involved in attention-reorienting and in comparing internal expectations with external events (Decety & Lamm, 2007). Interestingly, the rSMG (especially the posterior part) is also associated with processes that are not exclusive to social cognition, namely with proprioception, the vestibular system (Ben-Shabat, Matyas, Pell, Brodtmann, & Carey, 2015) and the visual system. Hence, it is suggested that rSMG contributes to conscious spatial orientation via integrating different information from different sensory modalities (internally & externally directed) into a coherent whole (Kheradmand, Lasker, & Zee, 2013). Until now, it is not completely clear to what extent rSMG might be involved in the integration of self- and other-related emotional relevant information and how it contributes to our emotional evaluation of others and ourselves.

It has been observed, that the recruitment of rSMG is beneficial for overcoming egocentrically biased emotion judgements (Silani et al., 2013): People's tendencies to give egocentrically biased judgements about the affective states of other persons when experiencing emotions of opposing valence dramatically increased when functioning of rSMG was temporary disturbed by the application of 1 Hz repetitive Transcranial Magnetic Stimulation (rTMS). Hence, rSMG might play an important role for empathic judgements that require conciliation of incongruent self- and other-related emotional representations. It furthermore has been observed that the mere presence of conflicting self- and other-related emotional representations seems to be sufficient to recruit rSMG, even if no empathic nor any emotion judgements are implemented (Steinbeis et al., 2014). This finding gives rise to the assumption that the rSMG already plays a role in early processes of self-other distinction, possibly differentiating the perceptual information which has relevance for one's own emotions from the information that is relevant to the emotions of others. In other words, rSMG generally might play a role in the estimation and calculation of information related to one's own emotions and distinguish this from information related to the emotions of others (Steinbeis et al., 2014).

Therefore, the extended tendency for egocentrically biased empathic judgements in incongruent affective states due to a disturbance of the functioning of the rSMG might reflect only one possible outcome of inaccurately working estimation processes. But, assuming that the rSMG is already recruited during the multisensory integration of perceptual information referring to one's own affective state on the one side and to the affective states of others on the other side, a disturbance of its functioning generally might affect how one estimates the relevance of other-related emotional information. A disturbance of rSMG might lead one to underestimate the relevance of other-related emotional information, regardless whether simultaneously processed self-related information are contradicting or accordant. This underestimation gets the most apparent when in an incongruent state to another individual. When in a neutral or congruent affective state, it may be the case that empathic judgements are far less prone to be biased by the one's own emotional experiences: In these situations, it might not be that important to dissolve self-related affective representations from other-related ones to get to an accurate empathic judgement (Silani et al., 2013). However, it is also conceivable that processes regarding the integration of self- and other-related emotional relevant information are at work even when these kinds of information are accordant. Further research is required to specify the exact role of the rSMG regarding empathic judgements during the perception of co-occurring self- and other-related emotional relevant information.

OBJECTIVE

In the broadest sense, the aim of this study is to further deepen our understanding of the neural mechanisms underpinning affective self-other distinction. We are interested in how the functioning of rSMG interacts with our ability to properly evaluate the affective states of others. To address this question concretely, we use continuous Theta Burst Stimulation (cTBS) to perturb activity in the rSMG and measure behavioral performance in the Empathy Touch Task. Note that, during task execution, we also measure changes in brain activity after cTBS via fMRI, but the analysis of the imaging data is beyond the scope of this thesis.

The method of cTBS, first described by Huang, Edwards, Rounis, Bhatia and Rothwell (2005), is a well-established form of patterned TMS that is able to induce long lasting (fifteen up to fifty minutes) effects on cortical excitability. Generally, cTBS is thought to have an inhibiting and suppressing effect on the neural activity on cortical structures under the coil (Huang, Rothwell, Chen, Lu, & Chuang, 2011). However, recent findings of Hamada, Murase, Hasan, Balaratnam and Rothwell (2013) suggest that the effects of cTBS can vary across individuals: They observed in a sample of 52 participants that the magnetic stimulation induced facilitating effects on cortical excitability just as often as it triggered inhibiting effects. The effects of cTBS seem to involve plasticity like changes in synaptic connections (Huang, Chen, Rothwell, & Wen, 2007) by altering activity in excitatory as well as inhibitory neuronal circuitry (Jacobs, Premji, & Nelson, 2012). The after-effects of cTBS are still not completely understood, but it has been shown that they are related to activity in GABAeric (Cárdenas-Morales, Nowak, Kammer, Wolf, & Schönfeldt-Lecuona, 2010) and glutamateric (Huang et al., 2007) systems, hence the association with inhibition and excitation. Nevertheless, cTBS has been proven to effectively inhibit cortical excitability and furthermore, functional connectivity with associated brain regions (Rahnev et al., 2013). Therefore, we expect that cTBS leads to long-term depression-like processes on synaptic plasticity, suppressing the excitability of the stimulated regions and thereby leading to an altered functioning of the targeted areas. Across two testing sessions, we once apply cTBS on the vertex (as a control condition) and once on the rSMG to investigate in a within-subjects design whether and how the temporary disturbance of the functioning of rSMG affects behavior in the Empathy Touch Task.

The Empathy Touch Task is based on a paradigm of Silani et al. (2013): Through simultaneous visuo-tactile stimulation of the participant and another person, congruent or incongruent emotions between the persons are evoked: A picture of a pleasant (e.g. soft, clean) or unpleasant (e.g. squishy, dirty) object gets presented on a screen in front of the participant while at the same time the participant's left hand gets touched with material that feels just like the depicted object. The picture of the object that the other person is stimulated with is also presented on the screen. After the stimulation participants either have to rate the intensity of the pleasantness (or unpleasantness) of their own emotional experience or of the experience of the other person. If the participant and the other person are both experiencing stimulation with pleasant or unpleasant objects, congruent emotions between the persons should be evoked, thus self- and other-related emotional relevant information are accordant. If one of the persons experiences stimulation with a pleasant and the other one with an unpleasant object, incongruent emotional states between the persons should be excited, meaning that self- and other-related emotional relevant information is contradicting.

The main goal of this thesis is to examine whether the tendency to give biased empathic judgements is higher when the functioning of rSMG is disturbed via cTBS. We suppose that the rSMG plays an important role in the integration of self- and other-related emotional relevant information during empathic judgements: When one is confronted with self- and other-related emotional relevant information at the same time, a disturbance of rSMG may lead one to perceive the information referring to others as disproportional irrelevant. A perturbation of the functioning of rSMG might bring us to overestimate the relevance of the information referring to our own affective state and thus to underestimate the relevance of other-related information. As a result, the not correctly working estimation processes might entail an altered understanding of the affective states of others. Thus, we suggest that a disturbance of the functioning of rSMG enhances the probability to be biased or distracted by self-related emotional relevant information when it comes to the understanding of emotional events that are experienced by another individual. In our experiment, this bias regarding empathic judgements might be expressed in different ways.

1. **How does rSMG contribute to other-related emotion judgements?**

Based on the consideration that rSMG might play an important role for other-related judgements, independent of whether self- and other-related emotional relevant information is contradicting or not, we expect our participants to generally evaluate other-related emotional events as less intensive after cTBS is applied to their rSMG. Under normal circumstances, rSMG might be involved as soon as participants are confronted with perceptual (e.g. visual) information that possesses relevance for another person's emotions and simultaneously experience an event which has meaning for their own emotions. We suppose that this involvement of rSMG is specifically important when it comes to the evaluation and understanding of affective states of others. Through the application of cTBS on rSMG, we expect to cause a disturbance in the processes of integrating self- and other-related emotional relevant information from different sensory channels. This disturbance might affect the perception of other-related information to the extent that the emotional relevance of these information is not completely recognized. As a result, other-related emotional events should be judged as less intensive. In other words, we expect the disturbance of functioning of rSMG via cTBS to express itself through deficits regarding the calculation and estimation of the meaning of other-related emotional relevant information. The restricted ability to fully comprehend the meaning of other-related emotional relevant information might lead subjects to evaluate other-related emotional events as less intensive than under normal circumstances. The involvement of rSMG should be less crucial regarding self-related emotional evaluation, since the evaluation of self-related emotional relevant events based on first-hand experience may be far less susceptible to be biased by concurrent available other-related information. Therefore, a disturbance of rSMG should not affect participants' judgements concerning self-related emotional events but rather exclusively regarding other-related events.

Considering the findings of Silani et al. (2013), a bias resulting from the disturbance of the rSMG with regard to other-related emotion judgements might only and specifically emerge when information referring to one's affective state is contradictory to information which refers to the affective state of others. When Silani et al. (2013) disturbed the functioning of rSMG via rTMS, they observed a drop in intensity ratings regarding other-related emotional events when participants simultaneously experienced self-related emotional events of opposing valence. However, such a drop in other-related intensity ratings was not observed when the valence of self- and other-related emotional events was congruent. This brings up the assumption that rSMG-associated integration processes concerning self- and other-related emotional relevant information are especially important when these kinds of information are not accordant. Hence, a disturbance of the functionality of rSMG might especially affect empathic judgements in situations of contradicting self- and other-related emotional relevant information.

Previous research (Silani et al., 2013; Steinbeis et al., 2014) supports the expectation that a drop regarding intensity ratings of other-related emotional relevant events after cTBS of rSMG especially emerges when self- and other-related emotional relevant information is of opposing valence. Nevertheless, it is also imaginable that cTBS of rSMG causes the tendency to generally rate other-related emotional events as less intensive, independent of whether self- and other-related information is contradicting or not. The rSMG-associated integration processes regarding self- and other-related information might be important for an adequate estimation of the emotional relevance of other-related information in general and not only when there is contrary self- and other-related emotional relevant information. We want to examine if rSMG-associated processes regarding other-related emotion judgements are indeed thus far specialized as it previously has been observed.

2. How consistent are the effects of cTBS over time?

Additionally to the above described main goal of the thesis, I would like to examine if the behavioral effects of cTBS of rSMG look differently in dependence of passed time after the application of cTBS. Through the chosen implementation of the Empathy Touch Task we are able to measure empathic behavior in one testing period early after the application of cTBS (between 5 and 20 minutes after the application) and in another later testing period (between 27 and 42 minutes after the application). Huang et al. (2011) observed that the suppression of motor evoked potentials caused through 40 seconds long cTBS can last up to 50 minutes. Hence, the excitability of rSMG (and maybe even neighboring cortical regions) should be inhibited in both testing periods. In this sense, we expect effects of cTBS on empathic behavior to occur in the early testing period as well as in the later testing period. Despite the observation that physiological effects of cTBS may last up to fifty minutes after application, there are several studies (Nyffeler et al., 2006; Cazzoli, Wurtz, Müri, Hess, & Nyffeler, 2009) reporting that behavioral effects caused by cTBS diminish or even vanish after thirty minutes. Furthermore, the elsewhere (Hamada et al., 2013) observed variability of effects of cTBS leaves room for the suggestion that the effects of cTBS in fact might be expressed differently over time.

METHOD

1. Participants

Forty healthy right-handed females (M_{age} = 21.88; SD_{age} = 3.23) were recruited through the University of Vienna's psychological research participation platform and bulletins in university buildings, receiving course credit and monetary compensation of 80 € for their participation. Since it recently was reported (Tomova, von Dawans, Heinrichs, Silani, & Lamm, 2014), that gender differences are likely to affect behavior in the Empathy Touch Task, we only recruited females to eliminate gender as one possible confounding variable. Interested candidates completed a TMS and MRI screening questionnaire, ensuring that participants do not suffer from any psychiatric or neurologic disorders and that they fit the well-established criteria for TMS application (Rossi, Hallet, Rossini, & Pascual-Leone, 2011) and MRI scanning (Kanal & Shellock, 1992). None of the finally included participants had any prior experience with TMS. General information about the course of the study and personality questionnaires (Interpersonal Reactivity Index, Davis, 1980; Bermond-Vorst Alexithymia Questionnaire, Vorst & Bermond, 2001; Autism-Spectrum Quotient, Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001; Questionnaire of Cognitive and Affective Empathy, Reniers, Corcoran, Drake, Shryane, & Völlm, 2011) were sent online to contemplable candidates prior to the experiment. The study was approved by the ethics committee of the Medical University of Vienna. Written informed consent was obtained from all participants.

2. Empathy Touch Task

2.1 Experimental setup

The experiment was conducted in a MRI environment (3 Tesla Siemens Prisma whole body scanner), making it impossible to run the task with two persons in one room at the same time. Nevertheless, to still provoke authentic incongruent or congruent emotions, it is best to have participants think that another person is simultaneously experiencing visuo-tactile stimulation. Similarly to the fMRI study of Silani et al. (2013), we paired each participant with a female confederate, who ostensibly performs the task in another MRI scanning room.

The main experimental task was constituted through the double perspective version of the Empathy Touch Task. During this task, participants laid in the scanner and visual stimuli were presented through a back-projection system consisting of a rear-view mirror mounted on the scanner's head coil. Each trial started with the presentation of a fixation cross (mean ISI=3825 ms). Directly afterwards, participants were presented with pictures of two objects on the left and right side of a screen (which was projected on the mirror) for 3 s. Visual presentation was time-coupled with tactile stimulation, which was executed through an experimenter sitting next to the scanner, touching the participant's left hand with material corresponding to the object presented on the left side of the screen. Tactile stimulation was performed at a frequency of 1 Hz. The picture on the left side was entitled with the label "You", whereas the picture on the right side was labeled "Your colleague". The picture on the right side referred to the visuo-tactile stimulation that the confederate ostensibly was receiving at the same moment. Immediately after the offset of visuo-tactile stimulation, participants had to judge the experienced pleasantness of stimulation on a Likert-type rating scale, ranging from very unpleasant (-4) over neutral (0) to very pleasant (+4), whereas the extreme ends of the scale were represented through pictures of a happy and a disgusted face. Participants had 4500 ms to enter their ratings through moving a cursor by pressing buttons on a response box with their right hand.

Whether participants had to judge the pleasantness of their own stimulation (self judgement) or the pleasantness of the stimulation experienced by the confederate (other judgement), was instructed to them at the beginning of each experimental run. One experimental run consisted of 40 trials. Ten different pleasant and unpleasant visuo-tactile stimuli were used per experimental run and each of the stimuli was applied twice to the participant, once leading to incongruent and once leading to congruent emotions between participant and confederate. Congruent emotions were elicited through visuo-tactile stimulation of participant and confederate with objects of the same valence, incongruent emotions were triggered by using stimuli of different valence. Figure 1 displays an exemplary representation of the task, including the different conditions regarding the congruency of administration of the stimuli, the valence of the target stimuli and the target perspective (other/self).

2.2 Materials

Overall 80 different pairs of visual and tactile stimuli were used across the two testing sessions. Note that, even though 80 individual pictures were used, given the similarity of some of these pictures, only 65 individual materials were adopted to build the corresponding tactile stimuli. All pairs were drawn from a larger set of 98 pairs, which were pre-rated with regard to the valence and intensity of elicited emotions and authenticity of the combination of visual and tactile stimuli. Pre-rating was performed by an independent sample (n=22). The 40 pairs that elicited the strongest positive emotions and the 40 pairs that elicited the strongest negative emotions were selected for this study.

All 80 pairs of visuo-tactile stimuli were subsumed into four distinct sets, each consisting of 10 pleasant and 10 unpleasant pairs (see Table 1 for a list of all pairs). Two of the sets were used during one session, the other two were used during the other session. The order of which two sets were used in the first session was counterbalanced across participants. Within one testing session, one set was used before the resting state period and one set was used afterwards. Each set of stimuli was used in two successive experimental runs (once in the other and once in the self judgement condition). The order whether a set was first used in the other or in the self judgement condition was counterbalanced across participants.

Before the application of cTBS and the execution of the double perspective version of the Empathy Touch Task (main experimental task), participants already were confronted with all stimuli in two different single perspective blocks in each session. These single perspective blocks were included in the experimental procedure to acquaint the participants with the stimulus material and the task. In one single perspective block, participants successively received visuo-tactile stimulation with all 40 pairs of stimuli that were used in the following session. They had to rate the pleasantness of their own sensations of the stimuli without being presented with a visual stimuli indicating any stimulation the confederate (or the supposed other participant) currently is receiving. In the other single perspective block, participants consecutively were presented with all 40 images referring to the pairs of visuo-tactile stimuli without receiving any touch in the meantime. They were told that the presented images refer to the stimulation the supposed other participant currently is receiving and they were asked to vicariously rate the sensations of the other person.

3. Finger Tapping Task

The Finger Tapping Task, if performed during fMRI measurements, can be used to identify the optimal location on the left motor cortex for stimulating the right first dorsal interosseous (FDI). Each of the six trials of the task starts with the presentation of a fixation cross for ten seconds and continues with the presentation of a rapidly blinking chessboard for the next ten seconds. Participants are instructed to alternately press their right index and middle finger on their thumb as soon as the blinking chessboard was presented, but leave their fingers still during the presentation of the fixation cross. The functional imaging data, which unfolds through contrasting the images of the different ten second periods, normally shows elevated activity in the left primary motor cortex (M1) and primary somatosensory cortex (S1) and in the primary visual cortex (V1) in both hemispheres.

4. TMS Procedure

4.1 General information

Single TMS pulses (for motor threshold estimation) and repetitive magnetic stimulation were applied with a previously positioned MRi-B91 Butterfly Coil (MagVenture, Farum, Denmark) which was connected to a MagPro R100 stimulator (MagVenture, Farum, Denmark). Navigation and positioning of the coil was performed by two experimenters with the aid of the frameless stereotactic Brainsight TMS Navigation system (Rogue Research, Montreal, Canada). Before every first TMS session, previously acquired T1 weighted structural scans (160 slices, TR= 2300ms, TE= 4.21ms, flip angle= 9°, 1x1x1.1mm voxel size) were supplied to the Brainsight TMS Navigation system and digital 3D curvilinear reconstructions of the participant's scull and brain were performed. At the beginning of each of the two TMS sessions, the digital reconstruction of the scull got co-registered with the actual head of the participant by means of an infrared positon sensor (mobile camera) detecting the required tracking tools (subject's headband with tracking balls, landmark pointer). Before the application of cTBS of rSMG in the one and cTBs of vertex in the other session, the intensity of the theta burst stimulation was adjusted to the active motor threshold (AMT) of participants. The AMT is defined as the minimal intensity of motor cortex stimulation required to elicit a reliable motor-evoked potential (MEP) of minimal amplitude in an active target muscle (Rossini et al., 2015). During the co-registration of the digital scull reconstruction with the actual head and during the estimation of AMT, participants were seated on a chair in the scanning-room next to the MRI-scanner.

4.2 Active motor threshold estimation

The functional imaging data (23 slices, 3.0mm thickness, no gap, 1.5x1.5mm in plane, interleaved slice acquisition, TR=2300ms, TE= 4.21ms) from the Finger Tapping task was used as an overlay on the structural reconstruction of the brain: The thereby observable elevated activation in left M1 was marked and a 2 x 7 circular grid of markers was built around it to curtail the optimal location for stimulating the right FDI. We asked subjects to press on a foam earplug with their right thumb and index-finger with about 25% of their maximal strength. Subsequently, we stimulated all the markers around M1 with single TMS pulses of the same intensity (40% of maximal stimulator output) and recorded MEPs from the muscle body of the right FDI through two self-adhesive silver/silver-chloride electrodes. A ground electrode was positioned at the underside of the right underarm in front of the elbow. The marker, whose stimulation led to the highest MEP, was chosen as the optimal stimulation site for the right FDI. We determined this stimulation site during the first TMS session and used the same site for AMT estimation in the second TMS session. To finally estimate the individual AMT of each subject we used a slightly modified method of Rossini et al. (2015). We began with the application of a single TMS pulse of 40% of maximal stimulator output at the optimal site and gradually increased the intensity by steps of 5% until the magnetic stimulus consistently evoked MEPs that exceed a peak-to-peak amplitude of 0.5 mV. Afterwards we lowered the intensity of TMS in steps of 1% until elicited MEPS were beyond 0.5 mV in 3 out of 5 trials only. The resulting intensity reflected our final estimation of the AMT. The mean AMT across all subjects and sessions was 56.8 % (SD = 8.445%).

4.3 cTBS application

Before the application of cTBS, participants changed their seat and already sat down on the bed of the MRI-scanner. This was done to minimize the time interval between the magnetic stimulation and the execution of the Empathy Touch Task. cTBS is a well-established form of patterned TMS, that is thought to produce relatively long-lasting reductions in cortical excitability (Rossini et al., 2015). During cTBS, a 40 seconds train of uninterrupted theta burst stimulations is given (Huang et al., 2005). Theta burst stimulations are characterized through the application of 3 pulses at a rate of 50 Hz, repeated every 200 ms. The magnetic stimulation was applied with an relative power of 80% of each participants' individual AMT, since this most likely induces inhibitory effects (Huang et al., 2005). The mean relative power of cTBS across all subjects and sessions was 45.44% (SD= 6.756%). Due to the frequent failing of MNI-coordinate transformation in the Brainsight system, the targets for cTBS were, based on the individual brain anatomy reconstructions, carefully selected by a well-trained experimenter. Figure 2 shows an illustration of the chosen targets for cTBS. In a manner similar to Silani et al. (2013), the vertex was stimulated to control for the nonspecific effects of auditory and tactile signals caused through the application of cTBS. Vertex was defined as the meeting point of the left and right central sulcus in the interhemispheric fissure. During cTBS of the vertex, the center of the coil was placed directly over it, with the connection of the cable pointing backwards (see Figure 2b.). The rSMG is part of the right inferior parietal lobe, located at the medial segment of it (Kwok & Macaluso, 2015). To set rSMG as a target for stimulation, we looked at the individual brain reconstructions and followed the right lateral sulcus to the superior end of it: We chose the gyrus that is located directly anterior to the dorsal end of the right lateral sulcus as our optimal target. During the application of cTBS on the rSMG, the center of the coil was located directly on target and the coil was oriented tangentially to the scalp with the connection of the cable pointing back and away from midline at 45 degrees (see Figure 2a). The mean spatial deviation from the target during the 40 seconds long stimulation phase across all subjects was 1.166 mm (SEM=0.149 mm), which speaks for a rather accurate positioning of the coil during stimulation of rSMG.

5. Experimental Protocol

The study was conducted at the Hochfeld MR Center Vienna (HFMRC) of the Medical University of Vienna between March the 9th and April the 20th 2016. All Participants took part in two testing sessions, with an interval of one week between the sessions. cTBS was applied on the vertex in one session and on the rSMG in the other session. The order of which target was stimulated in the first session was counterbalanced across participants.

Session 1. As soon as they arrived to their first session in the lobby of the HFMRC, participants were welcomed and got grouped together with a previously unknown female, who allegedly also participates in the study, but in fact was a confederate of the experimenters. Participant and confederate were told that they will both receive TMS and work on the same tasks, but in separate MRI scanning rooms. To maximize credibility of the role of the confederate, she received the same questionnaires and instructions as if she would really participate. To make sure that participants still fit the criteria for TMS application and MRI scanning (e.g. no alcohol or drug use during the last 24 hours) participant and confederate next completed the TMS and MRI screening questionnaires. Demographic information were inquired and written instructions for the Empathic Touch Task were handed out to both persons. An experimenter talked them through the instructions to make sure those were well understood and gave an overview regarding the study procedure, containing general information concerning TMS and MRI. The MRI scanner and the TMS setup were presented to both the participant and confederate, thereby strengthening the credibility of the confederate's role as an actual participant. Afterwards, the participant completed a few practice trials of the Empathic Touch Task outside of the scanner. The confederate was picked up by another experimenter to ostensibly train the task in another room. After the training, participant and confederate met again and as soon as they both dressed in MRI suitable coats, they were each picked up by an experimenter to allegedly participate in the experiment in two separate MRI scanning rooms.

As soon as participants resided inside the MRI-scanner, T1-weighted structural brain scans were acquired. Participants then completed the Finger Tapping Task. After that, participants rated all visuo-tactile stimuli (of the two sets that were used in this session) in two single perspective blocks. Next, a seven minutes long resting state measurement was performed. During this period, only a fixation cross was presented on the middle of the screen and participants were instructed to let their thoughts wander while fixating the cross. After that, participants left the MRI-scanner and were prepared for the TMS procedure. cTBS finally was applied either on the vertex or on the rSMG. After the application of cTBS, participants were carefully inserted into the MRI-scanner and the execution of the double perspective version of the Empathy Touch Task was prepared. Next, with reference to one of the two sets of visuo-tactile stimuli that were used in this session, two experimental runs of the task were executed (one regarding the self judgement condition and one regarding the other judgement condition). Whether the first experimental run was performed in the self or other judgement condition was counterbalanced across participants. After completion of the two runs, another seven minutes long resting state measurement was performed. After this period, another two experimental runs (again, one regarding the self judgement condition and one regarding the other judgement condition) were completed by participants. The other remaining set of visuo-tactile stimuli was employed for these runs. Participants were taken out of the scanner by one of the experimenters. Participants and confederate met again in the lobby of the HFMRC and the both got disbanded with the urgent request to return to the same place in exactly one week.

Session 2. Participants returned exactly one week after the first session to the HFMRC. They met again with the confederate, who supposedly also was going to take part in a second session. The course of the beginning of the second session was very similar to the one of the first session, but without the practice trials of the Empathy Touch Task and the presentation of the MRI scanning room and the TMS setup prior to MRI-scanning. In the first MRI scanning period, it was not necessary to acquire T1-weigthed images and execute the Finger Tapping Task again, so white matter macrostructure was acquired via diffusion tensor imaging (70 slices, TR= 8700ms, TE= 83ms, 1.6x1.6x1.6mm voxel size) instead. Then, participants completed the two single perspective blocks of the Empathic Touch Task in reference to all 40 visuo-tactile stimuli of the two sets that were used during this session. Before exiting the MRI scanner for the TMS procedure, a seven minutes long resting state measurement was performed. The TMS procedure of this session was almost equal to the one of the first session, but regarding the estimation of the AMT it wasn’t necessary to identify the optimal site for stimulating the FDI again (since this site was already known from the first session). Also, if cTBS was applied to the vertex in the first session, it was now applied to the rSMG (and vice versa). Next, participants were brought back into the scanner: The following procedure was equivalent to the one in the first session (two experimental runs – resting state – two experimental runs) but two different sets of stimuli were used in this session. After the testing procedure, participants were taken out of the scanner and they received their payment and got disbanded.

6. Statistical Analysis

The factor Valence (pleasant/unpleasant) depended on whether the stimulus, which was target of the intensity rating, was a pleasant or an unpleasant one. The factor Congruency (congruent/incongruent) depended on whether the actual visuo-tactile stimulation of participants and the alleged visuo-tactile stimulation of the confederate had the same or different valence. The levels of the factors Congruency and Valence varied from trial to trial. Forty trials composed one experimental run. Across one run, participants either gave other-related or self-related intensity ratings, leading to the experimental run dependent factor Perspective with the levels other and self. Importantly, two consecutive experimental runs varied with regard to the factor Perspective. If participants started the first of two subsequent runs with other-related intensity ratings, they continued with self-related ratings in the second run. Overall, participants completed eight experimental runs, four after receiving cTBS on the vertex in one session and four after receiving cTBS on the rSMG in the other session. The factor cTBS site was constituted through the session-dependent levels rSMG (experimental manipulation) and vertex (control condition). Furthermore, by splitting our sample with regard to whether rSMG or vertex was stimulated in the first session, we constructed the between-subjects factor Order of cTBS (rSMG 1^{st}/vertex 1^{st}). We included this factor in our analysis to investigate if there are systematic differences in the behavior of participants between the first and second testing session.

Importantly, two subsequent experimental runs (out of the four in one testing session) added up to one testing period. As already mentioned, a seven minutes long resting state period divided each session in two separate testing periods. Recall that the first testing period ranged over a time window early after the magnetic stimulation (from 5 to 20 minutes after the cTBS application) and the second testing period extended over a later time window after the magnetic stimulation (from 27 to 42 minutes after cTBS application). Notably, some studies (Nyffeler et al., 2006; Cazzoli, Wurtz, Müri, Hess, & Nyffeler, 2009) report that behavioral alterations caused by cTBS vanish after 30 minutes past the magnetic stimulation. Based on that, we suggest diverging behavioral effects of cTBS in the first testing period in comparison to the second one. Hence, to capture the strongest possible effect of cTBS (which we expect to occur in the first testing period), we analyzed participants' intensity ratings separately for the two testing periods.

We performed several ANOVAs with emotion intensity ratings in the experimental runs of the Empathic Touch Task as the dependent variable. Ratings between 0 and -4 (see section 2.1 *Experimental Setup*) were multiplied with -1 prior to the analysis to transform all ratings into positive values. Outlier analysis showed that one subject gave abnormally low intensity ratings in four experimental runs: Unfortunately this was caused by a not correctly working response box during the related measurements, so we excluded the subject from the following analysis. Due to further technical problems, the data of two other persons concerning the first testing period was incomplete. These subjects were excluded from the analysis, leaving us with a sample of n=37 for the analysis concerning the first testing period. The data set of one additional subject was lost regarding the second testing period, what left us with a sample of n=36 for the behavioral analysis in this testing period. Data analysis was performed with the statistic software SPSS version 20.0.

RESULTS

1. Effects of cTBS in the first testing period

Since behavioral effects of cTBS sometimes abate after around 30 minutes (e.g. Nyffeler et al., 2006) we analyzed intensity ratings separately for the first and second testing period. At the very beginning, a repeated measurements ANOVA with the factors cTBS site (rSMG/vertex), Perspective (Other/Self), Congruency (congruent/incongruent) and Valence (pleasant/unpleasant) was performed to examine how emotion intensity ratings in the Empathic Touch Task during the first testing period were affected by cTBS of rSMG. Two significant threefold interactions including the factors Valence and cTBS site were observed, namely Valence x cTBS site x Congruency ($F_{(1,36)} = 8.644$, $p = 0.006$, $\eta_p^2 = 0.194$) and Valence x cTBS site x Perspective ($F_{(1,36)} = 11.6$, $p = 0.002$, $\eta_p^2 = 0.244$). This indicates different effects of cTBS of rSMG if participants focused on the evaluation of pleasant or unpleasant stimuli. Hence, we consecutively executed separate ANOVAs, once with intensity ratings of pleasant stimuli as a dependent measure and once with ratings of unpleasant stimuli as the dependent variable. There also was a significant main effect of the factor Valence ($F_{(1,36)} = 9.282$, $p = 0.004$, $\eta_p^2 = 0.205$), indicating that intensity ratings overall were higher for unpleasant than pleasant stimuli. Furthermore, there was a main effect of the factor Congruency ($F_{(1,36)} = 15.393$, $p < 0.001$, $\eta_p^2 = 0.300$). This means that intensity ratings concerning congruently administered stimuli were significantly higher than the ratings concerning incongruently administered stimuli.

1.1 Regarding the evaluation of pleasant stimuli

In the following, a within-subjects ANOVA with factors cTBS site, Perspective and Congruency was performed with intensity ratings (in the first testing period) of pleasant stimuli as a dependent variable. The twofold interaction cTBS site x Perspective showed significant results ($F_{(1,36)} = 9.730$, $p = 0.004$, $\eta_p^2 = 0.213$). This interaction is driven by the circumstance that after cTBS of rSMG, other-related emotion intensity ratings were lower than after cTBS of vertex (see Figure 3). Self-related emotion intensity ratings of pleasant stimuli were independent of the factor cTBS site. Furthermore, the significant interaction cTBS site x Congruency was observed ($F_{(1,36)} = 5.757$, $p = 0.022$, $\eta_p^2 = 0.138$). Visual inspection of the results (see Figure 4) revealed that this interaction was caused through bigger differences between the intensity ratings of stimuli being presented in a congruent and in an incongruent manner after cTBS of vertex than after cTBS of rSMG. There was also a significant main effect of the factor Congruency ($F_{(1,36)} = 15.524$, $p < 0.001$, $\eta_p^2 = 0.301$). This means that stimuli scored higher intensity ratings if presented in a congruent manner than if presented in an incongruent manner. The interactions Perspective x Congruency ($F_{(1,36)} < 1$) and cTBS site x Perspective x Congruency ($F_{(1,36)} < 1$) were not significant. The absence of these interactions indicates the effect of the factor Congruency does not depend on the factor Perspective. Neither the main effect of the factor cTBS site ($F_{(1,36)} = 1.173$, $p = 0.286$, $\eta_p^2 = 0.032$) nor the one of Perspective ($F_{(1,36)} = 1.082$, $p = 0.305$, $\eta_p^2 = 0.029$) did reach significance.

Taking into account the factor Order of cTBS led to the execution of a mixed ANOVA with the within-subjects factors cTBS site, Perspective, Congruency and the between-subjects factor Order of cTBS (rSMG 1st/vertex 1st). Regarding the experimental runs in the first testing period, 20 participants received cTBS on the vertex and 17 participants got cTBS on the rSMG at their first testing session. The inclusion of the between-subjects factor Order of cTBS revealed the additional threefold interaction Order of cTBS x cTBS site x Congruency ($F_{(1,35)} = 7.738$, $p = 0.009$, $\eta_p^2 = 0.181$). Visual inspection of the results (see Figure 5) revealed that the cTBS site x Congruency interaction is only valid for the group of participants which received cTBS on the rSMG in the second testing session.

1.2 Regarding the evaluation of unpleasant stimuli

A second three factorial ANOVA with factors cTBS site, Perspective and Congruency and with intensity ratings of unpleasant stimuli (in the first testing period) as the dependent measure was executed. No interaction (cTBS site x Perspective, $F_{(1,36)} = 1.595$, $p = 0.215$, $\eta_p^2 = 0.42$; cTBS site x Congruency, $F_{(1,36)} < 1$; Perspective x Congruency, $F_{(1,36)} < 1$; cTBS site x Congruency x Perspective, $F_{(1,36)} < 1$) showed significant results and neither did the main effect of the factor cTBS site ($F_{(1,36)} < 1$). Seemingly, intensity ratings of unpleasant stimuli (in the first testing period) were independent of the target of cTBS. The analysis showed significant main effects of the factors Perspective ($F_{(1,36)} = 4.271$, $p = 0.046$, $\eta_p^2 = 0.106$) and Congruency ($F_{(1,36)} = 9.573$, $p = 0.004$, $\eta_p^2 = 0.210$). Other-related emotion intensity judgements were slightly higher than self-related judgements. Stimuli presented in an incongruent manner received lower intensity ratings than the stimuli presented in a congruent manner.

Once again, we reran the analysis with the additional between-subjects factor Order of cTBS, leading to a mixed ANOVA with the factors Order of cTBS, cTBS site, Perspective and Congruency and with intensity ratings of unpleasant stimuli as the dependent measure. The inclusion of the factor Order of cTBS revealed two additional interactions, namely Order of cTBS x cTBS site ($F_{(1,35)} = 10.435$, $p = 0.003$, $\eta_p^2 = 0.230$) and Order of cTBS x cTBS site x Congruency ($F_{(1,35)} = 7.877$, $p = 0.008$, $\eta_p^2 = 0.184$). These results indicate that after cTBS of vertex, participants rated unpleasant stimuli as equally intensive, independent if their vertex was stimulated in the first or second testing session (see Figure 6). Ratings after cTBS of rSMG concerning the intensity of unpleasant stimuli were significantly different in dependence of whether participants received cTBS on their rSMG in the first (M = 2.479, SE = 0.144) or second (M = 2.964, SE = 0.132) session ($t(35) = 2.484$, $p < .05$). Furthermore, the difference of intensity ratings between stimuli presented in a congruent and those presented in an incongruent manner was bigger in the first testing session, independent whether vertex or rSMG was stimulated in this session.

2. Effects of cTBS in the second testing period

Next, a second four factorial ANOVA was executed, including the factors Perspective (Other/Self), Congruency (Congruent/Incongruent), Valence (Pleasant/Unpleasant) and cTBS site (rSMG/Vertex). Emotion intensity ratings during the second testing period (after the resting state period) served as the dependent measure. There were significant main effects of the factors Valence ($F_{(1,35)} = 10.674$, $p = 0.002$, $\eta_p^2 = 0.234$), Congruency ($F_{(1,35)} = 12.051$, $p = 0.001$, $\eta_p^2 = .256$) and cTBS site ($F_{(1,35)} = 5.226$, $p = 0.028$, $\eta_p^2 = 0.130$). As one can see in the visualization of the results (see Figure 7), unpleasant stimuli were rated as more intensive than pleasant stimuli and stimuli scored lower intensity ratings if presented in an incongruent manner than if presented in a congruent manner. Also, stimuli scored lower ratings after the cTBS of rSMG than after cTBS of vertex. Any interactions (Congruency x Valence, $F_{(1,35)} = 3.279$, $p = 0.079$, $\eta_p^2 = .086$; cTBS site x Congruency, $F_{(1,35)} = 2.642$, $p = 0.113$, $\eta_p^2 = .070$; cTBS site x Perspective, $F_{(1,35)} < 1$; cTBS site x Valence, $F_{(1,35)} < 1$; Perspective x Congruency, $F_{(1,35)} < 1$; Perspective x Valence, $F_{(1,35)} < 1$; cTBS site x Congruency x Perspective, $F_{(1,35)} = 1.131$, $p = 0.295$, $\eta_p^2 = .031$; Perspective x Congruency x Valence, $F_{(1,35)} = 1.099$, $p = 0.302$, $\eta_p^2 = .030$; cTBS site x Perspective x Valence, $F_{(1,35)} < 1$; cTBS site x Congruency x Valence, $F_{(1,35)} < 1$; cTBS site x Perspective x Congruency x Valence, $F_{(1,35)} < 1$) and the main effect of Perspective ($F_{(1,35)} < 1$) were not significant. Mean intensity ratings were not significantly different for the self and other perspective.

In the following, we calculated two separate four factorial ANOVAs with the within-subjects factors Perspective, Congruency and cTBS site and the between-subjects factor Order of cTBS. In one analysis, intensity ratings of unpleasant stimuli (in the second testing period) were used as the dependent variable and in the other analysis intensity ratings of pleasant stimuli (in the second testing period) were used as the dependent measure. However, these analyses did not reveal any additional significant effects.

DISCUSSION

The vicarious experience of emotional relevant events and the consequential evaluation of affective states of others is not independent from our own affective state. Simulation and self-projection might indeed account for an important aspect when it comes to the interpersonal understanding and sharing of emotions, but processes that distinguish between information relating to the affective state of others and information relating to one's own affective state are also a crucial requirement for adequate empathic understanding and behavior. People naturally tend to perceive their own emotions as the most prominent and as a result they might be biased (through processes relating to their affective state) when evaluating the affective state of others and concurrently experiencing emotions themselves. In previous studies (Silani et al., 2013; Steinbeis et al., 2015), it consistently was observed that the intact and fully developed functioning of rSMG is a substantial requirement to not to project one's own emotions onto others in situations where this is not appropriate. Therefore, it seems plausible that rSMG is responsible in the integration and disentanglement of self-related and other-related emotional relevant information, but to what extend and under which circumstances has yet to be examined.

The frictionless functioning of rSMG is thought to play a pivotal role during self-other distinction processes regarding the emotional domain. The objective of this thesis was to examine how and to what extend a temporary disturbance of the functioning of rSMG via cTBS expresses itself in changes in behavior (measured via performance in the Empathy Touch Task) which is demanding a certain kind of self-other distinction regarding emotional relevant information. We assume that the rSMG plays an important role regarding processes of integration of self and other-related emotional relevant information. Such integration processes seem to be crucial for the adequate understanding of affective states of other persons, especially in situations when one is confronted with self and other-related emotional relevant information at the same time. The main goal of this thesis was to examine the importance of rSMG during other-related emotional evaluation in such situations. Previous research (Silani et al., 2013; Steinbeis et al., 2015) suggests that the rSMG specifically is recruited when self and other-related emotional relevant information are contradicting. However, rSMG generally might be involved in the estimation and recognition of the emotional relevance of other-related information, even when self and other-related information are accordant.

1. Effects of cTBS of rSMG on other-related emotion judgements

We expected that a disturbance of functioning of rSMG caused by cTBS inhibits the ability to fully comprehend the emotional relevance of other-related information when one is confronted with self and other-related emotional relevant information at the same time. So to say, when one is perceiving that another person experiences an event with emotional relevance but at the same time is experiencing another event with relevance for one’s own emotions, a disturbance of rSMG might bring one to generally underestimate the impact of the other-related emotional relevant information. Hence we posited that cTBS of rSMG leads participants to generally evaluate pleasant and unpleasant other-related emotional events in the Empathy Touch Task as less intensive than under normal circumstances, independent if self and other-related emotional relevant information were congruent or not. The results indicate that this posit is only partially correct. The supposed effect of the disturbance of rSMG via cTBS was only observed in a time window early (5 to 20 minutes) after the application of cTBS and only if participants focused on the evaluation of pleasant events.

Figure 3 shows that if functioning of rSMG was not disturbed (cTBS of vertex), participants tended to vicariously rate pleasant emotional events experienced by another person (indicated through visual information) as slightly more intense as if the same pleasant events are experienced at first-hand by participants themselves (via visuo-tactile stimulation). When functioning of rSMG was perturbed via cTBS, participants tended to rate pleasant emotional events which were experienced by other persons just as intense (or slightly lower) as if the same pleasant events were experienced by the participants themselves. This described effect was only observed in the first testing period (5 to 20 minutes after the application of Theta Burst Stimulation). In a way, cTBS of rSMG temporarily led participants to perceive or at least evaluate other-related pleasant emotional events as less intensive as it normally would be the case. The presumed involvement of rSMG in mechanisms which aim to integrate emotional relevant information from different sensory channels provides one possible explanation for this finding. If one simultaneously is busy with processing self and other-related emotional relevant information, a disruption of normal functioning of rSMG via cTBS might indeed cause a restricted ability to properly estimate the significance of other-related emotional relevant information. Due to this restricted ability, other-related emotional events are evaluated as less intense. The fact that, after a perturbation of functioning of rSMG subjects vicariously evaluated other-related pleasant emotional events just as emotionally intensive as they would evaluate these events for themselves (see *Figure 3)*, might indicate a greater reliance on self-related affective representations when functioning of rSMG is disturbed. As already stated, the disturbance in processing and integrating other-related emotional content from visual information during concurrent processing of self-related emotional content from other sources (e.g. tactile senses) could be a possible consequence of cTBS of rSMG. This disturbance in processes concerning the integration of other-related emotional relevant information in turn might result in a restricted ability to properly comprehend the emotional relevance of other-related information. It is conceivable that this restricted ability concerning the comprehension of the significance of other-related emotional events might be compensated through simulating how one self would experience the relevant events. The occurrence of such compensation mechanisms might account for the seemingly greater reliance on self-related affective representations during other-related emotion judgements when functioning of rSMG is disturbed. Yet, such conjectures are rather speculative and should be in the focus of following research projects.

As already mentioned, the supposed effect of lower other-related emotion intensity judgements was only observed when other-related emotional relevant information indicated pleasant emotional events. Interestingly, effects of cTBS of rSMG on behavioral responses in the Empathic Touch Task in the first testing period looked quite differently, depending on whether the target of the intensity judgement indicated a pleasant or an unpleasant emotional event. This is an unexpected finding, since previous studies (Silani et al., 2013; Steinbeis et al., 2015) repeatedly observed that the rSMG's involvement in processes that distinguish between self and other-related emotional relevant information generally does not depend on the valence of these emotional relevant information.

In the first testing period, participants independently of the cTBS manipulation rated unpleasant emotional relevant events as slightly more intensive when it was indicated that these events are experienced by another person than if the same events are experienced at first-hand by the participants themselves. Imagined touch experiences, based on a visual stimulus and evaluated with reference to the emotional reaction of other people, were evaluated as more unpleasant than the actual first-hand touch experiences. This might indicate that a mere presentation of the unpleasant visual stimuli elicited stronger emotions of unpleasantness than the visual and corresponding tactile stimuli combined. Also, it could be the case that participants on average judged the other person (confederate) as emotionally more responsive to an unpleasant touch stimulus. However, the relative emotional intensity of the visual stimuli in comparison to the tactile stimuli seems to contribute to the circumstance that other-related unpleasant emotional events were not judged as less intense, even after cTBS application on rSMG.

Based on findings from previous research (Silani et al., 2013; Steinbeis et al., 2014), one may suppose that the tendency to underestimate the significance of other-related emotional relevant information might especially increase when one simultaneously is processing opposing self-related emotional relevant information, for example when one is experiencing an emotional event of contrary valence to the event another person is experiencing. This expectations are based on the consideration that the integration processes regarding self- and other-related emotional relevant information, which are associated with the rSMG, are especially important for an adequate understanding of the emotions of others when self- and other-related information is not accordant. Contrary to the expectation of a general underestimation of the significance of other-related emotional relevant information when rSMG is disturbed via cTBS, the ability to adequately conceive the impact of other-related emotional relevant events might only and especially be affected when self- and other-related information are contrasting to each other.

We did not observe this supposed and in previous studies detected effect. The application of cTBS on the rSMG did not specifically alter participants' other-related emotion intensity ratings in situations when self- and other-related emotional relevant information implicated emotional events of opposing valence. Interestingly, previous studies which used a similar experimental paradigm (Silani et al., 2013; Tomova et al., 2014) already observed a slight decline in other-related intensity ratings with regard to opposing self- and other-related emotional relevant information under natural circumstances. However, we did not observe such a specific decline, independent whether functioning of rSMG was disturbed or not. The, at least in a time window early after cTBS application, observed tendency of participants to evaluate other-related emotional events as more intense than if the same events were experienced by participants themselves might provide one possible explanation for the missing of the specific decline in intensity ratings. Note that in the study of Silani et al. (2013) the opposite was the case, meaning that tactile stimuli consistently were rated as more intense than visual stimuli. Our results bring up the consideration that the here used visual stimuli (indicators of other-related touch experiences) were experienced as relatively intense in comparison to the tactile stimuli (first-hand touch experiences). This relative intensity of the visual stimuli compared to tactile stimuli might cause participants to be less biased through the received touch when they focus on the evaluation of the visual stimuli. In our experiment, the evaluation of other-related emotional events already was relatively unsusceptible to be biased through co-occurring self-related emotional events of opposing valence under natural circumstances. Thus, the relative intensity of visual stimuli might partially explain why a specific decline in other-related emotion intensity judgements due to concurrently processed self-related emotional relevant information of opposing valence was not observed, even after the disturbance of rSMG.

Although cTBS of rSMG tended to influence participants' general emotional evaluation differently whether they experienced congruent or incongruent emotional events in comparison to another person, there was no specific effect on other-related evaluation with regard to congruent/incongruent emotional events. In total, the observed bias of other-related emotion judgments through self-related information was less specific than previously (Silani et al., 2013) reported: The bias was independent of whether congruent or incongruent touch was received during the perception of other-related emotional relevant information.

2. Consistency of effects of cTBS on rSMG over time

Another concern of the study was to explore the temporal dynamics of the effects of cTBS of rSMG on behavioral responses in the Empathy Touch Task. The effects of a disturbance of functioning of rSMG via cTBS in the used version of the Empathy Touch Task depended on the relative time after the application of cTBS. The different results in the first and second testing period give rise to two conclusions: In the first place, cTBS of rSMG seems to impact intensity ratings in the Empathy Touch Task over a period longer than 30 minutes after magnetic stimulation. Second, the effects of cTBS of rSMG on the mentioned intensity ratings express themselves differently if measured in a time window early after stimulation (between 5 and 20 min. after stimulation) or in a time window later after stimulation (between 27 and 42 min. after stimulation). Even though cTBS of rSMG still had an effect on emotion intensity ratings (measured via the Empathic Touch Task) in the later time window after stimulation, there were no specific effects regarding other-related emotion judgements. During this time window, the used magnetic stimulation did not specifically alter how subjects evaluate the intensity of emotional relevant events that are experienced by other persons (cTBS site x Perspective, $F_{(1,35)} < 1$), but had a more general effect that comes with lower intensity ratings for emotional events relating to other persons and to the self. As time after the magnetic stimulation passes by, the disturbance of rSMG via cTBS expresses itself in lower intensity perception and/or evaluation of emotional events in general, independent if the events are self- or other-related.

This is a surprising finding, since in previous studies an altered functioning of rSMG has not been associated with changes in intensity perception concerning emotional relevant events relating to the self, but rather exclusively with changes in intensity perception concerning emotional relevant events relating to others. Remember that in our experimental setup, antecedent to every intensity judgement (concerning emotional events relating to the self or the other), the participant was simultaneously confronted with two kinds of stimuli which worked as indicators of emotional relevant events. One kind of stimuli (visuo-tactile) referred to the emotional relevant events regarding the participant's own affective state and the other kind of stimuli (visual) was used as indication for the emotional relevant events regarding another person's affective state. A recently (Steinbeis et al., 2015) ascribed role of rSMG is the accurate calculation and weighting of emotional relevant information relating to the self and in succession the disambiguation of this information from emotional relevant information relating to others. The here observed lower intensity ratings concerning both the other and the self may be an indication that the recruitment of rSMG may indeed play a role when it comes to the integration and processing of emotional relevant information from different sensory channels, but thereby possibly affecting our self-related emotional evaluation as well as other-related judgements. A disturbance of rSMG via cTBS might, at least in a late time window after magnetic stimulation, lead us to generally perceive emotional relevant information as less intensive, at least in situations in which we process emotional information from different sensory channels at the same time. It appears that a disturbance of rSMG might bring one to generally underestimate the significance of self- and other-related emotional relevant information. Regarding the more specific behavioral effects of cTBS of rSMG in a time window early after magnetic stimulation, it seems that the effects of cTBS first affect emotion judgements under very specific conditions. In a later time window after application, cTBS seems to have a depressant impact on our emotional evaluation in general. Seemingly, a disturbance of the rSMG-associated integration processes regarding self- and other-related emotional relevant information can have an impact for other- as well as self-related emotional evaluation. However, this is kind of speculative and further studies should investigate the extent to which the rSMG might be involved in emotional evaluation in general and the reasons behind the inconsistent effects of cTBS over time.

3. Inter-individual variability of the effects of cTBS

Additionally to the variability over time, there are good reasons to assume that cTBS of rSMG led to different effects across our participants, implicating that there was a certain inter-personal variability of the effects of cTBS.

One of these reasons stems from the observation that a seeming absence of any effects of cTBS of rSMG concerning the evaluation of unpleasant stimuli is no more supported if one splits the whole sample of participants into two groups with regard to the factor Order of cTBS. The fact that mean intensity ratings after cTBs of vertex are equally high in both groups confirms one experimental presupposition: Under natural circumstances (cTBS of vertex), intensity ratings do not differ between the first and second session (see *Figure 6*). Hence, there is no confounding effect caused by the experimental chronology on the perceived intensity of unpleasant events. The different intensity ratings concerning unpleasant emotional events after cTBS of rSMG in comparison to cTBS of vertex in both groups seem to imply that intensity ratings of unpleasant stimuli are in fact influenced by a disturbance of the rSMG. However, the significant difference of ratings after cTBS of rSMG between the groups might bring up the conjecture that cTBS of rSMG did influence both groups in different ways. There was a certain variability in the effects of cTBS between the both groups. Recall that even though cTBS generally is thought to suppress neuronal activity, there are also findings which emphasize that the effect of cTBS on cortical excitability can be highly variable across individuals. Hamada et al. (2013) observed that cTBS may have facilitating rather than inhibiting effects on cortical excitability and this appears logically since effects of cTBS are known to alter activity in excitatory and inhibitory neuronal circuitry (Jacobs et al., 2012). The results depicted in Figure 6 might imply that cTBS had rather suppressing effects in the group of participants which received the magnetic stimulation on rSMG at the first testing session and that the effects of cTBS of rSMG were rather excitatory in the group of people which received cTBS of rSMG at the second testing session. The analysis of the fMRI data might help to gain concrete insights concerning this.

Another reason to assume that cTBS affected participants in a different manner arises from the observation that only the group of participants which received cTBS on the vertex in their first testing session and cTBS on rSMG in the second session gave lower emotion intensity ratings of congruently administered pleasant stimuli after the application of cTBS (see Figure 5). Besides the circumstance that the magnetic stimulation of rSMG had no significant effects on mean emotion intensity ratings of pleasant stimuli being presented in an incongruent manner, this points out that self- and-other related emotional evaluation in the two groups of participants was affected differently through the magnetic stimulation of rSMG. It has been observed that the relative power of cTBS may be one possible cause of its inter-individual varying effects (McAllister, Rothwell & Ridding, 2009; Doeltgen & Ridding, 2011). However, the group of participants that received cTBS on rSMG at the first session (M = 46.24, SE = 1.499) and the group of participants that received cTBS on rSMG at the second session (M = 45.35, SE = 1.575) did not significantly differ regarding the relative power of cTBS (of rSMG). This was revealed by a non-significant t-test ($t(35)= 0.403$, $p > .05$).

It also is conceivable that the distance to target (in our case the rSMG) during magnetic stimulation might play a role when it comes to varying effects caused through cTBS. However, the distance to target in the group of participants that received cTBS on rSMG at the first session (M = 1.4 mm, SE = 0.216) was not significantly different from the distance to target in the group of participants that received cTBS on rSMG at the second session (M = 0.99 mm, SE = 0.22), $t(35)= 1.296$, $p > .05$. Seemingly, neither the relative power of cTBS nor the distance to target during magnetic stimulation does provide a good explanation for the different effects of cTBS in the two groups of participants.

4. Conclusion

Despite the different results regarding the evaluation of pleasant and unpleasant stimuli, we suggest that the functioning of rSMG affects our empathic as well as our general emotional evaluation.

Given the different effects of cTBS from individual to individual and with regard to elapsed time after application, we conclude that the manner, of how functioning of rSMG was perturbed, strongly varied in dependence of these aspects. The after-effects of cTBS are known to involve altered activity in excitatory as well as inhibitory neuronal circuitry (Jacobs et al., 2012), thus the used form of magnetic stimulation might not solely have caused inhibitory but as well facilitating effects on cortical excitability. The seeming inhomogeneity in how cTBS affected the participants narrows the conclusions which may get drawn on the basis of the reported data.

Nevertheless, we observed that a disturbance of rSMG via cTBS generally may affect processes of emotional evaluation. Thus, we conclude that rSMG actually is involved in processes regarding the multisensory integration of self- and other-related emotional relevant information. Contrary to the previous findings of Silani et al. (2013), a disturbance of rSMG did not solely affect processes regarding other-related emotional evaluation in situations of contradicting self- and other-related emotional relevant information. Moreover, the disturbance of rSMG via cTBS seemed to cause alteration concerning other- as well as self-related emotional evaluation. In a way, the disturbance of functioning of rSMG via cTBS was not exclusively associated with changes regarding empathic (other-related) judgements, but furthermore with altered self-related emotion judgements. By tendency, the influence of a disturbance of rSMG on emotional evaluation seemed to be independent whether other and self-related emotional relevant information were accordant or contradicting. The observed pattern of results might indicate that the impact of the rSMG-associated processes regarding integration of self- and other-related information on emotional judgements in general, and thus also on our self-related evaluation, may be bigger than previously suggested.

Seemingly, there is a certain relevance of rSMG for other- and self-related emotional evaluation. This implies that, in situations of the concurrent occurrence of self- and other-related emotional events, integration processes concerning self- and other-related emotional relevant information might not only play a role for empathic judgements but also for the direct experience of an emotional event. At least in the mentioned situations, processes relating to affective self-other distinction might not only be relevant for adequate understanding of the affective states of others but moreover might contribute to a candid and unbiased first-hand experience of an emotional event. The rSMG might not only be responsible for not projecting one's own emotions on someone else when this is not appropriate. Moreover, it generally might play a role in the recognition of the emotional relevance of sensory information. Further research should try to specify the role of the rSMG with regard to empathic judgements and emotional evaluation in general.

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APPENDIX

1. Figures

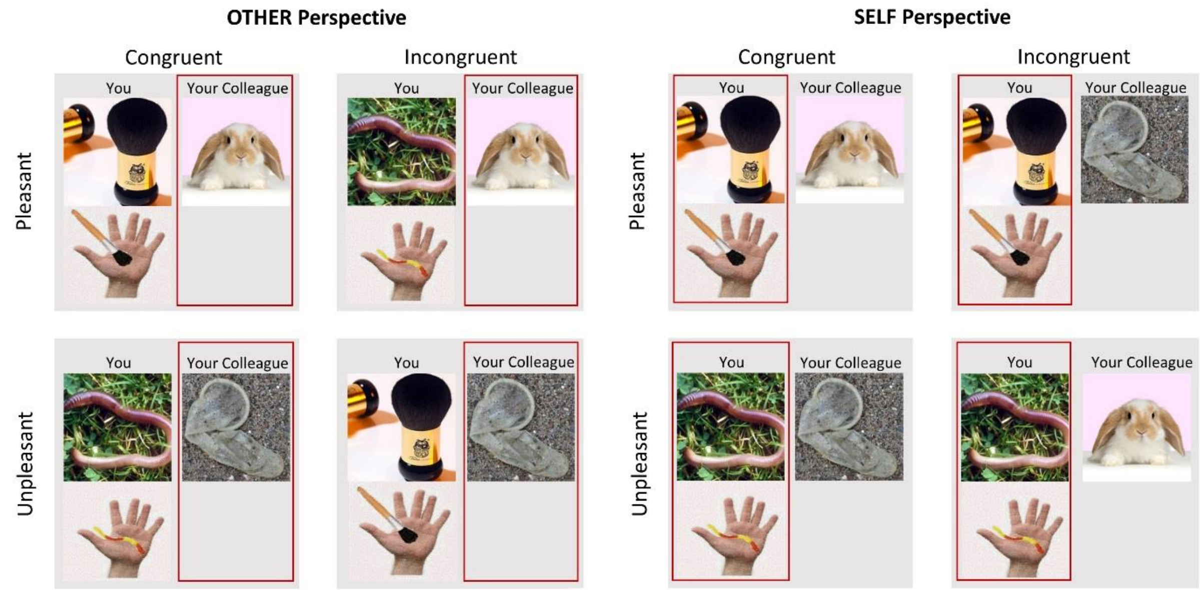

Figure 1. Exemplary representation of the Empathic Touch Task with the factors Perspective, Congruency and Valence. The upper half of each grey box displays the pictures that were presented to participants, the lower half indicates the touch they simultaneously were receiving. The red frames were included in the figure to point out the target perspective (Other/Self) but were actually not shown to the participants during the experiment.

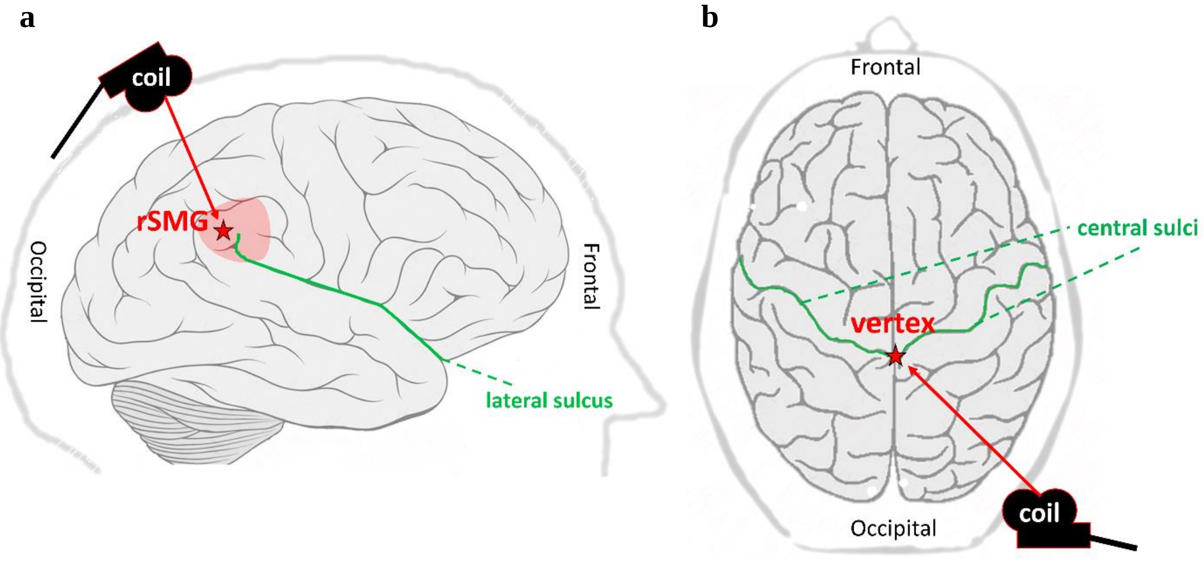

Figure 2. Illustration of the targets of cTBS on the cortex inclusive the orientation of the TMS coil for (**a**) the rSMG and (**b**) the vertex. The coil was located on the surface of the scull directly above the marked targets, whereby the center of the coil was situated straight above the center of the red star. Sulci are highlighted because they served as an orientation help during the setup of the targets.

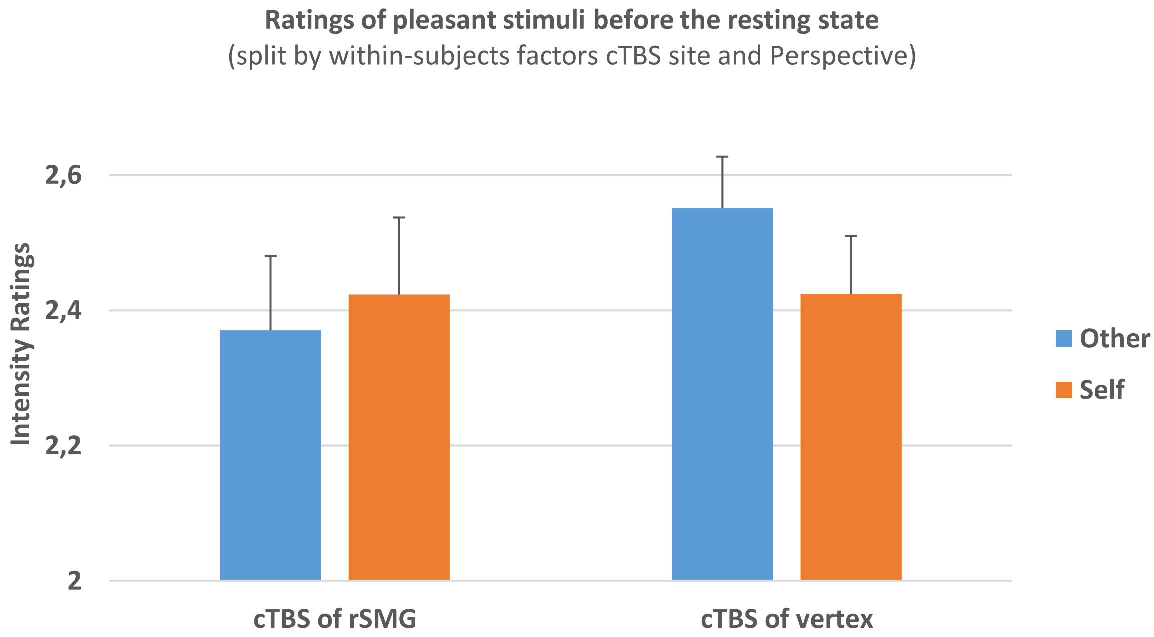

Figure 3. Mean intensity ratings (+SEM) in the pre resting state trials relating to the evaluation of pleasant stimuli. The significant interaction ($p < 0.01$) of the factors cTBS site and Perspective is caused by lower other-related emotion intensity ratings after the magnetic stimulation of rSMG.

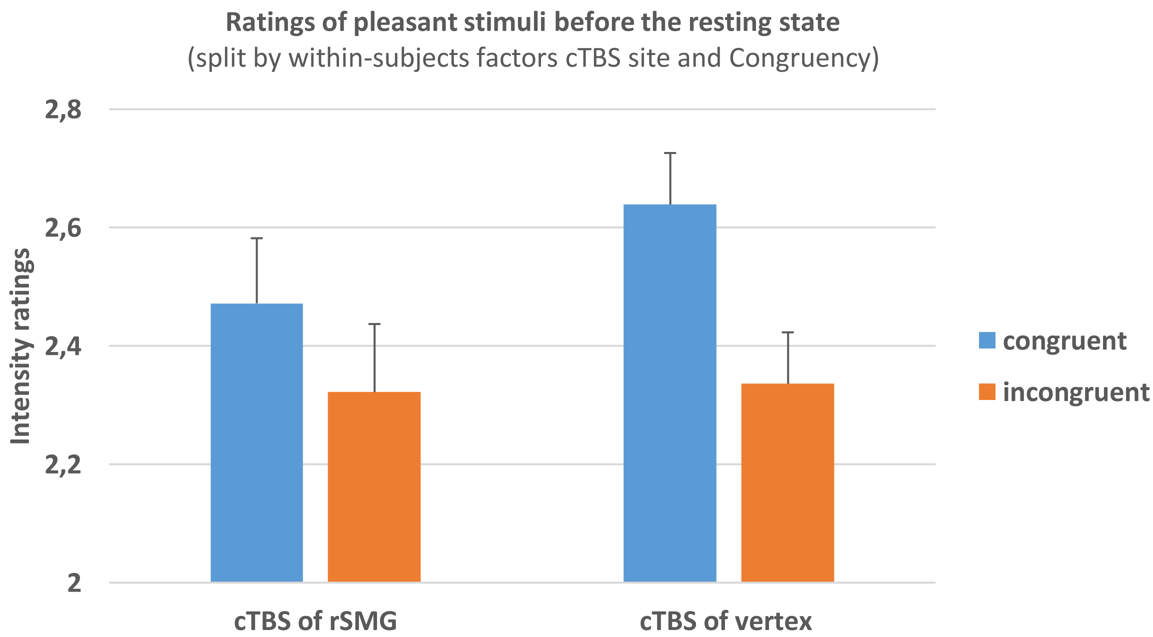

Figure 4. Mean intensity ratings (+SEM) before the resting state period relating to the evaluation of pleasant stimuli. The significant interaction ($p < 0.05$) of the factors cTBS site and Congruency is caused by lower emotion intensity ratings of congruently administered stimuli after the magnetic stimulation of rSMG.

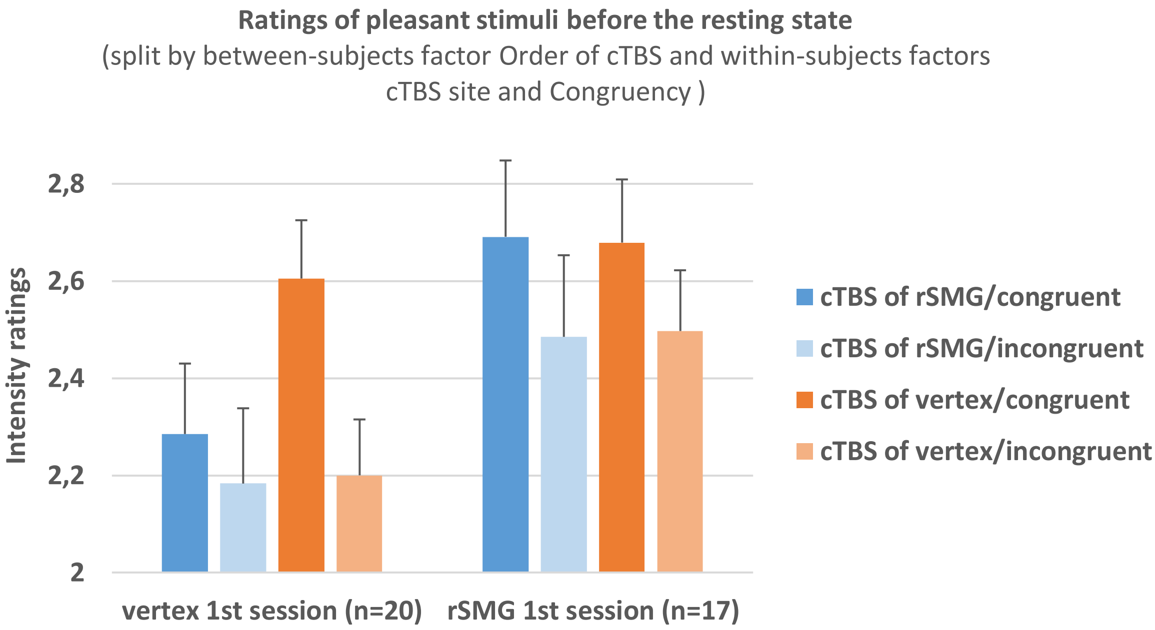

Figure 5. Participants which received cTBS on vertex at their first testing session and on rSMG at their second session showed bigger differences in their intensity ratings of congruently and incongruently administered pleasant stimuli after the stimulation of vertex than after the stimulation of rSMG. This was not valid for participants which received cTBS on rSMG at their first session and on vertex at their second session.

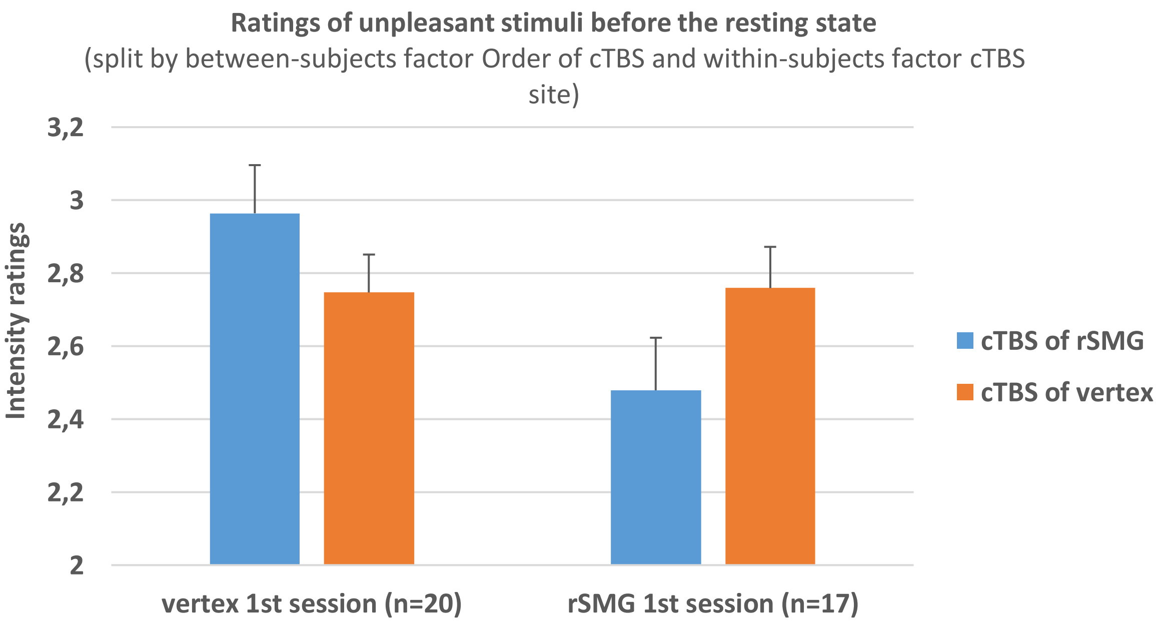

Figure 6. Intensity ratings of unpleasant stimuli before the resting state, split by the between-subjects factor Order of cTBS and the within-subjects factor cTBS site. Both groups rated unpleasant stimuli as equally intensive after vertex stimulation. Intensity ratings after cTBS of rSMG between the groups were quite different.

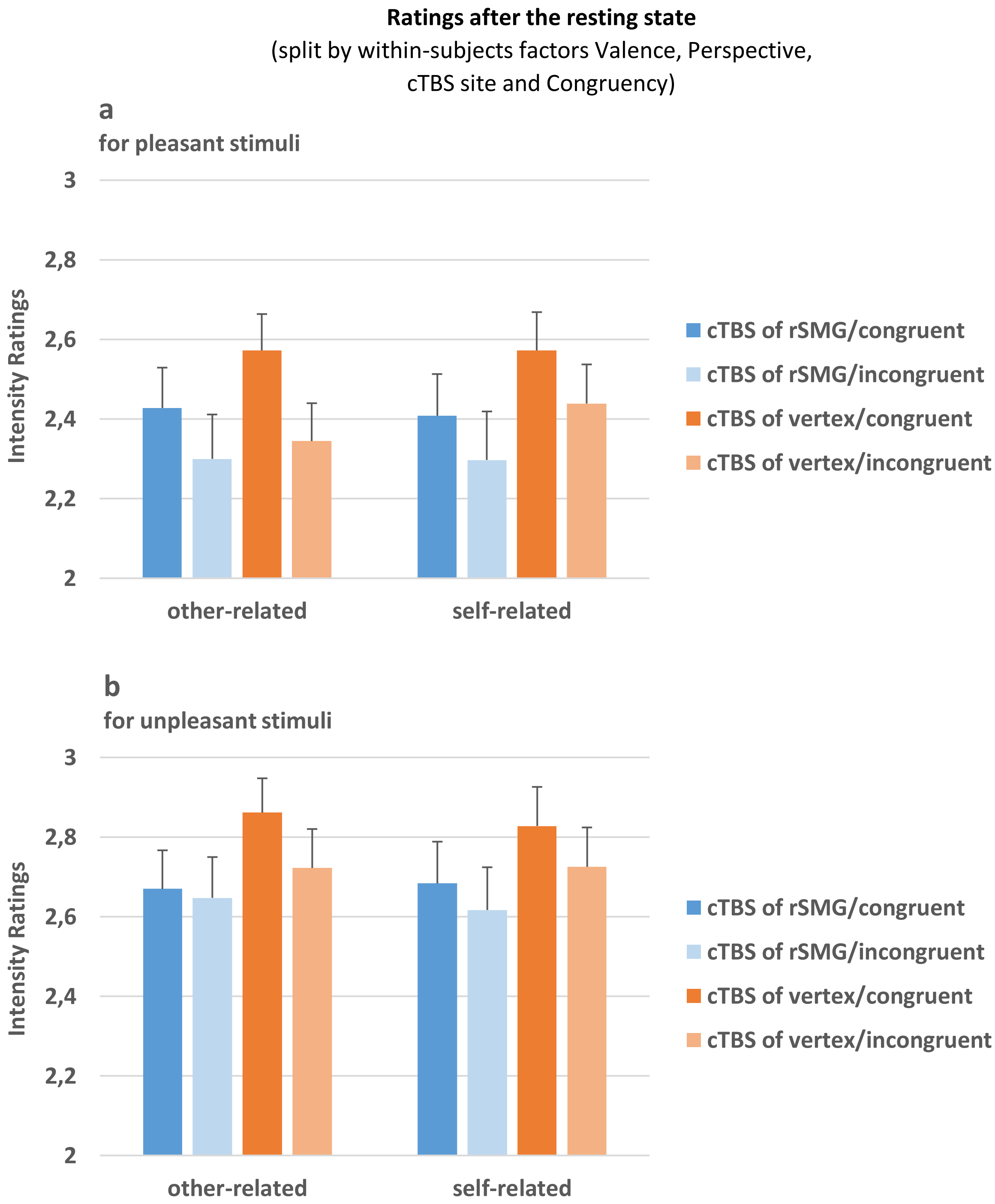

Figure 7. Emotion intensity ratings (mean +SE) after the resting state period split by valence of target stimuli (N=36). Unpleasant stimuli are consistently rated as more intensive than pleasant stimuli. Also, if stimuli are presented in a congruent condition, they score higher ratings. Intensity ratings after cTBS of rSMG are lower compared to the ones after cTBS of vertex. **a,** Ratings of pleasant stimuli. **b,** Ratings of unpleasant stimuli.

2. Tables

Table 1. List of used stimuli

Set 1		
Picture	*Material*	*Valence*
Feather 1	Feather 1	Pleasant
Massage stone	Massage stone	Pleasant
Seal	Synthetic fur	Pleasant
Grass	Artificial grass	Pleasant
Pearls 1	Glass pearls 1	Pleasant
Lotus	Artificial blossom	Pleasant
Pebbles 1	Smooth pebbles	Pleasant
Soft toy (bear) 1	Teddy bear	Pleasant
Cotton	Cotton wool	Pleasant
Microfiber cloth	Soft towel	Pleasant
Dirty underwear	Cotton panties	Unpleasant
Dirty Socks 1	Wool socks	Unpleasant
Wet Hair	Synthetic hair	Unpleasant
Old condom 1	Soapy plastic	Unpleasant
Dead fish 1	Wet artificial fish 1	Unpleasant
Bone marrow 1	Prepared dog bone	Unpleasant
Used tissue 1	Prepared tissue 1	Unpleasant
Rotten apple 1	Prepared rubber foam 1	Unpleasant
Blob-fish	Wet artificial fish 2	Unpleasant
Earthworm	Artificial worm	Unpleasant
Set 2		
Picture	*Material*	*Valence*
Jellybeans	Jellybeans	Pleasant
Terrycloth 1	Soft cloth	Pleasant
Baby brush	Baby brush	Pleasant
Leaf	Artificial leaf	Pleasant
Soft toy (bear) 2	Teddy bear	Pleasant
Cat	Synthetic fur	Pleasant
Cotton plant	Cotton wool	Pleasant
Glass stones	Glass pearls 2	Pleasant
Massage tool	Wooden heart	Pleasant
Bunny	Cashmere shawl	Pleasant
Eel	Toy snake	Unpleasant
Rotten strawberry	Prepared rubber foam 2	Unpleasant
Bone marrow 2	Prepared dog bone	Unpleasant
Old condom 2	Soapy plastic	Unpleasant
Mushroom	Toy slime (red)	Unpleasant
Slug 1	Toy slime (green)	Unpleasant
Callused skin	Droughty citron	Unpleasant
Molded bread 1	Prepared dry bread	Unpleasant
Rotten apple 2	Prepared rubber foam 1	Unpleasant
Salamander	Toy lizard	Unpleasant
Set 3		
Picture	*Material*	*Valence*
Q-tip	Fresh Q-tip	Pleasant
Sheep	Wool	Pleasant
Cushion	Cushion	Pleasant

Hot-water bottle	Wrapped heating pad	Pleasant
Shaving brush	Make-up brush	Pleasant
Velvet 1	Velvet rag	Pleasant
Angora	Angora wool ball	Pleasant
Wool ball 1	Wool ball 1	Pleasant
Pompom	Pompom	Pleasant
Terrycloth 2	Soft cloth	Pleasant
Dead fish 2	Wet artificial fish 1	Unpleasant
Used tissue 2	Prepared tissue 2	Unpleasant
Dead rat 1	Prepared synthetic fur 1	Unpleasant
Skin stretchmarks	Prepared artificial limb	Unpleasant
Maggots	Plastic maggots	Unpleasant
Used diaper	Prepared diaper	Unpleasant
Dirty socks 2	Wool socks	Unpleasant
Tongue	Toy slime (orange)	Unpleasant
Slug 2	Toy slime (green)	Unpleasant
Molded bread 2	Prepared dry bread	Unpleasant
Set 4		
Picture	*Material*	*Valence*
Felt	Felt cloth	Pleasant
Wool ball 2	Wool ball 2	Pleasant
Pearls 2	Glass pearls 1	Pleasant
Pebbles 2	Smooth pebbles	Pleasant
Kitten	Synthetic fur	Pleasant
Rose	Artificial rose	Pleasant
Dog	Synthetic fur	Pleasant
Velvet 2	Velvet rag	Pleasant
Silk	Silk cloth	Pleasant
Feather 2	Feather 2	Pleasant
Mold	Harsh cotton wool	Unpleasant
Gullet	Prepared modelling clay	Unpleasant
Oyster	Shell with toy slime	Unpleasant
Dead rat 2	Prepared synthetic fur 2	Unpleasant
Centipede	Toy centipede	Unpleasant
Old chewing gum	Dry chewing gum	Unpleasant
Stinkbug	Plastic bug	Unpleasant
Old cigarette	Prepared cigarette filter	Unpleasant
Skin eruption	Prepared artificial limb 2	Unpleasant
Liver	Modelling clay	Unpleasant

3. Abstract

3.1 English version

The aim of this study was to further investigate the extent to what the right supramarginal gyrus (rSMG) is involved in our empathic evaluation. We supposed that the rSMG is crucial for the comprehension of the emotional relevance of other-related information.

The study was conducted in a within-subjects design. In two separate sessions, we once applied continuous Theta Burst Stimulation (cTBS) on the rSMG and once on the vertex (control condition) on 40 young females. Afterwards, we measured other-related emotion intensity ratings in a task in which participants were presented with emotion eliciting other and self-related stimuli at the same time. Pleasant and unpleasant stimuli were used, leading to congruent and incongruent affective states between the participants and the persons they had to empathize with.

After cTBS of rSMG, participants specifically evaluated other-related pleasant stimuli as less intensive. Regarding unpleasant stimuli, the effect of cTBS was more ambiguous and not exclusive to other-related judgements. Furthermore, cTBS might have affected participants with certain inter-individual variability.

Despite partially heterogeneous results, we conclude that the rSMG is involved in integration processes concerning self and other-related information. These processes seem to be relevant for our empathic as well as our general emotional evaluation.

3.2 German version

Das Ziel dieser Studie war die Untersuchung inwiefern der rechte supramarginale Gyrus (rSMG) an unseren empathischen Beurteilungen beteiligt ist. Es wird angenommen, dass der rSMG wichtig für unser Verständnis der emotionalen Bedeutung von fremdbezogenen Informationen ist.

Das Experiment wurde in einem „Within-Subjects" Design durchgeführt. Vierzig jungen Frauen wurde an zwei separaten Untersuchungstagen „continuous Theta Burst Stimulation (cTBS)" einmal am rSMG und einmal am Vertex (Kontrollbedingung) verabreicht. Anschließend bearbeiteten die Versuchsteilnehmerinnen eine Aufgabe bei der sie gleichzeitig mit selbst- und fremdbezogenen emotional bedeutsamen Reizen konfrontiert wurden und fremdbezogene Emotionsbeurteilungen abgeben sollten. Angenehme und unangenehme selbst- und fremdbezogene Reize wurden eingesetzt. Dies verursachte teilweise übereinstimmende und teilweise nicht übereinstimmende Gemütszustände zwischen den Teilnehmerinnen und den Personen, auf welche sich die empathischen Beurteilungen bezogen.

Nach der Verabreichung von cTBS am rSMG beurteilten die Versuchsteilnehmerinnen fremdbezogene angenehme Reize als weniger intensiv. Es gab keine einheitlichen Effekte von cTBS bezüglich der empathischen Evaluation von unangenehmen Reizen. Es scheint, als ob cTBS von Versuchsperson zu Versuchsperson unterschiedliche Effekte nach sich zog.

Trotz uneinheitlicher Ergebnisse schlussfolgern wir, dass der rSMG in den Integrationsprozessen von selbst- und fremdbezogenen Informationen involviert ist. Diese Integrationsprozesse scheinen sowohl für empathische Beurteilungen als auch für das eigene emotionale Erleben relevant zu sein.