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Looking but not seeing: Increased eye fixations in behavioural-variant frontotemporal dementia

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ABSTRACT

Face processing plays a central role in human communication, with the eye region a particularly important cue for discriminating emotions. Indeed, reduced attention to the eyes has been argued to underlie social deficits in a number of clinical populations. Despite well-established impairments in facial affect recognition in behavioural-variant frontotemporal dementia, whether these patients also have perturbed facial scanning is yet to be investigated. The current study employed eye tracking to record visual scanning of faces in 20 behavioural-variant frontotemporal dementia patients and 21 controls. Remarkably, behavioural-variant frontotemporal dementia patients displayed *more* fixations to the eyes of emotional faces, compared to controls. Neural regions associated with fixations to the eyes included the left inferior frontal gyrus, right cerebellum and middle temporal gyrus. Our study is the first to show such compensatory functions in behavioural-variant frontotemporal dementia and suggest a feedback-style network, including anterior and posterior brain regions, is involved in early face processing.

1. Introduction

Face processing is integral to human social communication, relying on the ability to perceive, process, decode and contextualise a myriad of fluctuating cues informing identity, emotional state, gaze direction, age, gender and more. Despite the complexity of this process, humans are uniquely sensitive to faces, with automatic processing often happening with little to no conscious effort (Palermo & Rhodes, 2007). Given this efficiency, it is unsurprising that face processing is proposed to rely on a complex set of neural and cognitive systems (Bruce & Young, 1986; Haxby, Hoffman, & Gobbini, 2000). Extensive evidence exists for a core system of specialised

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neural regions that enable early face processing, which tend to involve the posterior, occipitotemporal brain regions (Haxby et al., 2000). Meanwhile, the neural structures underlying emotion processing such as the frontal lobe and amygdala have often been considered an extended system, involved in further contextualising and interpreting of facial information (Haxby et al., 2000).

More recently, a role for frontal brain regions in early face processing has been recognised (Adolphs, 2001, 2002). Yet the nature of the interactions between anterior and posterior brain regions is not well understood. Indeed, given the highly salient cues about emotional state provided by the eyes and mouth, it stands to reason that regions underlying emotion processing would be fundamentally intertwined with face processing. The eyes provide somewhat more elaborate cues than the mouth, where eyebrow position, whites of the eyes, pupil dilation and gaze direction can all signal different emotions (Ekman, 1992; Whalen et al., 2004). Moreover, use of eye information is crucial in discriminating between negative expressions, a skill that is vital for facilitating social interactions as well as threat-detection (e.g., discriminating fear from anger) (Smith, Cottrell, Gosselin, & Schyns, 2005).

Eye tracking studies have provided unique insight into the neural and behavioural mechanisms involved in face processing. Such studies have demonstrated that healthy adults engage in a systematic visual scanning pattern when viewing a face, with individuals typically showing a triangular viewing pattern focused on the eyes and mouth (Adolphs et al., 2005; Janik, Wellens, Goldberg & Dell'Osso, 1978; Spezio, Adolphs, Hurley, & Piven, 2007). Of relevance here, abnormal attention to facial stimuli and reduced visual gaze to the eyes has been demonstrated across a range of clinical disorders marked by social dysfunction, including autism (Pelphrey et al., 2002; Spezio et al., 2007), schizophrenia (Manor et al., 1999; Sasson et al., 2007), and populations with focal anterior brain lesions (Adolphs et al., 2005; Wolf, Philippi, Motzkin, Baskaya, & Koenigs, 2014). This reduced visual attention to the eyes when viewing emotional faces is argued to play a key role in impaired recognition of negative emotions in these clinical syndromes (Adolphs et al., 2005; Spezio et al., 2007; Wolf et al., 2014).

Behavioural-variant frontotemporal dementia (bvFTD) is a younger-onset neurodegenerative brain disorder characterised by atrophy in the frontal lobe, with the ventromedial prefrontal cortex and insula affected early in the disease (Rascovsky et al., 2011; Seeley et al., 2008). Clinically, individuals with bvFTD show pervasive changes in personality and behaviour including reduced empathy, increased apathy and disinhibition (Hutchings, Hodges, Piguet, & Kumfor, 2015; Lough et al., 2006; Piguet, Hornberger, Mioshi, & Hodges, 2011; Rascovsky et al., 2011). Deficits in emotion recognition have been well-established in bvFTD across different task modalities (for review see Kumfor & Piguet, 2012; Shany-Ur & Rankin, 2011). Performance tends to be worse for negative emotions and is associated with degradation of the bilateral amygdala, orbitofrontal cortex, inferior frontal gyrus and left insula (Couto et al., 2013; Kamminga et al., 2014; Kumfor, Irish, Hodges, & Piguet, 2013; Omar, Rohrer, Hailstone, & Warren, 2011; Van den Stock et al., 2015; Virani, Jesso, Kertesz, Mitchell, & Finger, 2013), regions considered a part of the extended face processing system.

Despite the vast majority of studies relying on facial stimuli to investigate social cognition in bvFTD, the potential mechanisms underlying this impairment have been remarkably understudied (Hutchings, Palermo, Piguet, & Kumfor, 2017). Two studies examined expression labelling of distorted faces in bvFTD patients, showing improved performance when viewing exaggerated facial expressions (Kumfor et al., 2011), and a decline in performance when key facial features were removed (Oliver, Virani, Finger, & Mitchell, 2014). Such evidence suggests that bvFTD patients may not utilise facial cues appropriately when looking at natural, unmanipulated faces. Meanwhile, functional MRI studies have shown reduced fusiform cortex activation in bvFTD patients, compared to controls, when viewing emotional faces (De Winter et al., 2016; Virani et al., 2013). Thus, existing evidence suggests that abnormal face processing may contribute to reduced emotion recognition in bvFTD.

The current study aimed to identify the neurobiological mechanisms underlying facial emotion recognition in bvFTD by using eye-tracking and structural MRI to examine early visual processing of faces in this group. It was hypothesized that (i) bvFTD patients would show fewer fixations to the eyes than controls, as has been observed in other clinical populations. We further hypothesised that (ii) patterns of facial scanning would be associated with facial affect recognition, and (iii) would correspond with integrity of the ventromedial prefrontal cortex and the fusiform cortex.

2. Materials and methods

2.1. *Participants*

Twenty bvFTD and 21 healthy control participants were recruited through Frontier, the frontotemporal dementia research clinic located in Sydney, Australia. In all patients, diagnosis was established by consensus following a clinical assessment with a behavioural neurologist, comprehensive neuropsychological assessment, structural brain imaging and met current consensus criteria for bvFTD (Rascovsky et al., 2011). In brief, bvFTD patients presented with behavioural and/or personality changes as well as cognitive deficits, and showed atrophy of the prefrontal cortices. Individuals with a diagnosis of possible bvFTD or with atypical presentation were excluded from the study.[1]

Individuals with a significant history of psychiatric or neurological conditions, substance abuse or medication with central nervous system effects were excluded from the study. Healthy controls scored above 88/100 on the Addenbrooke's Cognitive Examination-III (ACE-III) (Hsieh, Schubert, Hoon, Mioshi, & Hodges, 2013).

All participants or their Person Responsible provided informed consent in accordance with the Declaration of Helsinki. The South Eastern Sydney Local Health District and the University of New South Wales ethics committees approved the study. All participants volunteered their time and travel costs were reimbursed.

[1] Three bvFTD participants had a confirmed *C9orf72* expansion.