Transcranial magnetic stimulation studies of face processing

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Introduction

Neuropsychological patients exhibiting category-selective visual agnosias have provided unique insights into the cognitive functions of the human brain (Shallice, 1989; Moscovitch et al. 1997; Moro et al. 2008), and this has been especially true in the study of face processing (Bodamer, 1947; Farah, 2004). While cases of pure prosopagnosia resulting from cortical damage are extremely rare they still provide the strongest evidence that faces are processed in anatomically segregated neural networks in the human brain (Sergent and Signoret, 1992; McNeill and Warrington 1993; Rossion et al. 2003; Riddoch et al. 2008). Moreover, acquired prosopagnosics exhibiting selective deficits with specific aspects of face recognition (e.g. recognising facial identity or recognising facial expressions) provided evidence for the seminal cognitive model of face processing (Bruce and Young, 1986) as well as for subsequent cortical models of face processing (Haxby et al. 2000; Adolphs, 2002; Calder and Young, 2005). These models in turn provided cognitive frameworks with which to test how faces are recognised in the undamaged brain.

Over the past fifteen years experimental techniques such as event-related potentials (ERPs), magnetoencephalograhy (MEG) and functional magnetic

resonance imaging (fMRI) have been used to add to the evidence from neuropsychological and single unit studies to demonstrate where, when, and how faces are processed. However, unlike patient studies, neuroimaging techniques cannot demonstrate that a region is necessary for a particular cognitive function (Price and Friston, 2002). Transcranial magnetic stimulation (TMS), in contrast, can be used to draw causal inferences, as one of the effects of the cortical disruption induced by magnetic stimulation is to act as a "virtual lesion" lasting from tens of milliseconds up to approximately one hour, depending on the type of stimulation (Pascual-Leone et al. 2000; Walsh and Pascual Leone, 2003; Huang et al. 2005). TMS also avoids some of the potential difficulties of patient studies that can limit their interpretation such as individual differences in pre-morbid ability (Farah, 2004) and compensatory plasticity following the lesion (Robertson and Murre, 1999).

The greatest strength of TMS is that it can be delivered with a high degree of both spatial and temporal specificity (millisecond resolution). This specificity offers a unique advantage in psychological testing as TMS can be used to test where and when cognitive computations are performed (Walsh and Cowey, 2000; Walsh and Pascual-Leone, 2003). In this chapter we will briefly describe TMS, consider the small but growing number of studies that have used TMS to disrupt face processing, and discuss how TMS can be used in the future to better understand how faces are cortically represented in the human brain.

What is TMS?

Transcranial magnetic stimulation (TMS) is an experimental technique widely used in physiological studies of motor function and plasticity (Wassermann et al,

2008; Pascual-Leone et al. 2005). TMS can also be used to study cognitive processes by delivering an electromagnetic pulse over a targeted cortical area that can disrupt normal cognitive function (see figure 1). A TMS pulse is produced by generating a large, rapidly changing electrical current that is passed through a metal coil. The current generates a magnetic field perpendicular to the coil orientation. When the coil is placed on the scalp of an experimental participant the magnetic field passes through the skull and induces an electrical field within the underlying

cortex

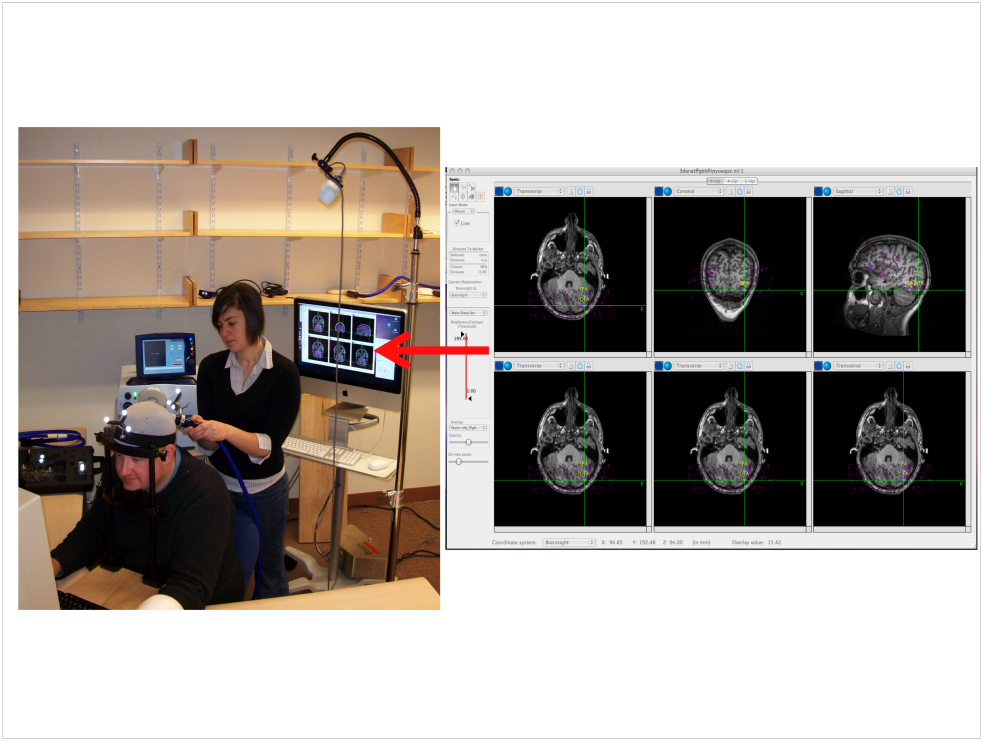

Figure 1. Where and how a specific cortical area can be targeted using a TMS coil (in this case TMS is being delivered over the right occipital face area). On the right are images from the Brainsight neuronavigation software used to identify the TMS target site. The subject's individual MRI scan is shown overlaid with the results of a face-selective functional localiser (faces minus objects). The Polaris camera (seen in the top right of the photo) identifies the precise location of the experimental subject and the TMS coil by sensing the location of the silver balls. This location information can be tracked online using the Brainsight software to ensure precise TMS coil placement over the targeted area throughout the experiment.

The size of the induced current depends on the amplitude and the rate of change of the current passing through the TMS coil. Typically the current in the coil is large, up to 8 kiloamperes (kA), with a swift rise time of roughly 200 microseconds (μs) and an overall duration of approximately 1 ms (Walsh and Cowey, 2000). The induced current alters the electrical state both inside and outside any affected nerve axons within range of the pulse (Nagarajan et al. 1993). The resulting voltage difference across the cell membrane causes it to depolarise, initiating an action potential. This difference raises the resting membrane potential of some neurons in the targeted cortical area while inducing others to fire.

The effects of the neural disruption induced by the TMS pulse on concurrent behavioural performance in experimental tasks can be measured using the standard behavioural tools of experimental psychology, e.g. performance accuracy, reaction times (RT), threshold procedures, etc. Furthermore by measuring performance during the delivery of TMS and when no TMS is delivered it is possible for subjects to act as their own experimental control group.

The spatial resolution of TMS

The exact spatial resolution of TMS cannot be stated in mm or cm because the effects depend on the initial state of the brain, the stimulation intensity and frequency and the measure being taken of the effects of TMS. What one can do, however, is make sound inferences based on what is known about cortical organisation. For example, phosphenes (perceived flashes of light induced by delivering TMS over V1) can be elicited with a resolution of 1-2 degrees of visual angle which equals a functional specificity mapped across 9-18mm of early visual cortex (Kammer, 1999).

Similarly, in the motor cortex muscles that are segregated by as little as 1 to 2 cm on the cortex can be selectively stimulated (Brasil-Nero et al. 1992; Wassermann et al. 1992; Singh et al. 1997). TMS has also been used to induce behavioural dissociations in spatially adjacent regions in the parietal cortex (Ashbridge et al. 1997), the left inferior frontal cortex (Gough et al. 2005) and the left occipitotemporal cortex (Duncan et al. 2009). The evidence from these studies demonstrates that the behavioural impairments of TMS in human studies can correspond with an effective spatial resolution of approximately 1cm to 2cm.

Identifying TMS target sites

In any TMS experiment it is important to accurately position the TMS coil to ensure that the induced neural disruption is focused on the intended targeted cortical area. Single pulses of TMS can be used to functionally identify early visual cortex (by inducing phosphenes) and motor cortex (by inducing muscle twitches) but no such induced signature techniques exist for face-selective areas such as the occipital face area (OFA) or the superior temporal sulcus (STS). The optimal method for individually identifying these target sites in subjects is by using a stereotaxic neuronavigation system (such as the Brainsight system seen in figure 1). Such systems allow individual structural and functional MRI data to be co-registered with a subject's head in real space. This allows the TMS coil to be accurately positioned over the desired TMS target site.

Although localizing target sites with functional MRI data is the most accurate method (Pitcher et al. 2009), other studies have used individual structural scans and identified target sites based on mean Talairach co-ordinates for functionally defined

areas reported in prior fMRI studies (Pitcher et al. 2007; 2008). A recent study that systematically compared different methods of TMS site localisation reported that the differences between such methods lay in statistical power and therefore in the number of subjects required to find significant effects rather than in qualitative differences in the experimental effects (Sack et al. 2009).

The temporal resolution of TMS

The disruptive effects of TMS in healthy human subjects are most commonly assessed by correlating the induced neural disruption with a behavioural task that is dependent on the stimulated region. As such the best demonstration of the temporal duration of any TMS disruption will be evident in the behavioural results (Amassian et al. 1993; O'Shea et al. 2004; Pitcher et al. 2007). The duration of a TMS pulse is very brief, approximately 1 ms. By contrast the physiologically measurable effects at the neuronal level have been shown to range from hundreds of milliseconds up to a matter of seconds (Moliazde et al. 2003). However, the effects recorded from single neurons over these longer time periods do not appear to be relevant behaviourally. The recordings in this study were made in anaesthetised animals and it is a common finding in human brain stimulation experiments that physiologically measurable effects that may last for several seconds in a passive subject do not survive if the subject uses the affected brain region / body part (Antal et al. 2007). For example, different TMS paired and quadpulse paradigms delivered over the motor cortex can change resting state motor evoked potentials (MEP) recorded from the hand and finger regions for several minutes after TMS if and only if the subject does not employ their motor cortex to move their hands and fingers (Silvanto et al. 2008). Thus the most important consideration when designing TMS experiments is the duration of

the impairment to the behavioural performance being measured. Any task in a standard experiment will typically require the involvement of multiple brain regions and these regions will exhibit peaks of neural activity at different times. As a result it is important that the TMS is delivered in the correct time window because otherwise the induced neural disruption could occur either too early or too late to cause a behavioural impairment.

One way to effectively address this problem is to deliver single pulses of TMS to the target region at different time points after stimulus onset or after the commencement of behavioural monitoring (Amassian et al. 1993). Plotting the temporal pattern of the induced impairments will demonstrate when the TMS is most effective which demonstrates when the targeted area is likely to be most active during task performance. While single pulse TMS can give a very precise temporal activation pattern for a targeted region it necessarily requires a large number of temporal conditions (single pulses of TMS delivered at different times from stimulus onset). One way to reduce these conditions and to expand the duration of any TMS induced disruption is to use more than a single pulse such that the disruptive effects of two pulses of TMS will summate and thereby increase the effect of the induced behavioural disruption. This is well established in the physiological domain and has been adapted for behavioural experiments. Double pulse TMS separated by 40 ms has proven to be a reliable protocol for demonstrating when a variety of functionally distinct cortical areas exhibit peak processing (Juan and Walsh, 2003; O'Shea et al. 2004; Pitcher at al., 2007: 2008; Juan et al. 2008; Kalla et al. 2008; Duncan et al. 2009).

The summation of multiple TMS pulses is further demonstrated in longer repetitive TMS protocols. Rushworth and colleagues (2001) and Göbel and colleagues

(2001) were the first to deliver TMS at a frequency of 10 Hz for 500 ms. The summation of five pulses of TMS has subsequently proven to be a robust TMS protocol across a wide variety of functionally distinct cortical areas (Campana et al. 2002; Bjoertomt et al. 2002; Lavidor et al. 2003; Muggleton et al. 2003; Wig et al. 2005; Beck et al. 2006; Pitcher et al. 2007; 2008; 2009; Duncan et al. 2009). Moreover the comparatively long duration of the impairment window makes it more likely that using this TMS paradigm will induce behavioural impairments.

The safety of TMS as an experimental tool

A concern in any TMS experiment is the health and safety of the subjects. The magnetic field generated by a TMS coil produces a loud clicking sound so earplugs are recommended for all experiments. Some subjects may experience headaches or nausea or may find the associated twitching and additional peripheral effects of TMS too uncomfortable. These subjects should be released from any obligation to continue in the experiment both for their own health and safety and additionally because such subjects are more likely to generate noisy data. More serious are the concerns that TMS may induce an epileptic seizure. As a guide, any subject with any personal or family history of epilepsy or other neurological condition should be precluded from participating in an experiment that does not involve investigation of that condition (Stewart et al. 2001).

Which face areas are accessible to TMS?

Functional magnetic resonance imaging (fMRI) studies have identified several areas in the human brain that exhibit a larger neural response to images of faces than

to images of objects (Haxby et al. 2000). These areas are thought to perform functionally different cognitive operations (Kanwisher and Yovel, 2006) and cortical models have been proposed that link these areas into distributed networks for face processing (Haxby et al. 2000; Adolphs, 2002; Calder and Young, 2005; Fairhill and Ishai, 2007) (figure 2.).

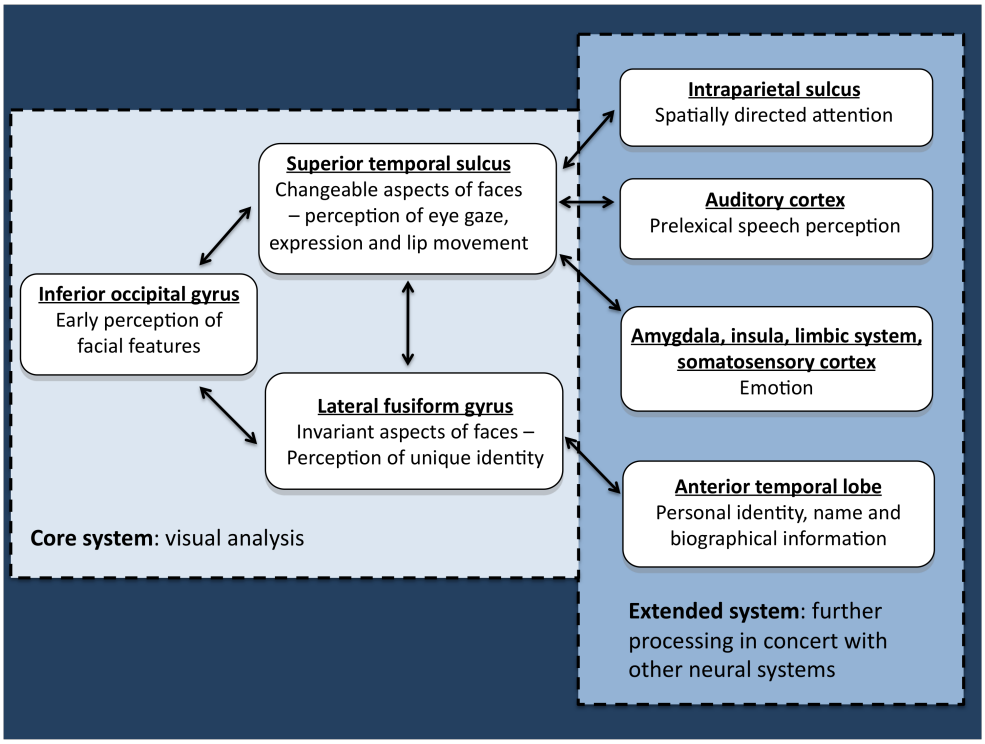

Figure 2. The extended face processing cortical network (Figure adapted from the original model in Haxby et al., 2000).

Not all of the face-selective areas identified with fMRI are accessible to TMS (see figure 3). The range of the disruptive effects of TMS can only be inferred from previous experiments but it seems that a cortical area that is greater than 2 to 3 cm from the cortical surface is unlikely to be affected by a TMS pulse. This makes it likely that functionally defined face-selective areas such as the fusiform face area (FFA) (Kanwisher et al. 1997) and the anterior temporal lobe (Kriegeskorte et al.

2007; Tsao et al. 2008) are outside the range in which TMS can induce cognitive disruption. However it remains possible that future studies may find a way to address this technical issue. In this chapter we will discuss studies that have disrupted the occipital face area (OFA), the superior temporal sulcus (STS), and the face regions in the right somatosensory cortex.

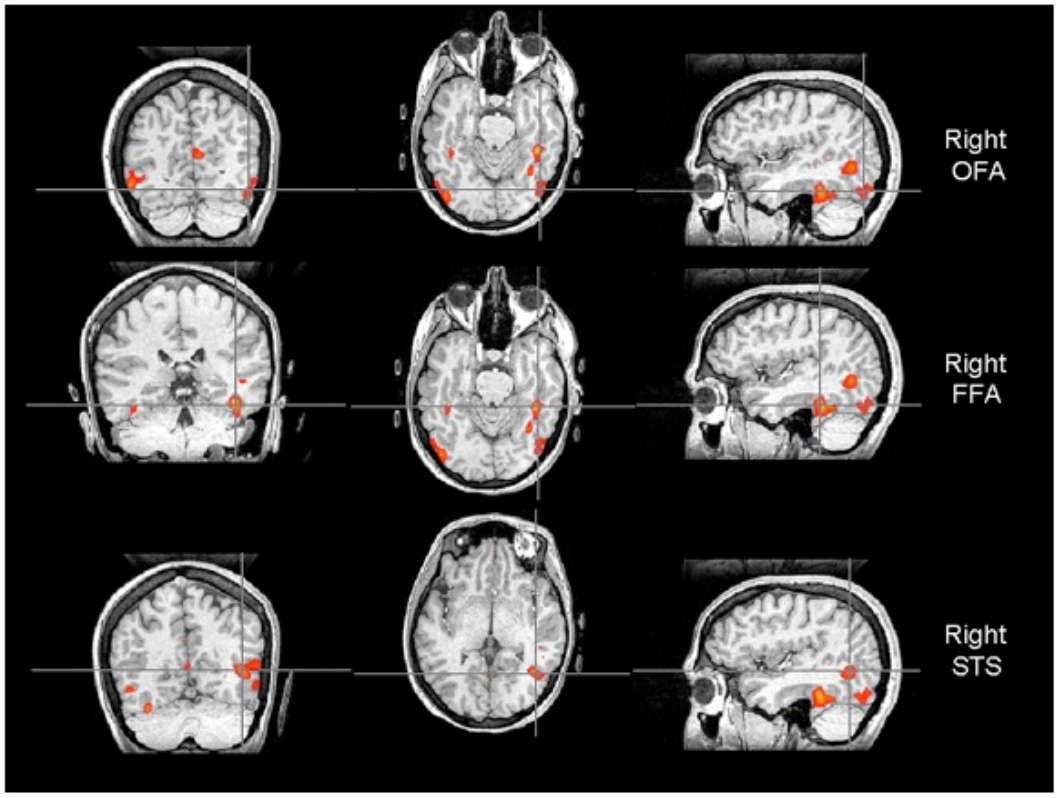

Figure 3. The three core face selective regions in the occipitotemporal cortex shown in one participant. From the top to bottom; the right OFA, right FFA and the face selective region in the right STS. The intersection of the gray lines identifies the area illustrated in each row. From left to right: coronal slice, horizontal slice and sagittal slice. The areas have been identified using a standard functional localiser (the subtraction was faces minus objects). As can be clearly seen in this subject the OFA and the face-selective in the STS are on the cortical surface and accessible to TMS. By contrast the cortical depth of the FFA probably makes it outside the range of TMS.

TMS studies of the occipital face area (OFA)

The occipital face area (OFA) is a functionally defined face-selective region most typically located in the inferior occipital gyrus (Gauthier et al. 2000). Cortical models of face processing (Haxby et al. 2000) propose that the OFA represents facial features prior to further analysis in downstream face-selective areas such as the FFA (Grill-Spector et al. 2004) and the anterior temporal lobe (Kriegeskorte et al. 2007). This hypothesis is supported by evidence that the OFA shows a much larger preference for faces presented in the contralateral visual hemifield than the FFA (Hemond et al. 2007; Hsiao et al. 2008), a characteristic consistent with the OFA being earlier in the visual processing stream than the FFA. The hypothesis is also consistent with a recent study that used dynamic causal modelling (DCM) to demonstrate that the inferior occipital gyrus (the area of the brain that contains the OFA) sends information to the fusiform gyrus (the area of the brain containing the FFA) (Fairhill and Ishai, 2007).

Also consistent with this hierarchical view are the functionally different fMRI adaptation responses exhibited by the OFA and the FFA (Rothstein et al. 2005). In this study the stimuli were a series of faces morphed at different gradations between images of two famous faces (for example, Margaret Thatcher and Marilyn Monroe). Subjects were presented with two successive faces that were either identical or varied by 30% along the physical morphing dimension. In half of the 30% steps, the faces were perceived as the same identity (both Marilyn or both Margaret) while on the other half the faces were perceived to be two different identities (Marilyn then Margaret or vice versa). The neural response in the OFA changed (it was released from adaptation) in response to a within-category change or to a between-category change. By contrast the neural response in the FFA changed in response to a between-

category change but not to a within-category change. This result indicates that the OFA is sensitive to physical changes in a face but not to identity changes and that identity computations are carried out in the FFA.

Neuropsychological evidence has demonstrated that the OFA is essential for accurate face processing. Bouvier and Engel (2006) performed a meta-analysis of neuropsychological patients exhibiting either cortical achromatopsia or prosopagnosia from reports that included details of behavioural testing and (in over half of the reported cases) detailed fMRI scans of the damaged brain areas. The majority of patients with face processing impairments had lesions encompassing the right inferior occipital gyrus (the cortical area usually containing the OFA in the undamaged brain) where fewer had lesions encompassing the right fusiform gyrus (the cortical area usually containing the FFA in the undamaged brain). Detailed single case studies of acquired prosopagnosics have complemented this lesion analysis by demonstrating that damage to the region typically encompassing the OFA (but importantly not to the right FFA) can cause severe prosopagnosia (Rossion et al. 2003; Steeves et al. 2006). While these neuropsychological studies suggest that the OFA is crucial for face processing the diffuse nature of the lesions in these patients makes specific claims about the functional role of the OFA problematic.

The spatial specificity of cortical disruption and its implications for any observed face-selective behavioural impairments are also issues directly relevant to TMS studies of the OFA. Demonstrating that any TMS impairment is specific to faces is important because the lateral occipital cortex, the region of the brain where the OFA is located, also contains functionally defined areas selective for other classes of visual object categories (see figure 4). These include an area selective for objects, the lateral occipital area (LO) (Malach et al. 1995), and another for bodies, the

extrastriate body area (EBA) (Downing et al. 2001). Moreover, distributed theories of object representation suggest that a face is represented across these functionally defined areas rather than only within areas showing a preferential response to faces (Haxby et al. 2001). It is therefore necessary to demonstrate that any behavioural impairment induced by delivering TMS over the OFA is face-selective and not the result of more general object recognition disruption.

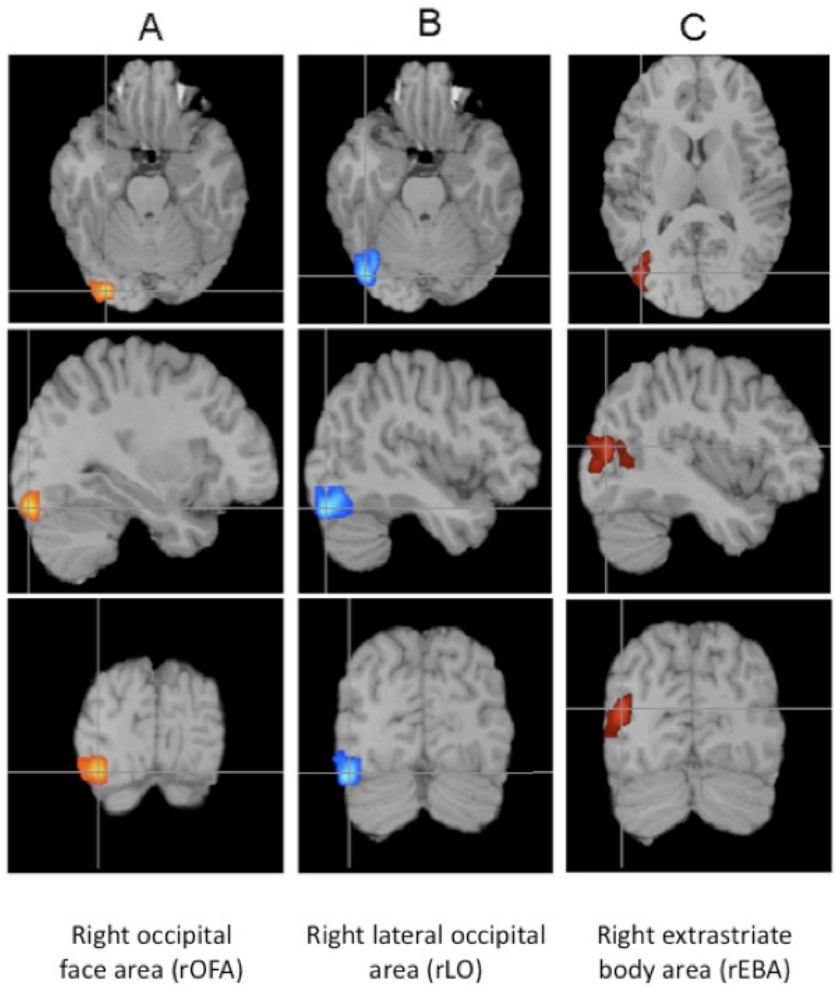

Figure 4. The three TMS target sites in Pitcher et al., (2009). The locations in one participant of (a) the rOFA in yellow (faces minus objects), (b) the rLO in blue (objects minus scrambled objects) and (c) the rEBA in red (bodies minus objects).

A recent study has demonstrated that TMS delivered over the OFA is capable of selectively disrupting face discrimination while leaving object and body discrimination unaffected (Pitcher et al. 2009). In this study TMS was delivered over the right OFA, right EBA and right LO while participants made delayed match-to-sample same / different discrimination judgements to computer generated face, body and object stimuli. Each stimulus category (faces, objects, bodies) consisted of paired images morphed between two distinct exemplars. On different trials the level of morph was varied to produce trials of differing difficulty. Prior to the TMS experiments each subject was scanned using a standard fMRI region of interest (ROI) functional localiser that included images of faces, objects, scrambled objects and bodies (Yovel and Kanwisher, 2004; 2005). The results of this localiser were used to identify the right OFA (faces minus objects), the right EBA (bodies minus objects) and the right LO (objects minus scrambled objects) individually in each subject. TMS was delivered concurrently with the presentation of a probe stimulus, at a frequency of 10Hz for 500 ms (see figure 5).

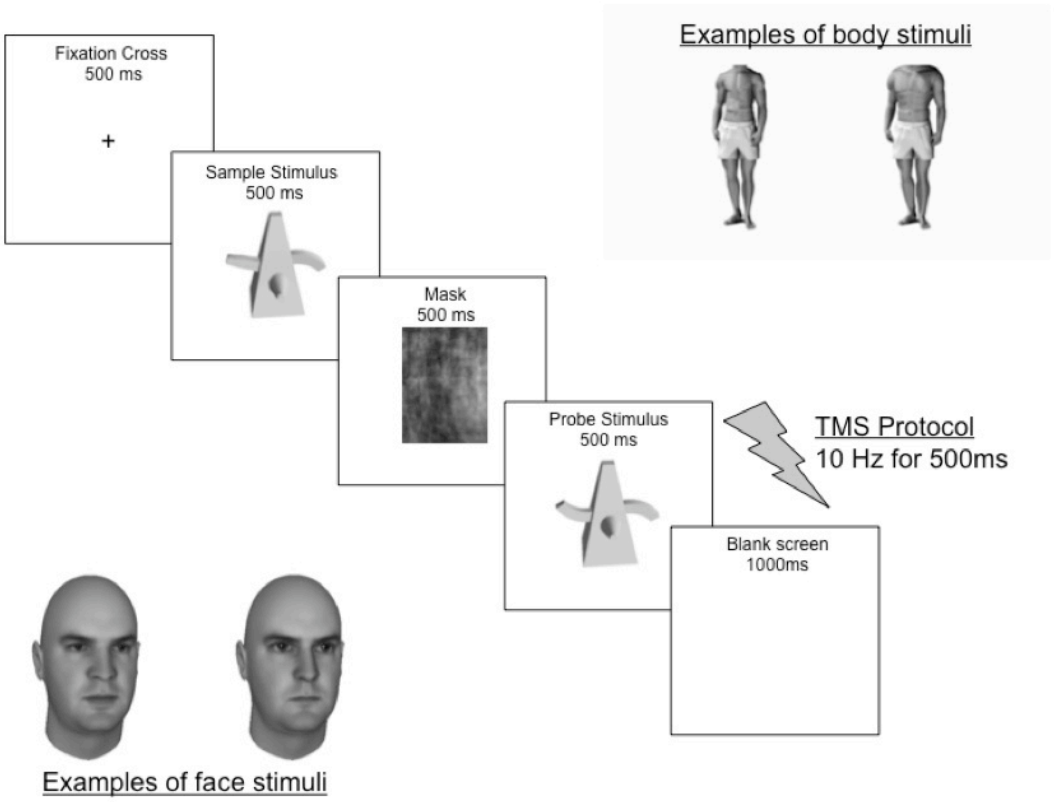

Figure 5. The trial procedure and examples of the stimuli used in Pitcher et al. (2009). The first TMS pulse was delivered concurrently with the presentation of the probe stimulus.

Behavioural impairments in each task were manifested only when TMS was delivered over the area selective for that class of visual stimuli (see figure 6). That is, TMS delivered over the right OFA disrupted face but not object or body discrimination, TMS over the right LO disrupted object but not face or body discrimination, and TMS over the right EBA disrupted body but not face or object discrimination. These results demonstrate that TMS possesses the necessary spatial resolution to selectively disrupt face processing at the right OFA.

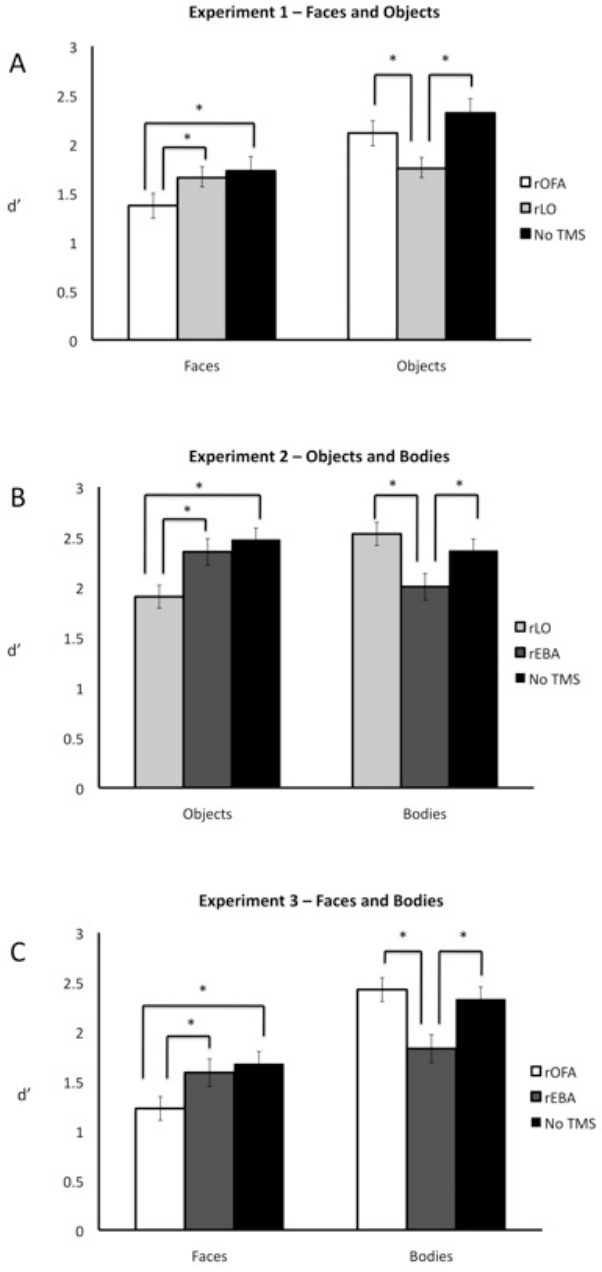

Figure 6. Results from Pitcher et al. (2009) (error bars denote standard errors). In each panel, performance on two tasks is compared in three conditions: TMS to a site selective for that category, TMS to a site selective for another category, and no TMS. An asterisk (*) denotes a significant difference in Bonferroni corrected tests. (A) Faces and Objects. Face task performance was disrupted only by TMS to rOFA, and object task performance was impaired only by TMS to rLO. (B) Objects and Bodies. Object task performance was impaired only by TMS to rLO whereas performance on the body task was disrupted only by TMS to rEBA. (C) Faces and Bodies. Performance on the face task was impaired only by TMS to rOFA, and body task performance was disrupted only by TMS to rEBA.

What information does the OFA represent and when is it active?

Cortical models of face processing propose that the OFA is the first stage of a face processing network and that it computes the early perception of facial features (Haxby et al. 2000; Calder and Young, 2005). Higher visual areas such as the FFA and the anterior temporal lobe are believed to compute the invariant aspects of a face such as facial identity at higher stages of the network. This theory is consistent with feed-forward models of visual perception that propose complex visual stimuli are recognised via a series of stages in which features of increasing complexity are extracted and analysed along the visual processing stream (Ullman et al. 2002; Grill-Spector and Malach, 2004). Thus establishing the precise temporal dynamics of different face-selective cortical areas will provide a better understanding of how these face recognitions mechanisms may function.

Electrophysiological studies indicate when different phases of face processing are performed but the inverse problem (Slotnick, 2004) makes directly linking these temporal components to functionally defined cortical areas identified in fMRI problematic. The N170 (Eimer, this volume), a key face-selective ERP component that peaks 170 ms after stimulus onset (Bentin et al. 1996), is believed to result from neural activity in the FFA (Horovitz et al. 2004) or possibly the STS (Henson et al. 2003) but not from the OFA. Magnetoencephalography (MEG) studies report a face-selective response that peaks 100ms after stimulus onset, the M100 component (Liu et al. 2002; Itier et al. 2006). The functional properties of the M100 are similar to those attributed to the OFA in fMRI studies (Liu et al. 2009), in that it is sensitive to face parts and is associated with successful face detection but not with identification (Liu et al. 2002). This converging evidence suggests the possibility that the OFA and the M100 may be generated by the same underlying neural activity.

The hypothesis that the OFA represents face part information approximately 100 ms after stimulus onset can be directly tested by delivering TMS pulses at different time points while subjects perform a face task (Amassian et al. 1993; Juan and Walsh, 2003; O'Shea et al. 2004; Duncan et al. 2009). Pitcher et al. (2007) conducted a TMS study in which subjects discriminated face stimuli that varied either the face parts (the eyes and the mouth) or the spacing between these face parts (see figure 7). Houses with varied parts and spacing (the manipulated house parts were the windows and the door) were used as control stimuli (Yovel and Kanwisher, 2004).

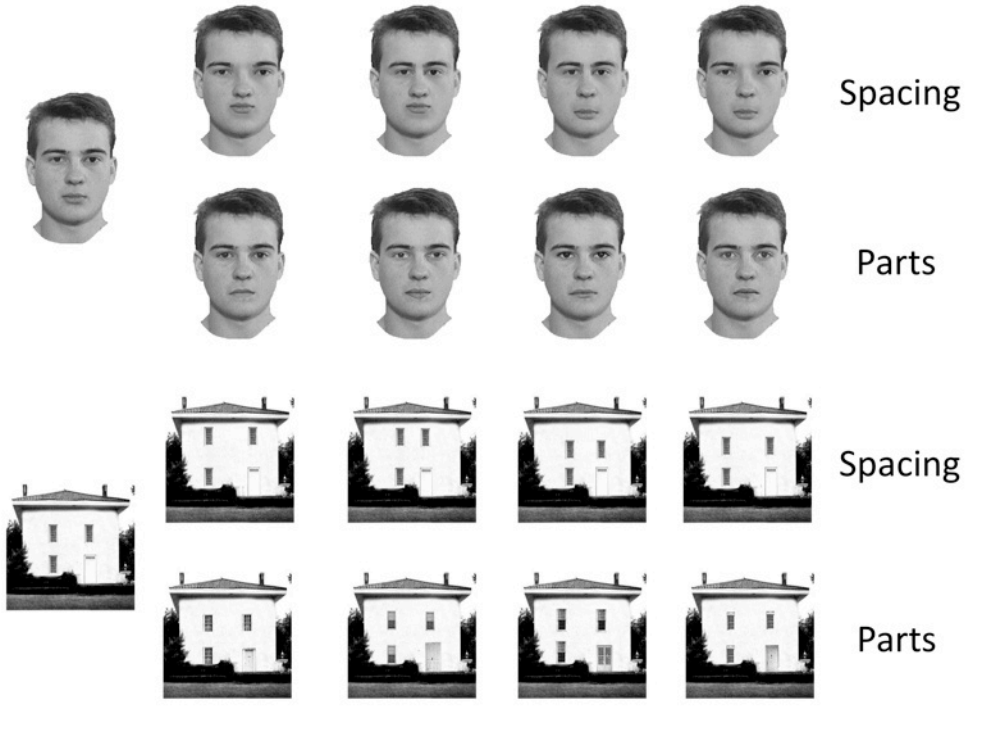

Figure 7. Examples of the face and house stimuli used in Pitcher et al., (2007). Faces or houses were manipulated in one of two different ways. For the part set, the shapes of the parts (eyes and mouth in faces, windows and doors in houses) were manipulated to generate four different stimuli that differed in parts, but shared the same configuration. For the configuration set, the spacing between these parts was manipulated to generate four stimuli that shared the same parts, but differed in configuration (these stimuli were originally used in Yovel and Kanwisher, 2004).

In the first experiment subjects performed a delayed match to sample same / different discrimination task. TMS was delivered at a frequency of 10Hz for 500 ms concurrently with the presentation of the second stimulus. This robust TMS protocol was used to establish whether the two sets of face stimuli were susceptible to disruption when TMS was delivered over the left and right OFA. The results demonstrated that only the face part stimuli were impaired and only when TMS was delivered over the right OFA. There were no impairments on the face spacing stimuli or the parts and the spacing house stimuli. There were also no significant impairments at the left OFA although there was a trend towards a face part impairment. This lack of a significant face effect at the left OFA is consistent with evidence from other methodologies which demonstrates that faces are preferentially processed in the right hemisphere (Young et al. 1985; Landis et al, 1986; Bentin et al. 1996; Yovel et al. 2003;). It is also worth noting that the left OFA is typically further from the surface than the right OFA. The induced face part impairment at the right OFA fits nicely with fMRI evidence that the OFA processes face parts (Liu et al. 2009) and the sensitivity of the M100 to face parts (Liu et al. 2002). The lack of impairment for the face spacing is seemingly inconsistent with a recent study which has demonstrated that the OFA codes information about the spatial relations of face parts (Rhodes et al. 2009). It is possible that the spacing information coded in the OFA is not behaviorally relevant to face discrimination, or alternatively the spacing task in our TMS study may have been insensitive to TMS disruption at the rOFA. Future studies will be needed to resolve this issue.

Pitcher et al. (2007) next tested when the OFA is active in the face processing stream by delivering TMS at different points after stimulus onset while subjects again

performed the face part task. Double pulse TMS separated by 40ms was delivered over the right OFA and vertex (as a control TMS site) in six distinct time windows after stimulus onset: 20 to 60ms, 60 to 100ms, 100 to 140ms, 130 to 170ms, 170 to 210ms and 210 to 250ms. These time windows were selected so that TMS pulses coincided with the M100 (Liu et al. 2002) and the N170 / M170 (Bentin et al. 1996; Liu et al. 2002) components reported in electrophysiological face processing studies.

The results showed a temporally discrete impairment window from 60 to 100ms; there were no impairments in any of the other time windows (see figure 8). Thus the TMS data provide convincing evidence that the OFA processes face parts and does so in an early and temporally discrete time period.

Figure 8. Results of the TMS timing experiment taken from Pitcher et al. (2007). Double pulse TMS was delivered over right OFA and vertex at six different time windows after stimulus onset while subjects made sequential delayed match-to-sample judgments about the face part stimuli shown in figure 7. The results show that TMS induced a disruption only when delivered 60 to 100ms after stimulus onset. This result suggests that the right OFA represents face parts early in the face processing stream.

TMS studies of facial expression processing

Cognitive and cortical models of face processing propose that categorisation of facial expressions relies on different computations than categorisation of facial identity (Bruce and Young, 1986; Haxby et al. 2000; Adolphs, 2002; Calder and Young, 2005; Calder, this volume; Kanwisher and Barton, this volume), and two studies have used TMS to examine how expressions are computed and cortically processed in the human brain. Pourtois et al. (2004) delivered single pulse TMS over the right somatosensory cortex while subjects performed a matching task involving happy or fearful facial expressions. They targeted right somatosensory cortex because neuropsychological and neuroimaging evidence suggests that it performs a role in facial expression discrimination (Adolphs et al. 2000; Winston et al, 2003). These findings fit with theories of embodied cognition, which suggest that the right somatosensory cortex is a component in a sensorimotor cortical network that internally simulates an observed expression and that this simulation contributes to identifying the expressions of others (Goldman and Sripada, 2005; Niedenthal, 2007).

TMS increased the time it took for subjects to match fearful but not happy expressions. It is not clear why the perception of fearful faces was impaired while the happy faces were unaffected but some evidence suggests that recognition of negative expressions is more dependent on the right hemisphere than positive expressions (Adolphs et al. 1996; Vuilleumier and Pourtois, 2007). It is also worth noting that Pourtois et al. (2004) also reported that TMS to right STS disrupts the perception of gaze but not expression. This finding is consistent with other evidence that STS is important for gaze perception (Haxby et al. 2000; Calder et al. 2007; Adolphs and Birmingham, this volume; Pelphrey and Vander Wyk, this volume), and more importantly it indicates that TMS to STS can disrupt face processing.

Pitcher et al. (2008) examined how facial expressions are represented across visual and non-visual cortical areas by delivering TMS over the right occipital face area and the right somatosensory cortex. In the first experiment subjects performed a delayed match-to-sample discrimination task in which two stimulus faces displayed the same identity across different expressions (identity task) or two stimulus faces displayed the same expression across different identities (expression task). The expression task and the identity task were behaviourally matched for performance accuracy. TMS was delivered concurrently with the presentation of the probe stimulus (as in Pitcher et al. 2009) at a frequency of 10 Hz for 500 ms. The results demonstrated that TMS impaired the expression task but not the identity task when delivered over the right OFA and the right somatosensory cortex.

The expression task impairments at right somatosensory cortex partially replicated the results of Pourtois et al. (2004), although TMS in the Pitcher study did not selectively impair any specific expression discriminations. This is possibly due to the inclusion of a broader range of expressions in this study (happy, sad, fear, surprise, disgust, anger) that reduced the statistical power in the subsequent analysis and future testing will be required to further clarify this point (Hussey and Safford, 2009). While there is no reason to suppose that the right somatosensory cortex should contribute to identity computations, the lack of identity impairment at right OFA in this study is perhaps surprising. Cortical models of face processing (Haxby et al. 2000; Calder and Young, 2005), fMRI studies (Hoffman and Haxby, 2000; Yovel and Kanwisher, 2005) and patient data (Rossion et al. 2003; Bouvier and Engel, 2006) suggest that the OFA is involved in identity computations. However, as discussed above, studies, including one involving TMS (Pitcher et al. 2007), indicate that the OFA represents face part information (Liu et al. 2009). In the identity task, same pairs

always differed in expression and hence discrimination based on face parts may not have been an effective strategy. This may have forced reliance on aspects of the face such as spacing between parts or surface reflectance that may be represented in other brain regions than right OFA.

In a follow-up TMS timing experiment Pitcher et al. (2008) used double pulse TMS separated by 40ms delivered at different time points to examine when the right OFA and the right somatosensory cortex contribute to facial expression discrimination. TMS was delivered in seven time windows while subjects performed the facial expression discrimination task. At right OFA TMS delivered 60 and 100 ms after stimulus onset impaired expression discrimination (see figure 9). This replicates the TMS timing impairment on the face part task reported in the earlier study (Pitcher et al. 2007) and again demonstrates that the OFA makes an early and temporally discrete face processing contribution.

TMS delivered over right somatosensory cortex induced impairments in two partially overlapping time windows at 100 and 140 ms and again at 130 and 170 ms. This result suggests that in comparison with the visual analysis at right OFA the expression processing at right somatosensory cortex may be a relatively sustained process. The timing of this effect demonstrates that the contribution from non-visual cortical areas to expression discrimination co-occur with visually mediated face computations such as those producing the face-selective N170 component (Bentin et al. 1996). This timing effect is also consistent with studies that have reported that cortical areas outside the visual system exhibit a response earlier than the N170 in visual tasks involving facial expressions (Eimer and Holmes, 2002) and emotionally evocative images (Kawasaki et al. 2001).

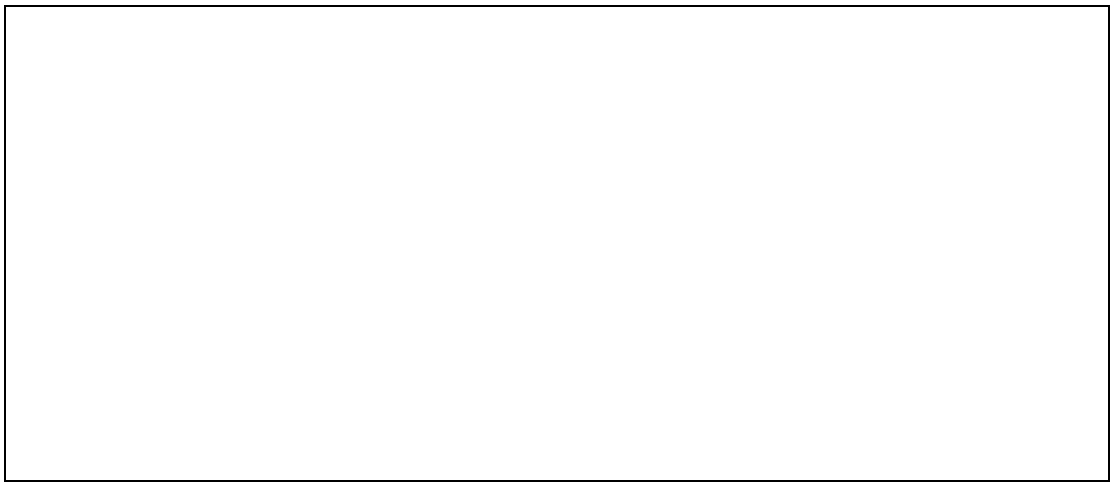

Figure 9. The results of the double pulse TMS timing experiments from Pitcher et al., (2008). TMS impaired expression discrimination at 60 and 100 ms when delivered over right OFA. By comparison the impairment at right somatosensory cortex was later and longer at 100 and 140ms and again at 130 and 170ms.

Future possibilities

Given the importance of face processing research, there are surprisingly few TMS face studies. We believe that the small number of studies described in this chapter demonstrate that TMS can be employed to examine both how and when faces are cortically represented in the undamaged human brain. Briefly disrupting these areas with TMS will allow experimenters to ask new types of questions about the cortical face processing network. For example cortical models propose that both feed-forward and feed-back mechanisms connect the face processing areas (Haxby et al. 2000; Fairhill and Ishai, 2007). Evidence for feedback processes and the timing of these processes could be demonstrated by showing early and later impairments in a study that delivered TMS over a stimulated region at different points from stimulus onset (Pitcher et al. 2007; 2008).

Perhaps one of the most exciting applications of the TMS research reported here is the potential to combine transient disruption of the OFA with neuroimaging

techniques such as fMRI or EEG. As was noted above, the OFA is believed to be the first stage of a face processing network and is thought to operate in combination with other face-selective areas, principally the FFA and STS. To date the FFA remains outside the range of TMS disruption and is largely studied using fMRI in humans. Disrupting the OFA via TMS and then measuring any subsequent downstream effects would offer a method of testing both the functional operation and the cortical connectivity in the face network. This could be achieved is by targeting TMS at the right OFA inside the fMRI scanner. This has been successfully achieved in both the dorsal premotor cortex (Bestmann et al. 2004) and the frontal eye fields (Ruff et al. 2006). However such studies are technologically challenging and require extensive resources. It may also be possible to disrupt the OFA using offline TMS techniques such as 1Hz TMS or using a theta stimulation protocol, the physiological effects of which can last up to an hour after stimulation (Huang et al. 2005) and the behavioural effects of which have been shown to outlast stimulation (Vallesi et al. 2007). Participants could be stimulated and quickly placed in the MRI scanner to search for any downstream effects. This technique has been successfully performed on the motor cortex (O'Shea et al. 2007).

TMS has also been successfully combined with EEG (Taylor et al. 2006; Fuggetta et al. 2009). The N170 (Eimer, this volume) is a key face-selective EEG component (Bentin et al. 1996) that is believed to result from neural activity in the FFA (Horovitz et al. 2004) or possibly the STS (Henson et al. 2003) but not from the OFA. TMS targeted at the OFA could potentially delay or reduce the N170 and thus demonstrate functional connectivity within the face network.

Summary and Conclusions

At present only a small number of studies have used TMS to examine face processing. We therefore began the chapter with a brief description of how TMS works and how it can be applied experimentally. We then described the existing studies that have used TMS to disrupt different cortical areas implicated in the recognition and discrimination of faces. These included the OFA, the face area in the right somatosensory cortex, and STS. Some of these studies have exploited the temporal precision of TMS to determine the temporal profiles of cortical areas in the face-processing network. We concluded by describing the exciting future possibilities that the continued application of TMS can provide for face processing research.

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