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Structural connectivity in a single case of progressive prosopagnosia: The role of the right inferior longitudinal fasciculus

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ABSTRACT

Progressive prosopagnosia (PP) is a clinical syndrome characterized by a progressive and selective inability to recognize and identify faces of familiar people. Here we report a patient (G.S.) with PP, mainly related to a prominent deficit in recognition of familiar faces, without a semantic (cross-modal) impairment. An in-depth evaluation showed that his deficit extended to other classes of objects, both living and non-living. A follow-up neuropsychological assessment did not reveal substantial changes after about 1 year. Structural MRI showed predominant right temporal lobe atrophy.

Diffusion tensor imaging was performed to elucidate structural connectivity of the inferior longitudinal fasciculus (ILF) and the inferior fronto-occipital fasciculus (IFOF), the two major tracts that project through the core fusiform region to the anterior temporal and frontal cortices, respectively. Right ILF was markedly reduced in G.S., while left ILF and IFOFs were apparently preserved. These data are in favour of a crucial role of the neural circuit subserved by right ILF in the pathogenesis of PP.

1. Introduction

The study of patients with a selective impairment in recognizing faces (acquired prosopagnosia) following right or bilateral temporo-occipital lesions has provided relevant information about the neural mechanisms involved in face processing (Bodamer, 1947; Barton et al., 2002; Bruce and Young, 1986; Damasio et al., 1982; De Renzi, 1986; Farah et al., 1995a,b; Rossion et al., 2003; Wada and Yamamoto, 2001). Such lesion studies, combined with functional imaging studies in normal individuals, have demonstrated that regions of the posterior fusiform gyrus, the inferior lateral occipital cortex and the posterior superior temporal sulcus (STS) are involved in face processing (e.g., Allison et al., 1994a, 1999; Barton, 2008; Kanwisher et al., 1997; Grill-Spector et al., 2004;

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Pitcher et al., 2009; Rossion et al., 2003; Sergent et al., 1992). Within these regions, that are part of the so-called ‘core system’ for face processing (Haxby et al., 2000), the fusiform gyrus seems to be especially important for processing facial identity. More recently, an important role in face recognition has also been ascribed to the anterior inferior temporal lobe (Allison et al., 1994b, 1999; Rajimehr et al., 2009; Tsao et al., 2008), particularly in individuals with developmental prosopagnosia (DP), who may show reduced volume of the anterior part of fusiform gyri (Behrmann et al., 2007; Garrido et al., 2009).

In a few studies, prosopagnosia has been described as the main manifestation of a neurodegenerative disorder (Barbarotto et al., 1995; De Renzi, 1986; Evans et al., 1995; Gentileschi et al., 1999, 2001; Gainotti, 2003; Tyrrell et al., 1990). Early patients with progressive prosopagnosia (PP) also showed visual agnosia, basic visuoperceptual deficits and impairments in other cognitive domains, associated with posterior cortical atrophy (De Renzi, 1986; Tyrrell et al., 1990). In subsequent years several patients with quite selective progressive disorders of face recognition have been described. In one patient with selective PP, Evans et al. (1995) interpreted their patient's picture as due to a visual, modality-selective, inability to access person-based semantic knowledge; however, the patient eventually developed (over 9 months) a multi-modal loss of person-based knowledge. Evans et al.'s patient showed prominent right hemisphere temporal lobe atrophy; analogous lesions were reported in further patients with PP who were affected by analogous multi-modal deficits of person (and face) recognition, not restricted to the visual modality (Barbarotto et al., 1995; Gainotti, 2003; Gentileschi et al., 1999, 2001).

A progressive defect in processing face configuration associated with mild visual agnosia, but with relative preservation of other cognitive domains and intact basic face perception skills, was described by Joubert et al. (2003), in a patient who showed atrophy of the right fusiform gyrus and parahippocampal cortex on quantitative volumetric measures of temporal lobes (Joubert et al., 2004). On the basis of this observation, the authors proposed that the critical region in the genesis of PP may lie more posteriorly than what was previously suggested, and involve the right fusiform gyrus selectively (Joubert et al., 2004).

This rare form of degenerative process may reflect a right hemisphere variant of semantic dementia. Actually, current clinical diagnostic criteria (Neary et al., 1998) consider PP with insidious onset and gradual progression, often associated to associative agnosia, as the hallmark of the prosopagnosic variant of frontotemporal dementia (FTD) (Neary et al., 1998), more recently defined right-temporal variant (rtFTD; Chan et al., 2009; Josephs et al., 2009; Miller et al., 1993).

In synthesis, several patients have been described with PP in the context of a degenerative disorder, and all of them showed atrophy in the right temporal lobe, but no specific study has investigated white matter tracts (WMT) in patients with selective PP (but see Migliaccio et al., 2012, for a DT study on posterior cortical atrophy). In neurodegenerative disorders neuropsychological deficits are usually considered as resulting from cortical degeneration. However, in recent years the cortical localization approach for cognitive functions is evolving towards network-based hypotheses, according to which cognitive disorders emerge from the interruption of the information flow within large-scale networks linking different cortical regions (Bartolomeo, 2011; Catani and ffytche, 2005). According to this approach, not only cortical lesions but also damage to WMT between cortical areas can induce network dysfunction and, hence, cognitive disorders (Mesulam, 2009).

Over the last few years, tractography has allowed hodological study of the brain and a re-interpretation of several neurobehavioral syndromes. In DP patients, Thomas et al. (2009) have found a bilateral reduction in structural integrity of the inferior longitudinal fasciculus (ILF) and of the inferior fronto-occipital fasciculus (IFOF), two major tracts that project through the core fusiform region to the anterior temporal and frontal cortices, respectively (Benson et al., 1974). However, Thomas et al. (2009) demonstrated that only the reduction in tract integrity of the right ILF (rILF), and to a lesser extent, of the right IFOF (rIFOF) correlated with errors in face recognition tasks, consistent with the notion that the right hemisphere is more prominent in face processing (for a recent review, see Gainotti and Marra, 2011). The ILF is a ventral associative bundle with long and short fibres connecting the occipital and temporal lobes namely lingual and fusiform gyrus (Catani et al., 2003). Damage to such a tract might disconnect visual processing in the occipital lobe from memory processing in the temporal lobe (Habib, 1986; Kawahata and Nagata, 1989; Meadows, 1974; Takahashi et al., 1995), thus giving rise to a form of associative prosopagnosia (Fox et al., 2008).

On the basis of evidence collected in DP, here we present a diffusion tensor imaging (DTI) study performed on a patient with relatively selective PP to the aim of investigating structural integrity of ILF and IFOF. In previous single case studies of patients with neurodegenerative disease, DTI was used for the purpose of following up progressive deterioration of WMT (Duning et al., 2009). DTI has also been used in a single patient with posterior cortical atrophy to demonstrate WMT damage (Migliaccio et al., 2011). Here, our specific working hypothesis was that connectivity between occipital and temporal lobes in the right hemisphere is disrupted in comparison with the left hemisphere.

2. Methods

2.1. *Case report*

G.S. was a 65-year-old, right-handed man with 7 years of formal education; he was a retired factory worker. He came to our observation in November 2010, complaining of progressive difficulties in recognizing familiar faces over the past 2 years. For instance, he knew and could immediately recall names of the examiners, but over a period of several weeks he never recognized them by their faces.

At the time of testing, G.S. was alert, cooperative and well oriented; his language was fluent and flawless. The patient was aware of his problems and described them in detail, but his relatives referred some early personality changes, with instances of social inadequacy (e.g.,: excessive or inappropriate jokes; childish behaviour); the total score on Frontal Behavioural Inventory (FBI; Alberici et al., 2007), administered to patient's son, was 12/72, i.e., below the cut-off point (28.6)