

Processing of featural and configural aspects of faces is lateralized in dorsolateral prefrontal cortex: A TMS study

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ABSTRACT

Facial recognition relies on distinct and parallel types of processing: featural processing focuses on the individual components of a face (e.g., the shape or the size of the eyes), whereas configural (or “relational”) processing considers the spatial interrelationships among the single facial components (e.g., distance of the mouth from the nose). Previous neuroimaging evidence has suggested that featural and configural processes may rely on different brain circuits. By using rTMS, here we show for the first time a double dissociation in dorsolateral prefrontal cortex for different aspects of face processing: in particular, TMS over the left middle frontal gyrus (BA8) selectively disrupted featural processing, whereas TMS over the right inferior frontal gyrus (BA44) selectively interfered with configural processing of faces. By establishing a causal link between activation in left and right prefrontal areas and different modes of face processing, our data extend previous neuroimaging evidence and may have important implications in the study of face-processing deficits, such as those manifested in prosopagnosia and autistic spectrum disorders.

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Introduction

We are exposed to thousands of faces and yet we are able to recognize those which are familiar from those which are not. Further, we can detect subtle changes in another's face, and we are able to recognize similarities in two people's faces, such as those occurring between brothers or sisters, parents and children. Facial processing is thus a quite sophisticated ability. Converging evidence suggests that face processing involves a complex network of cortical and subcortical areas (Gobbini and Haxby, 2007; Haxby et al., 2002; Ishai, 2008; Ishai et al., 2005; Natu and O'Toole, 2011). In particular, facial recognition seems to be based on distinct and parallel types of processing (Bombari et al., 2009; Mondloch et al., 2002; see Carbon, 2011): on the one hand, featural processing takes into account the identity of single components of a face (e.g., the shape or the size of the eyes), whereas configural processing considers the relations among those features (Carbon and Leder, 2005; Leder and Carbon, 2006; see Maurer et al., 2002 for a review). This latter type of processing can further be distinguished in: (i) sensitivity to first

order relations, i.e., the relative position of the different features with respect to each other (in a face, typically the two eyes are above the nose and above the mouth); (ii) holistic processing, i.e., binding all the features into a single percept (gestalt), and (iii) sensitivity to second order relations (or relational processing; Rhodes, 1988) which consists in perceiving the distance among features (e.g., the distance between the eyes or between the mouth and the nose). Paradigms investigating featural-based and relational-based (i.e., sensitive to second-order relations) processes, such as the “Jane faces task” (Maurer et al., 2007; Mondloch et al., 2002) employ stimuli differing in single features (e.g., varying the shape of the eyes) while keeping their distance constant, or varying the spacing between the features without changing the single elements of the face.¹ Humans are usually better in detecting differences between faces due to featural than relational changes (Carbon and

¹ It is worth noting that changes in spacing between facial elements may also slightly affect the way facial parts are perceived and that featural changes may also slightly affect how the whole configuration appears. Nonetheless, the validity of the featural and relational sets of the Jane faces task in selectively tapping on the corresponding processes has been extensively proven (Maurer et al., 2002, 2007; Mondloch et al., 2002, 2003, 2010). In particular, a critical validity test for the Jane faces task was the demonstration in Mondloch et al. (2002) (in which the test was first used) of higher inversion costs for the relational set than for the featural set, in line with long-standing evidence on inversion effects (e.g., Collishaw and Hole, 2000; Freire et al., 2000; Murray et al., 2000).

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Leder, 2005; Freire et al., 2000; Mercure et al., 2008; Mondloch et al., 2002, 2010); moreover, featural processing seems to emerge earlier in development compared to the ability to detect relational changes (Cashon and Cohen, 2004; Mondloch et al., 2002, 2003).

At the neural level, partially different neural circuits have been found to be involved in featural-based and relational-based facial recognition mechanisms. Examining brain activation during the execution of the Jane faces task, Maurer et al. (2007) reported a higher activation during same–different face judgments in areas of the right hemisphere, including the fusiform gyrus (adjacent to – but not overlapping with – the fusiform face area), the frontal and the inferior parietal cortex, when faces differed in terms of relational rather than featural aspects (see also Rotshtein et al., 2007). Left middle prefrontal activity instead was prominent for featural processing (Maurer et al., 2007; see also Lobmaier et al., 2008, for a left hemisphere predominant activation during featural processing of faces). This lateralization pattern is consistent with what is usually found for local/global processing of hierarchical stimuli (e.g., Martinez et al., 1997). Consistent with this, studies using ERPs have shown that the amplitude and the hemispheric lateralization of the N170 component – a negatively peaked component occurring approximately 170 ms after stimulus onset that differentiates faces and objects (see Bentin et al., 1996) – are modulated by presentation of featural or configural changes in face stimuli (Scott and Nelson, 2006; but see Mercure et al., 2008). Scott and Nelson (2006) found that the right hemisphere N170 was significantly greater for relational compared to featural processing, whereas the left hemisphere N170 exhibited the opposite pattern (Scott and Nelson, 2006). Using the Jane faces task, Mercure et al. (2008) observed that the P2 component was reduced in amplitude when elicited by a featural manipulation compared to a relational manipulation. Since the P2 component is likely to reflect the effects of visual cortical feedback (Kotsoni et al., 2006, 2007), the authors hypothesized that the larger P2 associated to configural processing may depend on faces with spacing manipulations relying to a higher degree on visual cortical feedback and thus requiring longer processing times compared to stimuli differing for single features only (Mercure et al., 2008).

However, ERPs and fMRI data are only correlational in nature, that is, they provide information on how manipulation of behavior may affect neural activity. Conversely, brain stimulation techniques such as TMS allow one to establish a causal link between a cortical site and a specific task, by directly modulating brain activity as the source of behavior. Here we used TMS to investigate the causal role of specific brain regions in featural and relational processing of faces. Specifically, we investigated the causal role of two regions in the dorsolateral prefrontal cortex, the right inferior frontal gyrus (rIFG, BA44) and the left middle frontal gyrus (lMFG, BA8), in featural and configural processing of faces using the Jane faces task (Mondloch et al., 2002). Participants were presented with two faces in sequence and had to decide whether they were identical or not (in case of a difference, the change could be featural or configural). rTMS was applied at 100, 150 and 200 ms after the appearance of the second face, in line with previous evidence showing differences in the ERPs pattern within this time window depending on the type of process – configural vs. featural – required (Mercure et al., 2008; Scott and Nelson, 2006). In a previous fMRI study (Maurer et al., 2007) during the execution of the Jane faces task (Mondloch et al., 2002) the rIFG has been implicated in the processing of second-order relations in faces, while lMFG has been associated to featural processing. If these regions in the DLPFC play a causal role in processing of faces, their stimulation should modulate participants' performance in same–different judgments for faces. More specifically, the rIFG should interfere with relational processing of faces (i.e., detecting changes in spacing between facial elements), but not with featural processing (i.e., detecting changes in the single features), whereas for the lMFG the opposite pattern is expected.

Method

Participants

Sixteen students of the University of Pavia (mean age: 22.06 years, SD: 1.53, range: 20–25, 4 males) took part in the experiment. Prior to the experiment, each participant filled in a questionnaire (translated from Rossi et al., 2011) to evaluate compatibility with TMS. None of the volunteers reported neurological problems, familiarity for seizures nor was taking any medication that could interfere with neuronal excitability. Written informed consent was obtained from all participants before the experiment. The protocol was approved by the local ethical committee and participants were treated in accordance with the Declaration of Helsinki.

Material and procedure

Participants were seated comfortably at a distance of 57 cm from a 17" TFT-LCD computer monitor (screen resolution: 1440×900 pixels; refresh rate: 60 Hz) and wore earplugs to minimize TMS click sound interference. Stimuli were part of the Jane faces task set (Mondloch et al., 2002) and consisted of nine gray-scale images (image resolution: 72×72 dpi) of Caucasian female faces, eight of which were derived from the photograph of a single face (called "Jane") (see Fig. 1A). "Jane's sisters" were obtained by either replacing Jane's eyes and mouth with matching features from different females (featural set, four pictures) or by varying the spatial position of the eyes or the mouth (relational set, four pictures; see Mondloch et al., 2002 for further details). Participants were asked to judge whether two shortly consecutive presented faces were identical or differed in some aspects, by pressing the corresponding key with the index or the middle finger of the right hand. Response speed was stressed in addition to accuracy. Each volunteer took part in four blocks of stimulation (one for each TMS condition, see below) for each set (featural or relational). The two sets were run separately to allow time for each style of processing to emerge but participants were not explicitly informed about the distinctions (see Maurer et al., 2007). The order of presentation of the blocks belonging to the two sets was counterbalanced across participants. Each block consisted of 40 face-pairs presented in random order. All the 20 "different" face-pair possible combinations were presented once (with the order of the two faces being inverted), while all the 5 "same" face-pair combinations were presented four times. The timeline of an experimental trial is shown in Fig. 1B. Face stimuli were presented in the middle of the screen (subtending a visual angle of approximately 12° in height and 8° in width). Each trial started with a 1000 ms long central fixation cross followed by a blank screen for 500 ms and by the presentation of the first face that remained visible for 200 ms. The presentation of the first face was followed by a blank screen lasting 300 ms (as in Maurer et al., 2007). Then, the second face was presented: duration of the second face presentation was not pre-determined but the face remained visible until participants responded ("same or different face?").

Before the experiment, a short slide presentation was displayed to explain the task. The difference in the identity between stimuli was emphasized, but no cues were given about the type of changes that could occur. Further, prior to each set presentation, short practice blocks were performed in order to familiarize participants with the task and with TMS. Practice blocks included 20 trials each (ten "different" face trials and ten "same" face trials); the face stimuli used in the practice blocks did not belong to the sets employed in the experimental blocks and consisted of four faces and their modified version, obtained by changing either featural or configural details. The software E-prime 2.0 (Psychology Software Tools, Pittsburgh, PA) was used for stimuli presentation, data collection and TMS triggering. The whole experiment took approximately 90 min.

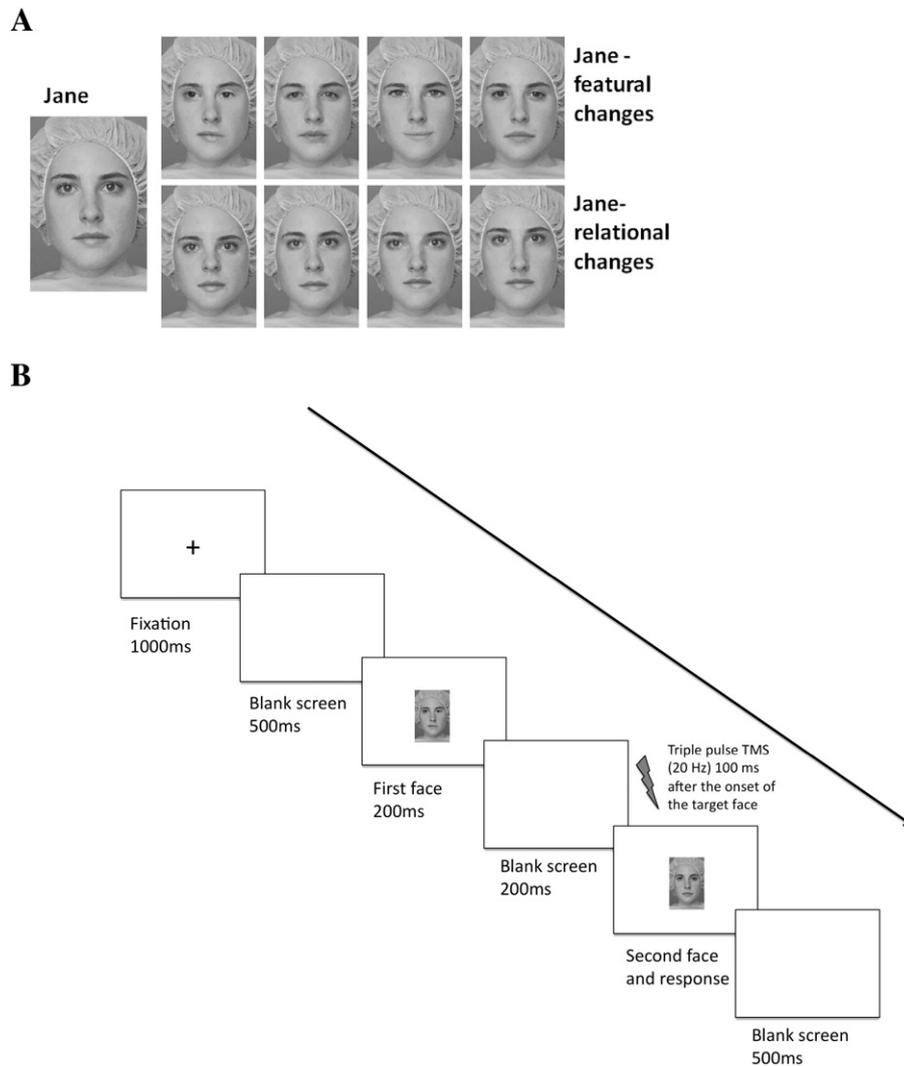


Fig. 1. A) The faces used in the Jane faces task. B) The timeline of an experimental trial. TMS was applied over the Vertex (control site) and over two sites of the DLPFC: the right inferior frontal gyrus (rIFG, BA44) and the left middle frontal gyrus (lMFG, BA8).

Transcranial magnetic stimulation

Online neuronavigated TMS was performed with a Magstim Rapid2 stimulator (Magstim Co Ltd, Whitland, UK) connected to a 70 mm butterfly coil at a fixed intensity of 60% of the maximum stimulator output. A fixed intensity was used in accordance with previous studies on visual perception (e.g., Pitcher et al., 2007; Silvanto et al., 2005); nonetheless, if participants reported discomfort or muscle twitches a lower intensity was used (minimum 55%, mean = 58%; SD = 2%, see Azañón et al., 2010).

Target cerebral areas were localized by means of stereotaxic navigation on individual estimated magnetic resonance images (MRI) obtained through a 3D warping procedure fitting a high-resolution MRI template with the participant's scalp model and craniometric points (Softaxic, EMS, Bologna, Italy). TMS was delivered to the right inferior frontal gyrus (rIFG; Talairach coordinates: $x = 43$, $y = 3$, $z = 37$), and to the left middle frontal gyrus (lMFG; Talairach coordinates: $x = -29$, $y = 14$, $z = 51$) on the basis of a previous fMRI study investigating neural correlates of featural and relational processing using the Jane faces task² (Maurer et al., 2007). The Vertex, corresponding to the median point of

the nasion–inion line, was used as a control area. For the rIFG and the lMFG, the coil was initially oriented with an angle of approximately 45° from the nasion–inion line and the handle pointing outwards, and hence adjusted for each participant in order to minimize discomfort. For the Vertex the coil was oriented tangentially to the scalp parallel to the nasion–inion line. The pitch and roll angles were set in order to minimize the distance between the scalp and the cerebral target. Three TMS pulses were delivered at 20 Hz 100 ms after the onset of the second face stimulus, with these parameters of stimulation leading to transient disruption of the underlying neural activity in the stimulated area (e.g., Bien et al., 2012; Schwarzkopf et al., 2011). Accordingly, stimulation occurred between 100 and 150 ms after the onset of the second face stimulus, in line with previous ERP studies suggesting that featural and relational processing should both occur within this time window (Scott and Nelson, 2006; see Mercure et al., 2008).

Results

Fig. 2A shows participants' mean percentage accuracy in each TMS condition (No TMS, Vertex, lMFG, rIFG) and set (featural, relational). Trials in which individual response latencies were beyond 3 standard deviations with respect to participant's mean performance in each

² Note that in Maurer et al. (2007) coordinates of activated brain regions were given in MNI space; these coordinates were converted into Talairach coordinates to be compatible with the neuronavigation system used here (Softaxic, EMS, Bologna, Italy).

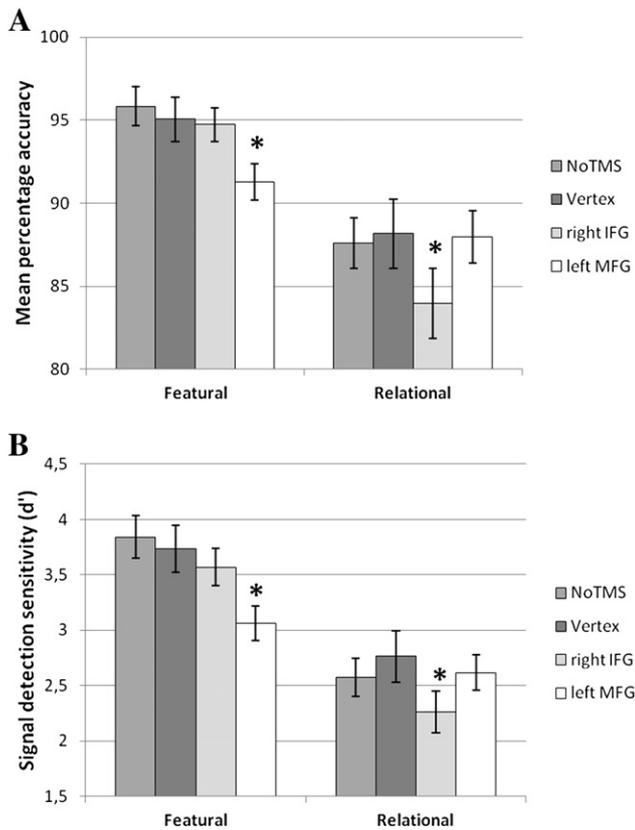


Fig. 2. A) Mean percentage of correct response accuracy and B) mean d' values for the featural and the relational sets for the four TMS conditions (No TMS, Vertex, IMFG, rIFG). Asterisks indicate the presence of a significant difference compared to both TMS over Vertex and TMS over the frontal gyrus in the other hemisphere. TMS over the rIFG selectively impaired participants' performance in the relational set, whereas TMS over IMFG selectively impaired participants' performance in the featural set. Error bars represent ± 1 SEM.

experimental block were excluded from the analyses (following this criterion, a total of 1.85% trials were overall excluded).

Planned pairwise comparisons ensured that accuracy in the No TMS and in the Vertex TMS condition was comparable in both the featural set, $t_{(15)} = .55$, $p = .59$, and the relational set, $t_{(15)} = .27$, $p = .79$. Vertex was hence taken as the unique control baseline condition in following analyses. A two-way repeated measures ANOVA was performed on mean accuracy with TMS condition (Vertex, IMFG, rIFG) and set (featural vs. relational) as within-subjects factors. The analysis yielded a significant effect of set, $F_{(1,15)} = 17.09$, $p = .001$, $\eta_p^2 = .53$, due to accuracy being overall higher in the featural than in the relational set. The main effect of TMS was also significant, $F_{(2,30)} = 4.59$, $p = .018$, $\eta_p^2 = .23$, indicating overall higher performance in the Vertex condition compared to the other two conditions. However, the effect of TMS depended on the experimental task, as indicated by the significant interaction TMS by set, $F_{(2,30)} = 8.27$, $p = .001$, $\eta_p^2 = .35$. The significant interaction TMS by set was analyzed by looking at the effect of TMS within each set. Bonferroni–Holm corrected post-hoc comparisons showed that in the featural set TMS applied to the IMFG significantly reduced accuracy compared to both the control Vertex condition, $t_{(15)} = 2.84$, $p = .024$, and the rIFG TMS condition, $t_{(15)} = 3.27$, $p = .015$, whereas no difference in accuracy was observed between Vertex and rIFG TMS, $t_{(15)} = .33$, $p = .74$. In the relational set, accuracy was significantly lower in the rIFG TMS condition compared to both the Vertex, $t_{(15)} = 4.30$, $p = .003$, and IMFG conditions, $t_{(15)} = 2.86$, $p = .024$, whereas participants made a comparable number of errors in the IMFG and Vertex TMS conditions, $t_{(15)} = .12$, $p = .90$.

Importantly, the results of the statistical tests using d' -prime values (d' , a measure of sensitivity, MacMillan and Creelman, 1991)

as the dependent variable were in agreement with the results of the analysis on correct responses (see Fig. 2B). In particular, a two-way repeated measures ANOVA with TMS condition (Vertex, IMFG, rIFG) and set (featural vs. relational) as within-subjects factors yielded a significant effect of set, $F_{(1,15)} = 22.99$, $p < .001$, $\eta_p^2 = .61$, a significant effect of TMS, $F_{(2,30)} = 6.36$, $p = .005$, $\eta_p^2 = .30$, and a significant interaction TMS by set, $F_{(2,30)} = 6.79$, $p = .004$, $\eta_p^2 = .31$, replicating the pattern found when accuracy was analyzed. Bonferroni–Holm corrected post-hoc comparisons showed that in the featural set sensitivity was lower for the IMFG TMS condition ($d' = 3.06$, $SD = .63$) than for both the Vertex ($d' = 3.73$, $SD = .85$), $t_{(15)} = 3.44$, $p = .012$, and rIFG TMS conditions ($d' = 3.57$, $SD = .66$), $t_{(15)} = 3.09$, $p = .014$, whereas no significant difference in sensitivity was reported between Vertex and rIFG TMS, $t_{(15)} = .87$, $p = .40$. In the relational set, participants' sensitivity was significantly decreased by TMS applied to rIFG ($d' = 2.26$, $SD = .75$) compared to both the Vertex ($d' = 2.76$, $SD = .92$), $t_{(15)} = 3.54$, $p = .009$, and IMFG conditions ($d' = 2.62$, $SD = .64$), $t_{(15)} = 2.49$, $p = .05$, whereas it was comparable between the Vertex and IMFG TMS conditions, $t_{(15)} = .82$, $p = .423$.

A further analysis was carried out on the response bias measure (c , see MacMillan and Creelman, 1991). In fact, it has been suggested that TMS may affect response bias more/rather than signal detection per se (for a detailed discussion, see Venezia et al., 2012). The bias was similar in the No TMS (mean $c = -.04$, $SD = .25$) and Vertex (mean $c = -.08$, $SD = .29$) conditions, $t_{(15)} = .61$, $p = .55$, ruling out possible unspecific effects of TMS on response bias. A repeated-measures ANOVA with set (featural vs. relational) and TMS condition (Vertex, IMFG, rIFG) as within-subjects variables on the response bias c revealed no significant effects of set, $F_{(1,15)} = .87$, $p = .37$, $\eta_p^2 = .05$, whereas the main effect of TMS was significant, $F_{(2,30)} = 3.93$, $p = .03$, $\eta_p^2 = .21$. Critically, the interaction set \times TMS condition was not significant, $F_{(2,30)} = 1.49$, $p = .24$, $\eta_p^2 = .09$. The significant main effect of TMS depended on TMS over IMFG (mean $c = -.28$, $SD = .25$) increasing participants' tendency to respond "different" (negative c values arising when the number of false alarm rate exceeds the miss rate, see MacMillan and Creelman, 1991) compared to the Vertex TMS condition, $t_{(15)} = 2.68$, $p = .05$ (Bonferroni–Holm correction applied). No difference in response bias was observed between the Vertex and rIFG (mean $c = -.14$, $SD = .32$) conditions, $t_{(15)} = 1.1$, $p = .24$ and between IMFG and rIFG, $t_{(15)} = 1.6$, $p = .29$.

Mean reaction times for correct responses were also analyzed (see Fig. 3). Planned comparisons revealed that response latencies were comparable in the No TMS and Vertex conditions, for both the featural, $t_{(15)} = 1.00$, $p = .33$, and the relational set, $t_{(15)} = .03$, $p = .97$. A two-way repeated measures ANOVA performed on mean RT for correct responses with TMS condition (Vertex, IMFG, rIFG) and set as within-subjects factors, only revealed a significant effect of set, $F_{(1,15)} = 21.28$, $p < .001$, $\eta_p^2 = .59$, indicating overall faster responses in the featural than

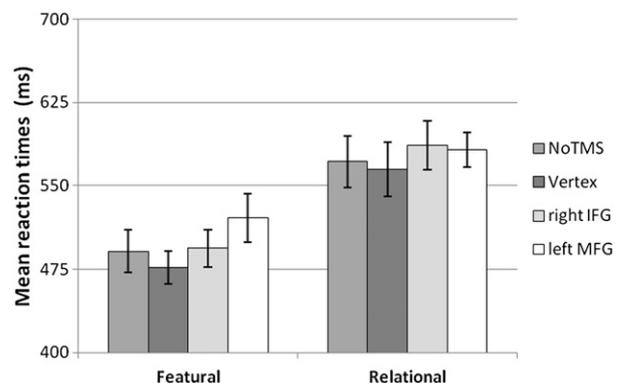


Fig. 3. Mean participants' response latencies in milliseconds (correct responses only) in each experimental condition. TMS did not significantly affect reaction times. Error bars represent ± 1 SEM.

in the relational set. Neither the main effect of TMS, $F_{(2,30)} = 1.27$, $p = .30$, $\eta_p^2 = .08$, nor the interaction TMS by set, $F_{(2,30)} = .52$, $p = .60$, $\eta_p^2 = .03$, reached significance.

Discussion

Our data provide evidence for a double dissociation between the left and right dorsolateral prefrontal cortex (DLPFC) in processing configural and featural aspects of faces. In particular, when TMS was applied over the right inferior frontal gyrus (rIFG, BA44), participants' accuracy was significantly lower compared to the control TMS condition (Vertex stimulation) and compared to TMS applied over the left middle frontal gyrus (lMFG, BA8) in discriminating identical versus different faces diverging for spacing between their features (e.g., distance between the eyes and the nose). No effect of rIFG TMS was observed on same–different judgments when faces differed for single features (e.g., the shape of the eyes and of the mouth). On the other hand, TMS applied over the lMFG significantly impaired participants' ability to discriminate faces differing for their single features compared to both Vertex and rIFG stimulation, but had no effect on processing spatial interrelationships between features. The same pattern was found when the response bias was accounted for by considering participants' response sensitivity (d') as the variable of interest. Our findings are in line with previous neuroimaging evidence (Maurer et al., 2007) that using the same task (the Jane faces task, originally used in Mondloch et al., 2002) showed higher activity in the rIFG when participants had to base their judgment on configural changes, whereas increased activity in the lMFG was associated to recognition judgments based on analysis of the single facial elements. Notably, the effect of TMS over rIFG is also in line with findings obtained with individuals treated for unilateral congenital cataract showing selective deficits in second-order relational processing (but not featural processing) following early right-hemisphere deprivation (due to left-eye cataract; Le Grand et al., 2003). More in general, the lateralization pattern found in the present study is consistent with the classical dissociation found between local and global processing of hierarchical stimuli (e.g., Martinez et al., 1997).

Participants' performance was overall higher in the featural set compared to the configural set, a result in line with previous studies employing the Jane faces task (e.g., Maurer et al., 2007; Mondloch et al., 2002). Our pattern of results rule out the possibility that the TMS effects we got depended on task difficulty: if this were the case, TMS should have selectively affected to a greater extent more demanding judgments (i.e., configural). In line with our data, in the fMRI study by Maurer et al. (2007) there was almost no overlap in cortical sites that showed modulations of activity dependent on task type (featural vs. configural) and regions where activity indexed task difficulty.

Our data are consistent with previous evidence pointing to the right IFG region as part of an extended network of face processing (Fairhall and Ishai, 2007): functional connectivity between the right inferior frontal and right FFA is critical in typical face processing (Fairhall and Ishai, 2007; Thomas et al., 2008), and the rIFG shows an increase in the fine tuning for faces with development (Joseph et al., 2011), as it is the case of the FFA (e.g., Aylward et al., 2005; Passarotti et al., 2007; Scherf et al., 2007). It has been proposed that the IFG may be the region where face-related semantic aspects are processed (Ishai et al., 2000, 2002; Leveroni et al., 2000), thus playing a critical role in face identification and in familiarity judgments (cf. Jiang et al., 2000). In fact, it has been suggested that identity judgments (e.g., familiar vs. not; famous vs. not), as well as other social inferences, rely heavily although not exclusively on configural processing of faces (see Cloutier and Macrae, 2007; Tabak and Zayas, 2012). Consistent neuroimaging evidence also points to the role of the left DLPFC in face processing. For instance, Bunzeck et al. (2006) found a category-specific correlation between neural and behavioral-facilitation in a repetition

priming task using faces and indoor/outdoor scenes as visual stimuli: in the left inferior frontal cortex the correlations were specific for scenes whereas in the left middle frontal gyrus (BA8) they were specific for faces. Using fMRI in combination with a delayed face recognition task, Druzgal and D'Esposito (2001) revealed a network including the left fusiform face and the left middle frontal gyrus that was more active when a probe face matched the remembered face at the time of decision. In line with this, in an fMRI investigation Li et al. (2009) reported the left DLPFC to be part of a distributed neural network involved in top–down face processing. Critically, our data add to this previous correlational evidence by providing first causal evidence for a selective involvement of the left and right DLPFC in processing different aspects of faces.

Prior fMRI evidence has suggested that configural and featural processing of faces is not dissociated in the face-selective fusiform face area (FFA), which is similarly sensitive to both types of face manipulations (Liu et al., 2010; Maurer et al., 2007; Rotshtein et al., 2007; Yovel and Kanwisher, 2004, 2008). Nonetheless, repetitive TMS over the right occipital face area (rOFA), another face-selective area located in the inferior occipital gyrus, interfered with discrimination of face parts but not with discrimination of spacing among these features (Pitcher et al., 2007). In particular, the detrimental effect of TMS on participants' accuracy was observed for (double-pulses) TMS delivered at 60 and 100 ms after stimulus onset, whereas stimulation given after 100 ms did not affect performance (Pitcher et al., 2007). These data suggest that the rOFA processes face-part information at an early stage of the face-processing stream, possibly due to a stronger reliance on high spatial frequencies for the feature-based type of processing (Goffaux et al., 2005; but see Goffaux and Dakin, 2010). Our data extend this previous evidence by shedding light on later stages of processing of face information. Previous studies measuring ERPs have found that the N170 and the P2 components discriminate featural versus configural processing (Mercure et al., 2008; Scott and Nelson, 2006), showing greater amplitude in response to spacing compared to featural changes in faces. Accordingly, in our study triple-pulse TMS (20 Hz) was delivered after 100 ms from the second face onset, therefore covering the time window indicated by ERP evidence as critical in processing featural vs. configural aspects of faces (Mercure et al., 2008; Scott and Nelson, 2006).

The Jane faces task may also be considered a paradigm to investigate change blindness (although in the original work by Mondloch et al., 2002, it was not conceived this way). In a typical change detection paradigm, participants are presented with a first array of stimuli that they have to maintain in working memory; a second array is then presented and participants need to compare the test stimulus with the retrieved memory representation for a decision. Previous TMS studies revealed a causal role of a parietal–frontal network in mediating visual awareness in this type of paradigm (e.g., Beck et al., 2006; Tseng et al., 2010; Turatto et al., 2004). Turatto et al. (2004) applied TMS over the left and right DLPFC at onset of the first stimulus with the stimulation covering the whole trial (first picture presentation, blank, target picture), and found a critical role for the right but not the left DLPFC in correct detection. Using a similar TMS paradigm, Beck et al. (2006) found a role for the right but not for the left posterior parietal cortex (PPC) in change detection. Notably, the right PPC seems to be more critical at the time of encoding of the first array (Tseng et al., 2010) than at the presentation of the second array, suggesting a specific role of PPC in encoding and maintaining information in visual short-term memory. In line with other TMS studies specifically investigating featural vs. configural processing of faces (see Pitcher et al., 2007) and consistent ERPs evidence (Mercure et al., 2008; Nelson and Scott, 2006), in our experiment we stimulated after the presentation of the second picture. On the basis of the above evidence we cannot exclude the possibility that TMS over the left and right DLPFC could have also impaired performance if applied during presentation of the first face. Although future experiments may clarify this issue, it is important to note that in previous TMS studies on change

blindness (Beck et al., 2006; Tseng et al., 2010; Turatto et al., 2004) stimuli consisted of an array of four faces, one of which could change between study and test: conversely, our task required participants to pay attention to a single face and to specifically process spacing and featural aspects. The role played by the left and right DLPFC in our task was specific for the type of face processing and went likely beyond storing information in working memory.

Notably, TMS did not affect reaction times. This was also the case of the TMS study by Pitcher et al. (2007) in which the OFA was targeted and that also reported effects of stimulation on accuracy, but not on reaction times. Conversely, we found TMS to affect participants' response criterion (c, Macmillan and Creelman, 1991). It has been suggested that TMS may in many cases affect response bias, an effect that might have gone undetected in many previous TMS studies that only considered TMS effects over accuracy and reaction times (see Venezia et al., 2012, for a detailed discussion on this issue). In our study, response bias did not differ between No TMS and Vertex conditions, ruling out possible unspecific effects of TMS over response bias. Nonetheless, our analyses showed that TMS applied over the left MFG significantly made participants more "liberal" in their response criterion (more false alarms than misses) compared to the Vertex control condition. Consistent evidence suggests that the left more than the right DLPFC is strongly involved in perceptual decision-making tasks (e.g., Heekeren et al., 2006; Philastides et al., 2011). TMS over the left MFG may have thus interfered with a general perceptual decision-making mechanism. Importantly though, this effect did not depend on the type of task (featural vs. configural), and cannot then be responsible for the effects we reported.

In sum, our study critically extends previous neuroimaging evidence demonstrating a dissociation in the dorsolateral prefrontal cortex in different aspects of face processing: in particular, we show that the right inferior frontal cortex is causally involved in configural processing of faces, whereas the left middle frontal gyrus is causally involved in featural processing of faces. By establishing a causal link between activation in frontal areas and processing of faces, our data may also have important implications in the study of face-processing deficits such as those observed in congenital prosopagnosia (Grüter et al., 2008) and autism spectrum disorders (Deruelle et al., 2004), in which configural processing may be particularly impaired (see also Lobmaier et al., 2010).

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