

TRANSCRANIAL MAGNETIC STIMULATION MODULATES LEFT PREMOTOR CORTEX ACTIVITY IN FACIAL EXPRESSION RECOGNITION AS A FUNCTION OF ANXIETY LEVEL

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Abstract

Recognition of emotional facial expressions is based on simulation and mirroring processes, and the premotor cortex is supposed to support this simulation mechanism. The role of this prefrontal area in processing emotional faces with different valence (anger, fear, happiness and neutral) was explored taking into account the effect of the lateralization model (more right-side activation for negative emotions; more left-side activation for positive emotions) of face processing and anxiety level (high vs low). High-frequency repetitive transcranial magnetic stimulation (rTMS, 10 Hz) was applied to the left prefrontal area to induce an increased activation response within the left premotor cortex. Twenty-nine subjects, who were divided into two different groups depending on their anxiety level (high/low anxiety; State-Trait-Anxiety Inventory (STAI)), were asked to detect emotion / no emotion. Accuracy (Acl) and response times (RTs) were considered in response to the experimental conditions. A general significant increased performance was found in response to positive emotions in the case of left-side stimulation. Moreover, whereas high-anxiety subjects revealed a significant negative-valence bias in absence of stimulation, they showed a more significant Acl increasing and RTs decreasing in response to positive emotions in case of left premotor brain activation. The present results highlight the role of the premotor system for facial expression processing as a function of emotional type, supporting the existence of a valence-specific lateralized system within the prefrontal area. Finally, a sort of “restoring effect” induced by TMS was suggested for high-anxiety subjects.

Keywords

• Emotional facial expression • Premotor cortex • Simulation process • Anxiety
• Transcranial magnetic stimulation (TMS) • Emotional valence

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Introduction

Simulation models of emotion recognition have suggested that understanding another's emotions expressed by face requires individuals to map the observed emotion onto their own representations which are active during the experience of the perceived emotion [1-3]. Supporting this perspective, functional brain imaging studies have indicated that perceiving another person's facial expressions correlates with increased activity in similar sensorimotor cortices, which mainly include two separate components: premotor and somatosensory cortices [4]. Cortical activations were interpreted as evidence that these regions contribute to explicit emotion processing by linking emotion perception with representations of somatic states previously engendered by emotions. Thus, it was suggested that visually recognizing the facial expressions of emotion will engage regions in the sensorimotor circuits that subserve the visual representations of the

perceptual properties of facial expressions and simulation of the motor behavior associated with such expressions (by premotor areas), as well as functions that serve to modulate the somatovisceral activity, and to link these two components to bodily experience the emotions (likely somatosensory systems). In particular, when a subject “simulates” the perceived emotions, premotor cortex may be more directly implicated in implicitly simulating the emotion-related motor behavior, to prepare the system to reproduce the emotional facial patterns [5-7].

TMS (transcranial magnetic stimulation) studies in healthy adults are consistent with these results [8,9]. Specifically, it was also found that premotor activity was related to the “valence” effect, pointed out by the different prefrontal responsiveness to some negative (i.e. fear) more than positive (happiness) or neutral faces [2,5]. These studies found a generic significant modification of frontal cortical network in response to emotional type,

but they did not directly explore the premotor cortex effect on facial expression simulation mechanisms [10-12].

Some recent studies revealed also a significant and distinct contribution by the left and right dorsolateral prefrontal cortex (DLPFC) in response to positive and negative emotional faces. It was found that, when activated, the left DLPFC improved the processing of positive emotions and reduced the processing of negative emotions [13]. Contrarily, right prefrontal stimulation (high frequency repetitive TMS, rTMS) resulted in impaired disengagement from angry faces, with significant DLPFC effect on attentional processing of negative emotional information [14]. The “valence-model” theory explains the relationship between emotional cue processing and the hemispheric lateralization effect, supposing withdrawal-related emotions are located in the right hemisphere, whereas approach-related emotions are biased to the left hemisphere [15-17]. Thus, different effects

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of left/right PFC on emotional face processing may be due to the emotional valence of the stimuli and to the distinct contribution the two hemispheres may have in manipulating such valence [18]. In comparison with previous research, in the present research a more specific analysis was conducted on the premotor cortex effect related to emotional face detection, to directly explore the contribution of the “simulation model” of emotion recognition based on the valence effect. Specifically we intended to verify the role of the left premotor cortex with respect to positive vs negative emotional faces.

A second main goal of the present research was to explore the relationship between anxiety level and emotional face comprehension based on simulation mechanisms. Indeed, anxiety level was previously found to be a significant effect of the personality component in emotional cue detection [19-21]. Therefore, we intend to investigate the effect of anxiety on information processing by performing an emotional recognition task. An exhaustive analysis of the prefrontal contribution in processing facial expression of emotion in relationship with anxiety behavior may be relevant in monitoring the dysfunctional role that some attentional mechanisms may have in clinical or sub-clinical subjects who show an unbalanced responsiveness toward aversive (mainly threatening) cues. In fact, it was shown that the frontal cortical area may be implicated in the anomalous implementation of attentional control over threat-related stimuli [22]. In cases of increasing level of anxiety in the clinical and pre-clinical field, it was hypothesized that disorder-relevant information and focusing selective attention on it would be an evoking and sustained factor for anxiety. It was supposed that heightened anxiety is associated with reduced recruitment of control mechanisms on emotional cues that are emotionally arousing, potentially aversive and threat-related [23,24]. It was also shown that an increased state of anxiety in healthy samples induces a reduced involvement of prefrontal control structures [22]. Thus, reduced activation of the PFC went along with reduced inhibition control of amygdala

which would be associated with the inability to suppress emotional or disorder-relevant information, inducing a sort of attentive bias toward the potentially aversive cues.

However, the promising and alternative “valence-model” theory allowed us to explain the relationship between anxiety and emotional information processing supposing withdrawal-related emotions, such as anxiety, are located in the right hemisphere, whereas approach-related emotions are biased to the left hemisphere [16,17]. Thus, an increased level of anxiety might be associated with dysfunctional right-hemispheric activity, with an increased activation, when aversive conditions are processed [24]. Contrarily, positive emotions would be subjected to a more normal processing mechanism without significant attentional bias. Recently, studies in healthy subjects have tried to test the valence hypothesis based on the assumption of increased right-hemispheric activity in anxiety disorder. In line with this hypothesis, recent evidence has shown that low frequency (inhibitory) TMS on the right DLPFC produced a decreased anxiety-related behavior (self-rated anxiety and contralateral increased theta EEG) [25]. Moreover, in this case TMS significantly reduced vigilant attention for fearful faces [26].

An adjunctive hypothesis might integrate this valence effect by considering the contribution of the simulation mechanisms implicated in emotional facial expression recognition. In fact, we may suppose that this left/right “unbalance effect”, related to the anxiety level, could be also supported by anomalous activation of the somatosensory areas, and in particular of the premotor component. Therefore, we may suppose impairment in automatic mechanisms related to facial mimicry and simulation. In this case, a sort of mimicry bias in simulating the facial expression to be recognized may intervene in favor of more negatively valenced emotional patterns. Based on these hypotheses, we suppose that not only the attentional bias may characterize the performance of high-anxiety subjects, supported by the generic prefrontal unbalanced activation, but that a more specific dysfunctional simulation mechanism, with increased somatosensory response to negative

emotions, could intervene to modulate the subjects’ biased recognition process.

No previous study has explored the impact of these simulation mechanisms in relationship with anxiety in a clinical or sub-clinical sample, since a more generic effect of the DLPFC was considered in relationship with anxiety levels [11,20]. In the present research the rTMS (repetitive TMS) method was used to produce an increased responsiveness of the left frontal premotor cortices. In comparison with previous research that adopted a low-frequency stimulation paradigm, finalized to the inhibition of PFC circuit, in the present research we intended to induce an increased effective performance in emotional facial detection, by using a high-frequency paradigm. This innovative approach consists in potentiating the spontaneous simulation process in response to emotional faces, supported by frontal premotor area.

Thirdly, the high-frequency rTMS method was used to confirm the hypothesis of a direct contribution of the premotor area in emotional face processing in relationship with levels of anxiety. The TMS paradigm may be used to increase the cortical excitability of the left hemisphere to enhance the response to positive emotional cues and to guarantee a better recognition. The left hemispheric activity “potentiation” could induce a sort of restored balanced somatosensory behavior for both negative and positive categories in high-anxiety subjects. In the present study anxiety levels in healthy subjects was used as an independent group variable to test the effect it has in the retrieval process in case emotional positive and negative cues are processed. As a consequence, by the stimulation of the left hemisphere in high-level anxiety subjects, we should reduce the right superiority related to negative-valenced faces, thus inducing a normalization of the interhemispheric imbalance. In other words, in performing the left-side stimulation we intend to restore a vacant equilibrium between the two hemispheres, by potentiating the approach-emotions responsiveness (regulated by the left side) and to contrast the withdrawal-emotions bias (regulated by the right side). We hypothesized that this effect was expected on both accuracy and RTs measures,

with a significant equivalence of attentional allocation to the two stimulus categories for high-anxiety subjects (unbiased performance). Thus, the cortical modulation induced by TMS may furnish a proficient tool to restore anxiety-related dysfunctional mechanisms, showing potential neuroplasticity effects on sub-clinical subjects.

Subjects and methods

Subjects

Fifteen females and 14 males (21-28 years; $M = 23.34$; $SD = 0.11$) participated at the experiment. We included young sub-clinical subjects who were all right-handed [27] and with normal or corrected-to-normal visual acuity. Exclusion criteria were history of psychopathology (Beck Depression Inventory, BDI-II, 1996) [28] for the subjects or immediate family. State-Trait-Anxiety-Inventory (STAI) [29] was submitted after the experimental session. No neurological or psychiatric pathologies were observed. Two expert clinicians applied a semi-structured interview and evaluated the general psychopathological profiles of the subjects and their direct family members, in a preliminary phase of the research. No payment was provided for subjects' performance. They gave informed written consent for participating in the study and the research was approved by the Ethical Committee institution where the work was carried out.

Materials

Stimulus materials were taken from the set of pictures by Ekman and Friesen [30]. They were black and white pictures of a male/female actor (four different exemplars for each emotional type and neutral face balanced for gender), presenting respectively a happy 34 JJ-4-07, angry 38 JJ-3-12, fearful 37 JJ-5-13, or neutral face. After the experimental section, the subjects were asked to analyze the stimuli viewed to evaluate the significance (type of emotions), the arousing power, and the valence attributed to each face. The emotional categories were correctly recognized (respectively 99% for happiness, 97% for anger, 97% for fear, 92% for neutral faces). The subjects also expressed (on a seven-point Likert scale)

their evaluation on arousing power (happiness $M = 5.54$; $SD = 0.32$, fear $M = 6.43$; $SD = 0.47$, anger $M = 6.32$; $SD = 0.87$ and neutral stimuli $M = 1.23$; $SD = 0.30$) and on valence (happiness $M = 6.68$; $SD = 0.33$, fear $M = 1.08$; $SD = 0.38$, anger $M = 1.13$; $SD = 0.44$, and neutral stimuli $M = 3.53$; $SD = 0.36$). The univariate repeated measures analysis of variance (ANOVA) applied to arousal showed significant differences between the emotions ($F_{3,28} = 7.89$, $P \leq 0.01$; $\eta^2 = 0.36$). *Post hoc* comparisons (contrast analyses) showed different responses between emotional and neutral stimuli (for all comparisons $P \leq 0.01$). On the contrary, no differences were found between the three emotions. Also the valence differed across emotions ($F_{3,28} = 8.70$, $P \leq 0.01$; $\eta^2 = 0.39$). *Post hoc* analyses showed that anger and fear were found to be more negative than happiness, whereas happiness was considered more positive than the other emotions and the neutral stimuli (for all comparisons $P \leq 0.01$).

Procedure

Subjects were seated comfortably in a moderately lighted room with a monitor screen positioned approximately 60 cm in front of their eyes. Pictures were presented in a randomized order in the center of the computer monitor, with a horizontal angle of 9° and a vertical angle of 11.8° (E-prime 2.0 software, Psychology Software Tools, Pittsburgh, PA, USA, temporal resolution 10 ms). Each facial stimulus was presented for 150 ms, preceded by a fixation point (a centered cross). Subjects were required to distinguish between emotion/no emotion feature ("do you see an emotion or not?") by focusing attention on each expression [8,31]. They were instructed to make a two-alternative forced-choice response, by pressing a left/right button. Accuracy and speed were stressed. A familiarization phase allowed them to comprehend the significance of the task and to learn the detection procedure.

STAI measure

After the experimental phase subjects were asked to answer the STAI. It is a self-report assessment composed of 40 items where the subject is required to evaluate how he feels about common daily situations, on a four-point Likert-scale. The STAI differentiates between

the temporary condition of "state anxiety" (S-Anxiety subscale, 20 items) and the more general and long-standing quality of "trait anxiety" (T-Anxiety subscale, 20 items), and provides two different total scores, related to the two subscales. STAIs were scored using norms from the *Manual for State Trait Anxiety Inventory* [29]. Based on the STAI total scores (range 27-48) we distinguished 2 groups referring to trait-anxiety: high trait-anxiety group and low trait-anxiety group. The two groups were composed by considering high-anxious group scores equal to or greater than 43, whereas low-anxious group scores equal or less than 39 [32,33].

rTMS stimulation

We used a transcranial magnetic stimulator (Magstim Rapid², The Magstim Company Limited, Spring Gardens, Whitland, Carmarthenshire, UK) with a 70 mm figure-of-eight coil (maximum output 1.2 T). The center of the coil, which produced the maximum electric field, was positioned perpendicularly to the cortical site to be stimulated. The accurate localization of the rTMS pulse was confirmed using a Brainsight frameless stereotactic system (Brainsight Magstim, Softaxic Optic 2.0, E.M.S. srl, Bologna, Italy, optical digitizer: Polaris Vicra, NDI Medical, Waterloo, Ontario, Canada). This scan procedure suggested that TMS was applied over the BA6 (Talairach -4,12,56 coordinates) (Figure 1). Due to the stimulation parameters and the known effect of rTMS on the scalp, we may exclude a significant and systematic effect on more medial cortical structures (such as the medial prefrontal cortex or cingulate cortex; for specific details on the TMS parameters see [34]).

TMS pulses were set at an intensity of 120% of the motor threshold, defined as the TMS intensity that caused a visible twitch at the muscle of the right hand in 80% of the delivered pulse (two series of ten pulses) over the left primary motor cortex (M1). Two control conditions were included in the experimental design to control the simple stimulation effect (sham condition with absence of TMS stimulation) and the location effect (control site condition with Pz stimulation). Pz was considered as a control area of stimulation

since in the present contribution we examined the frontal component of the stimulation process. A different block for each stimulation condition was randomly run. One-second rTMS stimulation (high frequency - 10 Hz) was time locked to the stimulus. In total, there were 100 stimuli in each experimental condition (each expression type was presented twenty-five times for condition). Stimuli were totally randomized across condition and emotional type. Thus subjects received 100 trains of 10-pulse for each condition, with an inter-train interval of 5 seconds. A trial started with the stimulation and the presentation of a fixation point, followed by the stimulus presentation composed by the stimulus and a blank screen (500 ms), according to the recommendation for repetitive stimulation [35]. Subjects could respond starting from the onset of the stimulus.

Data analysis

Two factorial repeated measures ANOVAs (IBM SPSS Statistics 19, SPSS Inc., Chicago, IL, USA) with three independent factors (Trait, low/high-anxiety subjects; Condition, stimulation/control site/sham; E, emotional content, four types) were applied on the dependent measures of accuracy (Accuracy index, Acl = total of correct response/total occurrence) and RT measures. Type I errors associated with inhomogeneity of variance were controlled by decreasing the degrees of freedom using the Greenhouse-Geisser epsilon. The normal distribution of the data was assessed by using skewness and kurtosis test in a preliminary statistical phase.

Accuracy index (Acl)

Significant effects were found for Trait ($F_{1,28} = 6.09, P \leq 0.01; \eta^2 = 0.34$). High-anxiety subjects showed a better accuracy in comparison with low-anxiety subjects (Table 1). Moreover Trait x E interaction effect was significant ($F_{3,56} = 8.45, P \leq 0.01; \eta^2 = 0.39$). As shown by paired contrast (Contrast analysis) effects, high-anxiety subjects revealed a better performance for negative stimuli (anger and fear) than positive (happiness) and neutral stimuli (all comparisons $P \leq 0.01$). Contrarily, low-anxiety subjects did not show significant differences

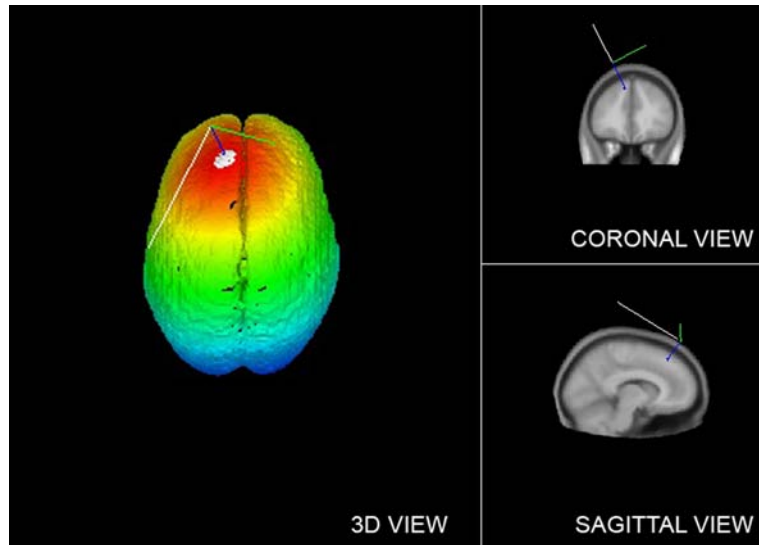


Figure 1. Coil position on the scalp (axial, coronal and sagittal view) and brain stimulation site (Talairach coordinates: -4,12,56).

Table 1. Mean correct response (Acl, percentage values) and response times (RTs, msec), for each Trait, stimulation Condition, and Emotional type.

	Acl		RTs		Acl		RTs	
	<i>high-anxiety</i>				<i>low-anxiety</i>			
Stimulation	M	(SD)	M	(SD)	M	(SD)	M	(SD)
Anger	0.95	0.09	410	1.32	0.87	0.10	436	1.47
Fear	0.94	0.07	420	1.23	0.88	0.07	433	1.27
Happiness	0.94	0.08	390	1.45	0.92	0.09	430	1.23
Neutral	0.88	0.07	444	1.20	0.87	0.11	435	1.38
Pz	M	(SD)	M	(SD)	M	(SD)	M	(SD)
Anger	0.96	0.08	422	1.17	0.88	0.13	429	1.10
Fear	0.95	0.10	428	1.25	0.89	0.11	432	1.20
Happiness	0.88	0.12	435	1.28	0.87	0.10	436	1.31
Neutral	0.85	0.10	436	1.30	0.85	0.09	440	1.30
Sham stimulation	M	(SD)	M	(SD)	M	(SD)	M	(SD)
Anger	0.94	0.07	428	1.15	0.86	0.13	431	1.22
Fear	0.95	0.06	425	1.23	0.88	0.09	433	1.20
Happiness	0.87	0.11	432	1.31	0.88	0.08	437	1.29
Neutral	0.86	0.11	433	1.38	0.84	0.11	438	1.12

(Figure 2). Moreover, a significant interaction effect Trait x Condition x E was observed ($F_{6,56} = 7.09, P \leq 0.01; \eta^2 = 0.37$). As shown by contrast comparisons, firstly a general increasing of performance for positive stimuli was observed for both groups in case of stimulation than

Pz and sham (all comparisons $P \leq 0.01$). In addition, for high-anxiety subjects, whereas in Pz and sham conditions anger and fear were better recognized than happiness (respectively $F_{1,28} = 6.09$, $P \leq 0.01$; $\eta^2 = 0.31$; $F_{1,28} = 7.09$, $P = 0.023$; $\eta^2 = 0.34$) and neutral faces ($F_{1,28} = 7.45$, $P \leq 0.01$; $\eta^2 = 0.37$; $F_{1,28} = 8.92$, $P \leq 0.01$; $\eta^2 = 0.39$), in stimulation condition happiness showed an increased degree of recognition and it did not differ from the negative stimuli (respectively for anger $F_{1,28} = 1.20$, $P = 0.25$; $\eta^2 = 0.08$, and fear $F_{1,28} = 1.11$, $P = 0.32$; $\eta^2 = 0.07$).

RT data

Trait \times E interaction effect was found to be significant ($F_{3,56} = 9.55$, $P \leq 0.01$; $\eta^2 = 0.40$): high-anxiety subjects showed decreased RTs in response to negative emotions (anger and fear) than positive emotions and neutral faces (all comparisons $P \leq 0.01$) (Table 1). It was also observed a significant interaction effect Trait \times Condition \times E ($F_{1,56} = 8.81$, $P \leq 0.01$; $\eta^2 = 0.38$): a consistent reduction of RTs was revealed in stimulation condition for high-anxiety subjects in response to happiness in comparison with anger ($F_{1,28} = 5.89$, $P \leq 0.01$; $\eta^2 = 0.35$), fear ($F_{1,28} = 8.08$, $P \leq 0.01$; $\eta^2 = 0.38$) and neutral ($F_{1,28} = 9.32$, $P \leq 0.01$; $\eta^2 = 0.41$) faces. No other comparison was statistically significant (Figure 3).

Discussion

In the present experiment, facial expression recognition was explored taking into account the level of anxiety, by comparing the performance of high-anxiety subjects with that of low-anxiety subjects. The role of the left premotor area and the contribution of simulation mechanism were considered. It was found that the cortical potentiation of this prefrontal area, by a high-frequency rTMS, consistently affects the detection of facial stimuli. This effect on recognition was relevant in response to specific emotional patterns (for positive emotions). The improved performance in response to happiness was observed for both low- and high-anxiety subjects. As shown by the statistical results, this trend may be directly imputable to an accentuated response to a specific category of emotional valence (the positive stimuli). However, a different behavior

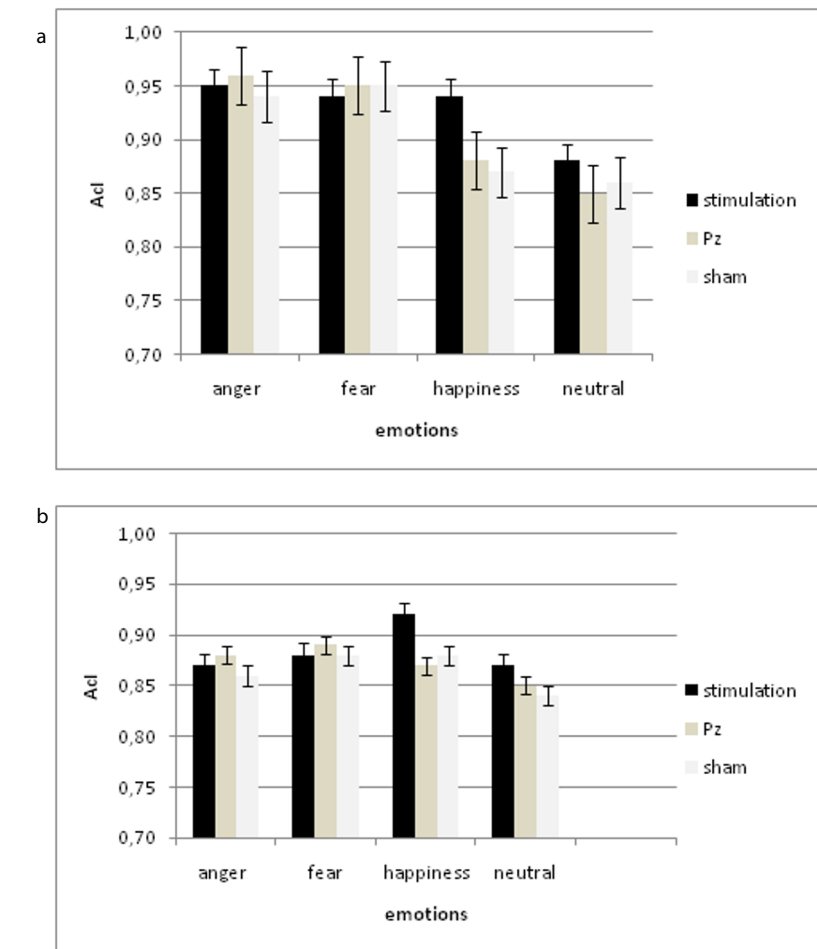


Figure 2. Acl (mean and SD) for stimulation, Pz control and sham effect, as a function of different emotional types (anger, fear, happiness, neutral), respectively for high-anxiety (a) and low-anxiety subjects (b).

in responding to emotional cues as a function of anxiety level was observed. High-anxiety subjects revealed a generally more increased effectiveness (Acl; RTs) in retrieving positive emotional patterns, since their “negative bias effect” observed in absence of cortical stimulation was eliminated in favor of a more balanced response in the case of the left premotor area potentiation.

About the premotor brain activation, the present research showed a general effect of this prefrontal area in modulating the emotional faces recognition. With respect to brain response to facial cues, we observed an increased facility in processing emotional expressions when the frontal motor circuit was potentiated. This result was confirmed by the simultaneous decreasing of RTs and by the increasing of Acl. Based on these results, we

may suppose that the TMS stimulation could facilitate a better detection by potentiating the “simulation” response and its link with the sensorimotor system [6]. It was previously found that the premotor areas are mainly implicated in inducing a coherent motor behavior which is finalized to “reproduce” the facial patterns observed [2,5]. Thus, a specific competence may be ascribed to this frontal cortical system, which may allow a functional “mirroring” and simulation behavior to produce a functional face recognition.

However, a main point elucidated by the present research was that the premotor contribution in face comprehension was valence-dependent. In fact, the “facilitation effect” observed for Acl (increased) and RTs (reduced) was detected in response to a specific emotional category, i.e. for happiness.

Therefore, it may be suggested a specific relationship between the left premotor area and the selective processing of some emotional cues exists. Thus, this mechanism could be considered more specifically positive-valence related and not generically responsive to emotional facial expressions. In contrast with the present results, a recent TMS study using happy and fearful faces reported that somatosensory cortex stimulation only impaired the discrimination of fearful faces [36]. However, it should be pointed out that previous research used an inhibitory rTMS and, more critically, they did not distinguish the lateralization effect, modulating the left or right premotor cortex. In contrast, in the present research we more directly verified the presence of a lateralization effect relating to the emotional category, by applying the stimulation on a specific hemisphere. By stimulating the left side we more accurately tested the role of the two hemispheres in face processing as a function of the emotional valence. As shown, in comparison with no stimulation condition (sham and control conditions) left premotor stimulation induced a general increased facilitation for positive emotions.

The valence-effect was more accentuated for high-anxiety subjects, who were revealed to have a higher increased gain than low-anxiety subjects as a consequence of the left premotor stimulation. The enhancement of the left activity produced an increase in both effectiveness (higher Acl) and efficiency (reduced RT). This result becomes more significant if compared with the general trend observed for high-anxiety in normal conditions (without stimulation), that is the observed negative bias toward the potential threatening information. Evidence of the assumption that anxiety facilitates the detection of negative aversive information comes from previous studies on attentional bias [37,38], in which anxious individuals preferentially attended to or had delayed disengagement from threat-related stimuli. More specifically, anxiety could impair attentional control and anxious individuals preferentially would allocate attentional resources to aversive information. This attentional unbalance between positive vs negative cues may contribute to maintaining high levels of anxiety, and it may constitute

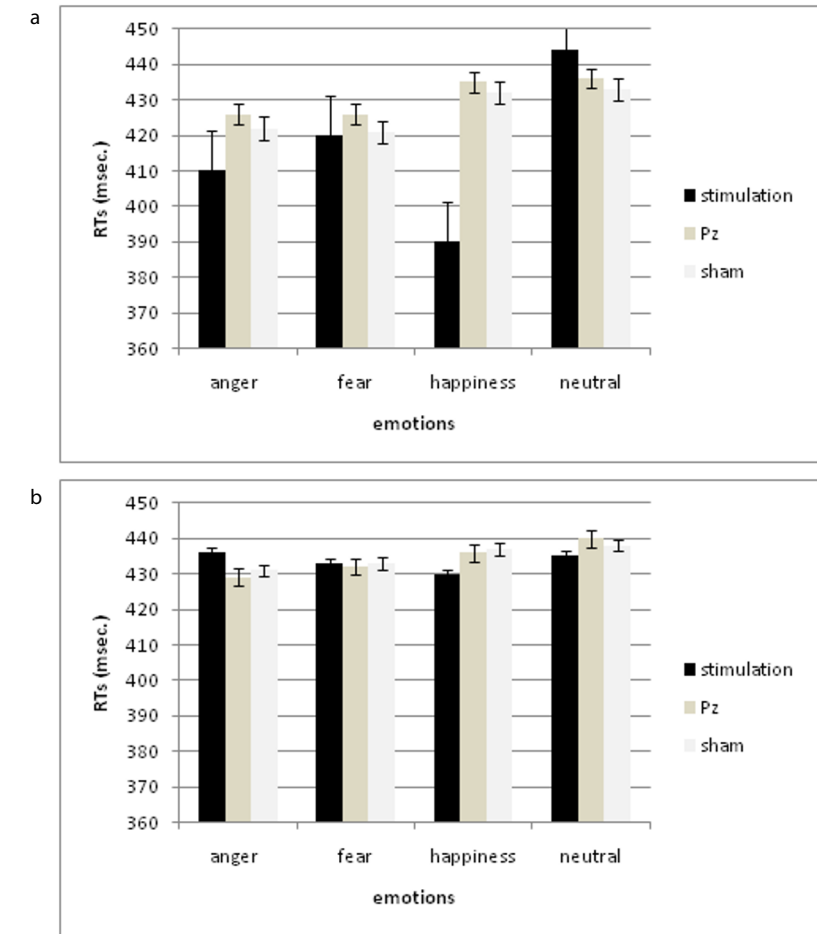


Figure 3. RTs (mean and SD) for stimulation, Pz control and sham effect, as a function of different emotional types (anger, fear, happiness, neutral), respectively for high-anxiety (a) and low-anxiety subjects (b).

a sort of reinforcement of anxiety behavior [39,40].

Taken together our results might confirm the reduction of the “unbalance effect” related to bias toward the negative cues. Moreover, this restored balance may be more directly related to the contribution of some simulation mechanisms, mediated by the premotor cortex. Indeed, the valence model of emotional cue processing in relationship with the mirroring functions may explain the increasing of both accuracy and RT measures in high-anxiety subjects, by pointing out the distinct role the left and right hemispheres have in emotional cue processing for these subjects [16]. When a sort of functional condition is restored between the two cortical systems deputed to elaborate

respectively the positive and negative emotional cues, the high-anxiety subjects’ performance shows a significant reduction of the pre-existing bias, making their behavior more similar to that of the low-anxiety subjects.

Thus, the negative-bias revealed in high-anxiety subjects may be contrasted by left premotor stimulation which restores the “normal” brain functions related to emotional cue processing. An interesting study that has applied a low frequency TMS paradigm (cortical depotentiation) on the frontal left hemisphere revealed an increased attentional negative bias and a clear anxiety behavior [41], which could confirm the distinct role of left and right sides in processing emotional cues in relationship with the anxiety profile, and contemporary

the significant effect of TMS in regulating the anxiety behavior. However, in that research the specific effect of premotor cortex on emotional face processing was not considered. It should be considered that the present research results may be explained by supposing a significant over-activity by the right DLPFC, an effect that the left-side TMS stimulation may partially counterbalance, or by supposing a significant under-activity by the left hemisphere that the TMS stimulation may restore. Both of these explanations seem to be plausible, and we suggest that the result may fit and support the hypotheses of a significant premotor dysfunctional activity. For this reason the present study could be replicated by inducing a cortical perturbation of the right DLPFC by adopting a potential inhibitory paradigm. In fact, the reduction of the attentional bias toward the negative cues should be obtained

also by reducing the cortical excitability of the right hemisphere, that was deputed to respond to aversive and potentially threatening information, and that was shown to be hyper-responsive in high-anxiety subjects.

To summarize, premotor area activity was shown to be implicated in emotional recognition and it functions as a neural correlate of the underlying “resonance mechanism” when emotions are observed. The prefrontal implication is interpretable as a functional mechanism of mirroring the emotional condition displayed by other people, where somatosensory sharing similar emotional responses allows a direct form of understanding other people by simulating their emotions. More specifically, positive emotions may be better recognized when the left hemisphere is activated generating a consonant shared response by the observer.

Anxiety-related bias, that is increased responsiveness to negative emotional patterns in high-anxiety subjects, may be modulated by left premotor cortex potentiation. A sort of restored balance may operate increasing the mimicry functions toward positive patterns, mainly supported by the left hemisphere.

However, as shown in previous research, the impact of the “simulation mechanism” should be tested by using some integrative measures, such as facial feedback, by acquiring the electromyography facial response (EMG): we propose an integration between the autonomic measures and the cortical prefrontal activity, that showed an ability to signal the presence of a somatosensory response to facial patterns [10]. These integrated effects may allow a complete overview of the motor and somatic behavior which supports the mirroring function in emotional face comprehension.

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