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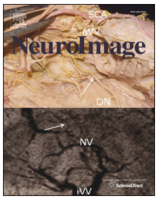

When gaze opens the channel for communication: Integrative role of IFG and MPFC

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ABSTRACT

Recent advances in the field of cognitive neuroscience have revealed that direct gaze modulates activity in cortical and subcortical key regions of the 'social brain network', including the inferior frontal gyrus (IFG) and the anterior rostral medial prefrontal cortex (arMPFC). However, very little is known about how direct gaze is processed during live interaction with a real partner. Here, for the first time we used an experimental setup allowing the participant inside an MRI scanner to interact face-to-face with a partner located in the scanner room. Depending on condition, the participant and the partner were instructed either to look at each other in the eyes or to direct their gaze away from the other. As control conditions, participants gazed at their own eyes, reflected in a mirror, or gazed at a picture of the partner's eyes. Results revealed that direct gaze by the partner was associated with activity in areas involved in production and comprehension of language and action, including the IFG, the premotor cortex (PM), and the supplementary motor area (SMA). Activations in these areas were observed regardless of the participant's gaze behavior. In contrast, increased activity in arMPFC, an area involved in inference of other mental states during social interaction and communication, was only observed when the participant reciprocated the partner's direct gaze so as to establish mutual gaze. Psychophysiological interaction (PPI) analysis revealed effective connectivity between the IFG and the arMPFC during mutual gaze. This suggests that, within a larger network concerned with the processing of social gaze, mutual gaze with a real partner is established by an increased coupling between areas involved in the detection of communicative intentions, language, and social interaction.

Introduction

Successful communication between two people depends first on the recognition of the intention to communicate. There are many ways by which this intention can be conveyed. A subtle yet effective way to initiate a conversation without actually speaking is to look directly at the other person (Cary, 1978). From infancy, humans are extremely sensitive to direct gaze and appreciate its significance in the initiation of communicative acts (Senju and Johnson, 2009; Senju et al., 2008). For example, it has been demonstrated that 6-month-old infants only follow the adult's gaze towards an object—a potential communicative referential signal—when such an act is preceded by ostensive cues like infant-directed speech or direct gaze (Senju et al., 2008).

In adults, neuroimaging evidence suggests that direct gaze modulates activity in several cortical and subcortical key regions of the 'social brain network' (Frith, 2007), including the superior temporal sulcus (STS), the anterior rostral medial prefrontal cortex (arMPFC), and the amygdala (Senju and Johnson, 2009). Yet, the precise neural mechanisms underlying the processing of direct gaze during *real interaction*, remain unexplored to date. Indeed, until recently, social cognition has been mainly studied from a detached, observational perspective in tasks involving inert social stimuli (Becchio et al., 2010; Hari and Kujala, 2009; Schilbach et al., 2013). In line with this tradition, early fMRI studies seeking to ascertain the neural basis of the effect of direct gaze adopted simplified paradigms in which static displays of faces and eyes or brief video clips were presented to passive observers (for

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a review, see Frischen et al., 2007). In recent years, more interactive paradigms have been developed by combining eye-tracking and virtual reality technologies (e.g., Schilbach et al., 2010; Wilms et al., 2010) and using live video feeds (e.g., Redcay et al., 2010; Saito et al., 2010; for a review, see Babiloni and Astolfi, 2014; Pfeiffer et al., 2013). These paradigms allow participants not only to react to the other's gaze, but also to observe an agent moving its eyes in a gaze contingent fashion—that is, in response to the participant's own gaze behavior. Despite their usefulness in characterizing gaze-contingent responses, however, they do not allow true face-to-face interaction and may thus lack 'the potential for real social interaction' (Skarratt et al., 2012).

In the context of a 'live' encounter, the other's gaze is not something that can be subsumed into a strictly visual representation of eye direction: it has an impact on the observer's own system that sets the observer up for further response (Gallagher, 2014). Accordingly, perception of the other's gaze presents not just a perceptual pattern. It involves complex interactive behavioral and neural response patterns and affords a 'unique type of interaction' (Gangopadhyay and Schilbach, 2012), which may remain beyond the reach of paradigms manipulating gaze contingency within virtual and video setups.

To capture this specific aspect of gaze-based interaction arising out of active engagement with a 'live' person, here we used an experimental setup allowing the participant inside an MRI scanner to *interact face-to-face with a real partner*. The partner—a co-experimenter—stood in the scanner room, close to the machine, behind the participant, within his/her social space (Hall, 1966). His face was visible to the participant through a 45° oriented mirror located inside the scanner in front of participant's eyes. Depending on condition, the participant and the co-experimenter were instructed to look at each other in the eyes (so to reciprocate the partner's direct gaze and establish mutual gaze) or to turn their gaze away (so to avoid the partner's direct gaze). As controls, participants had to gaze at a picture of the partner's eyes or at their own eyes as reflected in a mirror. In both these situations, participants saw a face with a direct gaze without encountering any true interaction with another person.

Consistent with the proposal that being looked at by live person elicits a response from the observer (Gallagher, 2014), we expected that, in comparison to both averted gaze and control conditions, direct gaze by the co-experimenter would activate regions critical for preparing a communicative response. These areas include the inferior frontal gyrus (IFG), the premotor cortex (PM), the left anterior insula (AI), and the supplementary motor area (SMA; Alario et al., 2006; Brendel et al., 2010; Riecker et al., 2005). The IFG, in particular, has been consistently implicated in both comprehension and production of language and action (Fadiga et al., 2009; Fazio et al., 2009). Its role in social gaze, however, is less clear as only some of the studies examining direct gaze have shown increased activity in this region (Kuzmanovic et al., 2009; Pelphrey et al., 2004; Pierno et al., 2006, 2008; Saito et al., 2010; Tanabe et al., 2012). A recent proposal (Pfeiffer et al., 2013) relates IFG to the establishment of a communicative intent and suggests that IFG activity may open the 'channel for social interaction' (Cary, 1978), providing some kind of 'readiness potential' for initiating a gaze-based interaction (see also, Saito et al., 2010).

With this in mind, we hypothesized a functional association between IFG and mentalizing areas implicated in social interaction and communication (Amodio and Frith, 2006; Frith and Frith, 2006, 2010) during mutual gaze. More specifically, we expected that during mutual gaze, recruitment of the IFG would increase in coupling with that of the arMPFC, a key region of the 'social brain network', consistently activated across a wide range of mentalizing tasks (Amodio and Frith, 2006) and proposed to play a prominent role in modulating the processing of visual information in social contexts (Schilbach et al., 2013). To test this hypothesis, in addition to the conventional univariate analysis, we conducted psychophysiological interaction (PPI, Friston et al., 1997) analysis using IFG as seed region.

Materials and methods

Participants

Twenty one right-handed volunteers (9 women and 12 men; average age: 23) were recruited at the University of Minnesota. None of them had a history of neurological, major medical, or psychiatric disorders. Before the study participants gave their written informed consent. Specific information about the study was provided after the experimental session. Experimental procedures and scanning protocols were approved by the Institutional Review Board and conducted in accordance with the principles of the revised Helsinki Declaration (World Medical Association General Assembly, 2008). None of the individuals taking part in the experiment experienced any discomfort during fMRI acquisition.

Procedure and design

During the entire experiment, the participant (*P*) laid in supine position in the bore of the MRI scanner, while an experimenter (*E*), who was the same person for all the experimental sessions (male, aged 54), sat in the scanning room. The distance between *P*'s head and *E*'s head was about 150 cm and was constant throughout the study. A large mirror was positioned in the back of the scanner's bore at a distance of approximately 50 cm from the scanner. P viewed the large mirror via a tilted mirror attached to the top of the head coil at a distance of 15 cm from *P*'s eyes. When the large mirror was positioned obliquely (at 45°), *P* could see *E*'s gaze reflected in the head coil mirror, with a clear view of *E*'s gaze direction. A white carton board, held up by *E*, ensured that only the upper part of *E*'s face (from the nasal bone to the forehead) was visible to *P*. When the large mirror was positioned orthogonally to the main axis of the scanner's bore, *P* could see his/her own gaze (from the nasal bone to the forehead) reflected in the head coil mirror. The distance between the eyes of *P* and those of *E* was the same as twice the distance between the eyes of *P* and the large mirror. This ensured that for the participant the image of his/her own eyes had the same size as the image of *E*'s eyes.

The experiment consisted of five different conditions, each one described by the gaze behavior of *P* and *E*. In the (*Look, Look*) condition, *P* and *E* were instructed to establish mutual gaze by looking at each other directly in the eyes. In the (*Look, Not Look*) condition, *P* looked at *E*, whose gaze was oriented 30° left away from P. In the (*Not Look, Look*) condition the opposite took place: at the beginning of the trial, *P* was instructed to direct his/her gaze 30° away from *E* and look at the magnet bore, while *E* looked straight at P. Despite the gaze behavior of *E* being the same as in the (*Look, Look*) condition, *P*'s view was therefore completely different. Based on instructions, *P* knew that *E* was looking at him/her, but he/she could not discriminate E's gaze direction. In the (*Look Picture*) condition, *P* was asked to look at a still picture displaying *E*'s face and eyes looking straight ahead. The pictured pasted on a white carton board, was held up by *E* at the eye level, thus covering his real face. Finally, in the (*Look Yourself*) condition, the participant was asked to look at his/her own eyes reflected in the mirror. In all five conditions, the gaze direction was constantly monitored by another co-experimenter via a camera to guarantee the correct execution of the task. Each participant was randomly assigned to one of two possible experimental sessions. In the first session, each condition, lasting 30 s, was presented four times. In the second session, each condition was presented six times and lasted 15 s. In both sessions, a 20 second break, in which participants were asked to keep their eyes closed, was included after each condition. Within each session, trials were presented in pseudorandom order (maximum of two trials of the same condition in a row).

MRI data acquisition

The experiment was carried out on a whole body 3 Tesla scanner (Magnetom Trio, Siemens Medical Center, Erlangen, Germany) equipped with a standard Siemens 32-channel coil. Functional images were