CORTEX 56 (2014) 111–120

Available online at www.sciencedirect.com

ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex

Special issue: Research report

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

Dario Grossi [a], *Andrea Soricelli* [b], *Marta Ponari* [a], *Elena Salvatore* [c], *Mario Quarantelli* [d], *Anna Prinster* [b,d] *and Luigi Trojano* [a,*]

[a] *Neuropsychology Laboratory, Department of Psychology, Second University of Naples, Caserta, Italy*
[b] *IRCCS Fondazione SDN, Istituto di Ricerca Diagnostica e Nucleare, Naples, Italy*
[c] *Department of Neurological Sciences, School of Biotechnology, Federico II University of Naples, Italy*
[d] *Biostructure and Bioimaging Institute, CNR, Naples, Italy*

ARTICLE INFO

Article history:
Received 1 May 2012
Reviewed 29 August 2012
Revised 11 September 2012
Accepted 16 September 2012
Published online 29 September 2012

Keywords:
Diffusion tensor imaging
Inferior longitudinal fasciculus
Inferior fronto-occipital fasciculus
Progressive prosopagnosia

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;

* *Corresponding author*. Neuropsychology Laboratory, Department of Psychology, Second University of Naples, Via Vivaldi 43, 81100 Caserta, Italy.
E-mail address: luigi.trojano@unina2.it (L. Trojano).
http://dx.doi.org/10.1016/j.cortex.2012.09.010

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)

discriminating frontotemporal lobe degeneration from other dementias.

Neurological examination was normal. MRI showed a predominant right temporal atrophy associated to mild cortical atrophy of remaining supratentorial cortices (Fig. 1). The analysis of biomarkers in cerebrospinal liquor (ELISA test; Innogenetics, Ghent, Belgium) revealed normal levels of phosphorylated tau (p-tau 181: 28.6 pg/mL; normal values: <33) and β-amyloid 1–42 (749.3 pg/mL; normal values: 492–1088).

General neuropsychological assessment did not reveal impairments of verbal and spatial memory, spatial exploration of personal and extrapersonal space, visuoconstructional skills, abstract logical abilities, verbal fluency and executive functioning (Table 1). G.S. then underwent a specific neuropsychological assessment of face processing, visuospatial perception, imagery and semantic knowledge.

2.1.1. *Assessment of face processing*

2.1.1.1. Face matching. On the Benton Facial Recognition Test (Benton et al., 1983), G.S.' performance was in the 'borderline' range after adjusting raw score for age and educational level (Table 2). It is interesting to note that he performed flawlessly on the trials in which camera angle and lighting were held constant, suggesting that his face recognition impairment could not be accounted for in terms of elementary visual deficits. G.S. emphasized that he always tried to rely on details such as ears or eyebrows in order to succeed on this task.

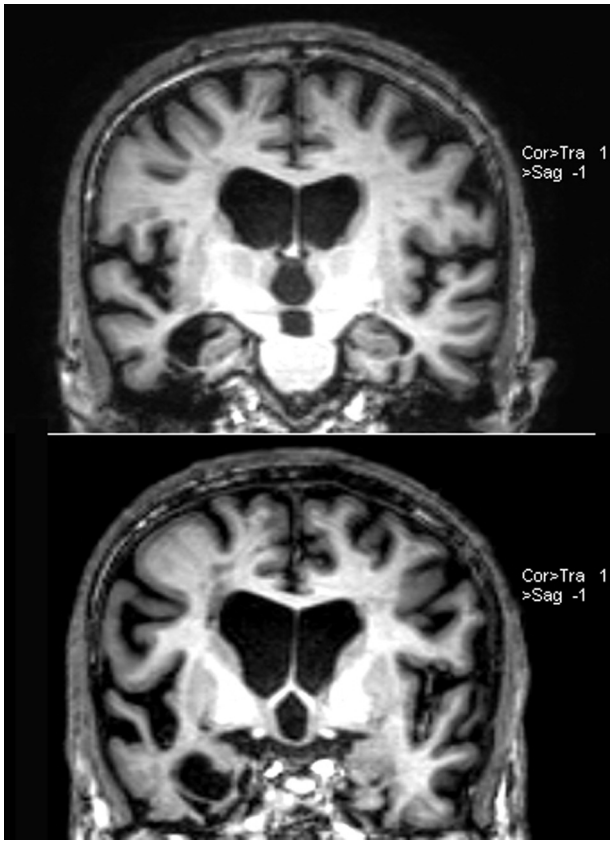

Fig. 1 – Coronal reformats of the 3D-T1w-volume at the level of the midportion of the hippocampus (top) and of the amygdala (bottom), showing on the right side a relative sparing of the hippocampus, with a dilation of the temporal horn of the lateral ventricle, likely due to loss of adjacent white matter, parahippocampal gyrus and amygdala.

Table 1 – Results of the formal neuropsychological assessment.

Test	Nov 2010	Feb 2012	Normal cut-off*
Mini Mental State Examination (MMSE)[a]	28/30	28/30	≤23
FAB[b]	14.40	13.40	≤13.40
Raven coloured progressive matrices (PM)[c]	24	28	≤14.75
Story recall[d]	10.8/16	11.4/16	≤4.50
Corsi Visuospatial span[d]	4	6	≤3.50
Digit span[e]	5	5	≤3.50
Verbal word span[d]	3	4	≤2.75
Copying simple drawings[d]	11.75	12.75	≤7.75
Rey complex figure[f]			
Copy	29.9/36	36/36	<23.76
Immediate recall	9/36	10.50/36	<6.44
Delayed recall	8.2/36	13.25/36	<6.33
Phonemic verbal fluency[c]	26.2	27.2	<17.35
Semantic verbal fluency[d]	15.25	14	≤7

Note. *Normal cut-off values refer to age- and education-adjusted Italian norms; no G.S.' score was below cut-off.
[a] Measso et al., 1993.
[b] Appollonio et al., 2005.
[c] Caltagirone et al., 1995.
[d] Spinnler and Tognoni, 1987.
[e] Orsini et al., 1987.
[f] Caffarra et al., 2002.

2.1.1.2. Famous face recognition, naming and identification. To assess famous face processing, G.S. was administered the *Famous face recognition and naming test* (Rizzo et al., 2002), that evaluates both visual recognition of known people and verbal recognition of their names. As for visual recognition, the test included 50 photographs depicting famous people randomly intermingled with 50 pictures of unknown people. Photographs were presented one at a time, and G.S. was asked: (a) to make a fame judgement, (b) to name the 50 famous people, and

Table 2 – Processing of unfamiliar and familiar faces.

	G.S.' scores	Normal cut-off
Unfamiliar faces		
Benton Facial Recognition Test[a]	40/54	41
Familiar faces		
Famous face recognition and naming test[b]		
Naming	0[c]	≤14.50
Semantic information	0[c]	≤22.17
Semantic information from name	24.75	≤20.68
False recognitions	0	≥14.16
False recognitions from name	0	≥12.92

Note. Normal cut-off values refer to age- and education-adjusted Italian norms.
[a] Benton et al., 1983.
[b] Rizzo et al., 2002.
[c] Denotes a score below age- and education-adjusted cut-off.

(c) to provide some semantic information about the person, in particular, whether the person was alive, if he/she was Italian, and to which professional category the person was associated. G.S. was not able to distinguish famous from unknown faces (Table 2), and could neither name nor identify even celebrities with very distinctive and unique facial features from their photographs (e.g., Michael Gorbaciov). G.S. spontaneously referred to the gender of every single face he was presented with (e.g., "I have never seen her/him" or "I don't know who he/she might be"), showing that his gender perception was preserved. When all visual stimuli were presented, the test assessed recognition of auditorily presented names of the same famous people, intermingled with 50 unknown names. When asked to perform a fame judgement and to provide as much information as he could about the celebrities upon verbal presentation of their names, G.S. performed in the normal range, meaning that his semantic knowledge about famous people was at least relatively preserved.

2.1.2. *Assessment of visuospatial perception*

2.1.2.1. VISUOSPATIAL ABILITIES. On the *Battery for Visuospatial Abilities* (BVA, known in Italy as *TERADIC*; Angelini and Grossi, 1993; Grossi and Trojano, 1999; Grossi et al., 2002; Trojano et al., 2004), exploring perceptual and representational visuospatial abilities, G.S.' scores were well within the normal control range according to published norms on tasks assessing discrimination of line length and orientation, coding of relative position of points within squares, mental rotation, and analysis and recognition of complex abstract figures (Table 3). G.S. was relatively impaired in one subtest assessing discrimination of angle width, and in one 'representational' subtest assessing mental construction of abstract figures.

2.1.2.2. VISUAL OBJECT PROCESSING. On tasks assessing visual object recognition from the Birmingham Objects Recognition Battery (BORB; Riddoch and Humphreys, 1993), G.S. showed selective difficulties (Table 4). He could correctly name only about 25% line drawings (19/76), with no difference between living (10/38) and non-living (9/38) items; during the task, the patient often provided stimulus' superordinate category (e.g., "container" for saltshaker or pot) or a prototypical exemplar of the same category (e.g., "dog" for lion, sheep or kangaroo). G.S. achieved low scores on the Object decision task (subtest 10: to decide whether a line drawing depicts a real item or not) and on the Associative match task (subtest 12: to associate items with strong semantic, but not visual, relationships), implying that his visual knowledge of objects and his knowledge about semantic relationships among objects were impaired. However, he performed within the normal range when he was asked to match items of the same class (Item match task, subtest 11: to associate items with different visual features but referring to the same concept, e.g., two visually different keys), that also share many visual properties (G. Humphreys, personal communication). Thus, it is likely that G.S. relied on his spared visuoperceptual skills in performing the task. In addition, he showed spared object constancy, i.e., the ability to judge that an object remains the same when viewed from different positions (subtest 8, Foreshortened view task).

2.1.3. *Mental imagery*

2.1.3.1. MENTAL CLOCK TASK. When required to imagine 20 pairs of analogue clock faces based on verbally presented times, and to judge which of the two hand settings defines the larger internal angle (Formisano et al., 2002; Grossi et al., 1989; Paivio, 1978; Trojano et al., 2000), G.S. made no errors.

2.1.3.2. DRAWING OF HIS OWN HOUSE. To assess visual memory, he was asked to draw a plan of his own apartment, illustrating its general outline, the spatial relations between the rooms, and their relative dimensions. Compared to the one performed by his son, G.S. drew an accurate plan of the house.

Table 3 – Assessment of visuoperceptual abilities.

	G.S.' scores	Normal cut-off
BVA[a]		
Visuoperceptual tasks		
Line length judgement	16/20	15
Line orientation judgement	6/10	4
Angle with judgement	1/10*	4
Point position identification	11/12	8
Spatial representational tasks		
Mental rotation	10/10	4
Complex figure identification	10/10	6
Hidden figure identification	8/10	5
Mental construction	11/20*	13
BORB[b]		
Foreshortened view (subtest 8)	21/25	16
Object decision (subtest 10)	23/32*	28
Item match (subtest 11)	30/32	26
Associative match (subtest 12)	16/30*	22
Picture naming (subtest 14)	19/76*	64

*Denotes a score below age- and education-adjusted cut-off.
[a] Angelini and Grossi, 1993.
[b] Riddoch and Humphreys, 1993.

Table 4 – Results of DTI in patient G.S. and in a group of normal controls (HC; $n = 7$).

		G.S	HC
Lines	**rILF**	.4[a]	8.00 ± 4.62 (3.0–16.4)
	lILF	4.9	8.44 ± 2.91 (3.3–12.0)
	rIFOF	8.5	6.98 ± 3.52 (3.4–13.9)
	lIFOF	7.3	5.56 ± 2.12 (3.5–9.5)
FA	**rILF**	.902	.931 ± .040 (.880–.978)
	lILF	.875	.918 ± .040 (.872–.981)
	rIFOF	.898	.973 ± .042 (.896–1.017)
	lIFOF	.951	1.007 ± .048 (.920–1.034)
ADC	**rILF**	1.151[b]	.967 ± .042 (.902–1.027)
	lILF	.961	1.024 ± .020 (.998–1.048)
	rIFOF	1.150	1.000 ± .102 (.920–1.203)
	lIFOF	1.013	.988 ± .072 (.932–1.136)

Note. Normalized values of number of lines, FA and ADC are separately reported for left and right inferior longitudinal fasciculus (l/rILF) and left and right inferior fronto-occipital fasciculus (l/rIFOF) in G.S. and HCs. For HC mean ± SD (and range) are reported.
[a] Denotes a value falling outside the range of HC.
[b] Denotes a value falling outside the range of HC and significantly above the means of HC (one-tailed Bayesian p value = .003). All the other statistical comparisons did not show significant differences between G.S.' and HC's values, and are not reported.

2.1.3.3. Face description from memory. We also assessed whether G.S. could retrieve visual details of famous people's faces whom he did not recognize. Our patient could provide several visual details about famous people he could not recognize, although it was quite difficult to exclude that he relied on verbal semantic memory.

2.1.4. *Semantic memory*

2.1.4.1. Verbal semantic matching. Access to semantic knowledge from written material was assessed by the verbal version of the *Pyramids and Palm Trees Test* (Howard and Patterson, 1992), requiring subjects to associate semantically related words. G.S. scored 45/52 (86.5%), a performance marginally below that of normal controls (90% correct responses or more).

2.1.4.2. Naming on verbal definition. G.S. was asked to produce abstract or concrete nouns corresponding to verbal definitions read aloud by the experimenter (Novelli et al., 1986). He scored 25.5/28 for concrete words and 7.5/10 for abstract concepts; his overall score (33/38) was slightly below the normal cut-off (33.25).

2.1.5. *Summary of the first assessment*

G.S. showed spared basic visuoperceptual and visuospatial abilities, and spared visuospatial imagery, but was affected by relatively selective defects in face and visual object processing. In particular, G.S. was totally unable to name or identify faces of famous people. When names of the same famous people were provided, G.S. could retrieve precise semantic information about almost half of them, a performance within the normal range. Therefore, our patient proved to be unable to access person-based semantic knowledge via the visual modality, but could access the same knowledge by verbal modality. Moreover, G.S. showed a minor impairment in processing unknown faces, particularly when he could not rely on perceptual details, but had to resort to a configurational analysis. This defect of face processing was associated with mild visual agnosia (not clinically relevant) for both living and man-made objects. In contrast, the patient showed preserved semantic knowledge about the objects he could not recognize when he was provided with their names.

2.1.6. *Follow-up*

Fifteen months after the first evaluation (February 2012), G.S. underwent a new clinical and neuropsychological assessment. The patient was still cooperative and well oriented, and his language was fluent and flawless, but he was highly distractible, with increasing difficulties of staying on task. Although patient's subjective complaints were still limited to difficulties in recognizing familiar faces, his caregivers reported increasingly frequent episodes of social inadequacy, impulsivity, aggressive behaviour and disinhibition. The most evident personality changes with respect to the first evaluation reported by patient's son at the FBI were in the disinhibition subscale (restlessness, irritability, excessive jocularity, impulsivity, aggression, hyperorality, hoarding); the total FBI score (32/72) was above the cut-off score thought to identify FTD patients (28.6; Alberici et al., 2007). Neurological examination was still normal.

General neuropsychological assessment did not show changes in verbal and spatial memory, spatial exploration, visuoconstructional skills, abstract logical abilities, verbal fluency and executive functioning (see Table 1).

G.S.' performance on the Benton Facial Recognition Test was substantially unchanged (38/54): G.S. still emphasized that he relied on details such as general face shape, ears or eyebrows to perform the task, and performed well with faces presented in the same perspective and with the same lighting conditions.

To further investigate G.S.' impairment in face recognition, and to assess the relative contribution of perceptual processes and memory to his recognition impairment, he was assessed on the Cambridge Memory Test for Faces (CMTF; Duchaine and Nakayama, 2006), and the Cambridge Face Perception Test (CFPT; Duchaine et al., 2007). G.S.' scores were compared to those of 7 age-matched healthy control (HC) participants (mean age: 68 years, range: 61–77), using the modified *t*-test devised by Crawford and Garthwaite (2002) for use with single cases.

The CFMT includes a study phase in which subjects are required to familiarize with six target faces presented in three different views; after the study phase, subjects are asked to recognize target faces in 54 forced-choice items, consisting of novel views of one of the six target faces along with two non-target faces. G.S. scored 31/72; this score was significantly below the mean score of the HCs ($m = 52.4$, SD = 6.7; $p = .024$). In the CFPT, subjects are required to arrange six frontal views of men's faces according to their similarity to a ¾ profile view of a target face. The test images are morphs of six different individuals with the target face. Each combination of target and test faces are presented once upright and once inverted, allowing to assess presence of the "face inversion" effect (i.e., better performance for upright than for inverted faces), that is robust in normal adults (Yovel and Duchaine, 2006) and typically developed children (Taylor et al., 2004), but is lacking in patients with acquired prosopagnosia (Farah et al., 1995b) and DP (Schmalzl et al., 2009). Scores for each item are computed by summing the deviations from the correct position for each face. G.S.' score for upright trials (total deviations: 90) was significantly above the mean score of the age-matched control group (mean deviations: 45.5, SD = 12.6; $p = .016$) and very close to chance performance (93.3 deviations). While controls showed a robust inversion effect (mean deviations for inverted trials: 65.5, SD = 6.7), G.S. performed better with inverted trials, and his score was not significantly different from controls (total deviations: 76; $p = .193$).

On tasks assessing visual object recognition from BORB, G.S. did not show any relevant change in performance with respect to the first evaluation. G.S. could correctly name 18/76 drawings. Moreover, he performed below normal cut-offs on the Object decision task (subtest 10: 16/32) and on the Associative match task (subtest 12: 16/30), but still performed within the normal range on Item match task (subtest 11: 31/32) and showed spared object constancy (subtest 8: 20/25).

2.1.7. *Summary of the follow-up assessment*

After 15 months, the neuropsychological picture had remained relatively stable. A more extensive assessment of G.S.' face recognition abilities at the follow-up showed an impaired memory for faces, with associated deficits in perception of facial similarity. However, the patient could still perform a perceptual analysis of face details with high accuracy, as

shown by his normal performance on the 'inverted faces' condition of the CFPT. Visual object recognition abilities had remained generally stable. The only relevant change concerned severity of behavioural and psychological symptoms, particularly those of the disinhibition type.

As it will be discussed to a longer extent below, G.S.' clinical picture at the time of the first evaluation conforms to that described at early stages of PP. This gave us the opportunity of testing the hypothesis about the role of rILF and rIFOF in PP by means of DTI.

2.2. *DTI data acquisition*

G.S. was scanned using a 3T Philips Achieva scanner equipped with a 8 channels phased-array head coil. The DTI sequence was based on a single-shot spin-echo, echo-planar imaging (EPI) sequence with diffusion sensitizing gradients applied on either side of the 180° refocusing pulse. Diffusion weighted images were acquired with diffusion gradients oriented along 32 non-collinear directions. Specific DTI parameters were: Repetition Time (TR) = 9330 msec, Echo Time (TE) = 102 msec, flip angle = 90°, Field of view (FOV) = 256 × 256 mm^2, acquisition matrix size = 128 × 128, 50.2 mm thick axial slices (.7 mm gap), pixel size = 2 × 2 mm^2, diffusion weighting b = 1000 sec/mm^2. Two repetitions of the complete set were collected and averaged to increase signal-to-noise without introducing motion artefacts. Sensitivity Encoding (SENSE) factor of two was used to reduce scan time to 11′29″ and to minimize distortion related to EPI (van den Brink et al., 2003). During each scanning session, along with the DTI acquisition, high-resolution anatomical scans were acquired. The high-resolution anatomical scan (T1-weighted 3-D Magnetization-Prepared Rapid Acquisition Gradient-Echo sequence (MPRAGE)) was used for co-registration with the b = 0 image. Specific T1 scanning parameters: inversion time = 832 msec, TR = 6.7 msec, TE = 3.1 msec, flip angle = 8°, FOV = 256 × 256 mm^2, matrix size = 256 × 256, slice thickness = 1.2 mm, number of slices = 170, Turbo factor = 240, orientation of slices was sagittal, acquisition time was 10′53″.

Seven age-matched HCs (5 males, 68 ± 6 year, age range 61–77) underwent the same DTI acquisition protocol within a multi-centre research study focussing on memory impairment. Local ethical committee approval and written informed consent were obtained before the study.

2.2.1. *DTI post-processing*

Computation of the diffusion tensor and fibre tracking was performed using Extended MR WorkSpace R2.6.3.1 (Philips Healthcare), operating on a Microsoft Windows platform. The diffusion tensors were calculated by solving a linear equation system using least square fitting. Parameters for tract definition were .15 minimum Fractional Anisotropy (FA), 27° Max Angle Change.

We employed a multiple region of interest (ROI) approach to visualize and quantify the fibres within the tract of interest as this approach has been shown previously to ensure robust recovery of the major fibre tracts in the human brain (Mori et al., 2002; Huang et al., 2004). For each hemisphere we demarcated the ROIs along three coronal planes. In particular, the fibre tracts for the ILF and IFOF were extracted by specifying two ROIs for each tracts: a common ROI encompassing the ventral aspect of the occipito-temporal cortex, inferior to the floor of the posterior horn of the lateral ventricles, for both tracts was designed in a coronal plane tangential to the posterior edge of the splenium of the corpus callosum; a second ROI for the ILF was designed in the coronal plane located where the fornix descends towards the mammillary bodies, encompassing the whole temporal lobe; a third ROI for the IFOF was designed on a coronal plane posterior to the tip of the rostrum of the corpus callosum, encompassing the whole frontal lobe. As IFOF and ILF share a common pattern in their most posterior parts, IFOF fibres were removed from the ILF to avoid inclusion of spurious fibres in the latter. Additionally, to correct for head size and global white matter volume, for each subject a Whole-Brain white matter ROI (WB) was derived by connecting all the voxels with FA ≥.55, starting from a seed manually placed in the centre of the corpus callosum.

3. DTI results

All tracts were successfully identified in all subjects. DTI reconstruction of ILF and IFOF bundles in patient G.S. demonstrated a severe reduction of fibres in rILF versus left ILF (lILF), while IFOFs were relatively symmetric (Figs. 2 and 3).

For each tract the total number of fibres, FA and Apparent Diffusion Coefficient (ADC), as derived from the tractography analysis, were normalized dividing by the corresponding parameters obtained from the whole set of fibres crossing the WB ROI (detected using the same parameters as for the single tract definition). The resulting ratios were used to compare G.S. with the group of HC. For statistical analysis we choose a

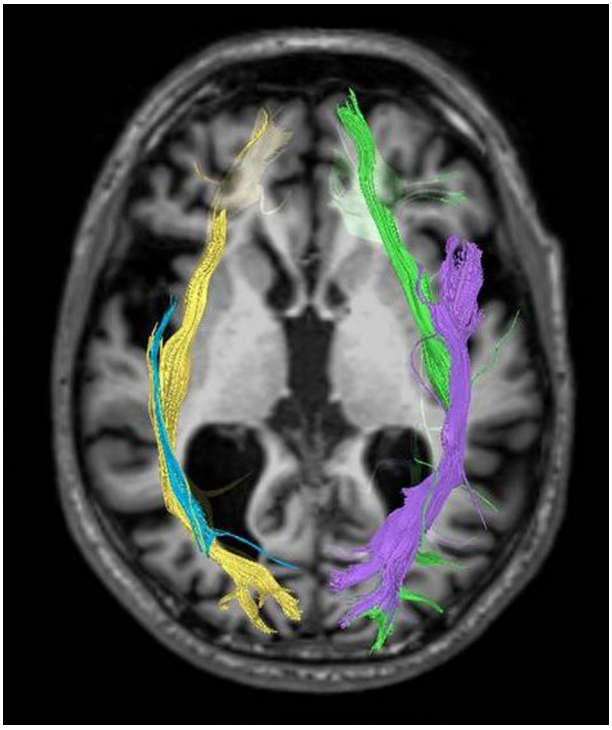

Fig. 2 – Axial sections and lines tractography. LILF is in purple, RILF is in light blue, LIFOF is in green, RIFOF is in yellow.

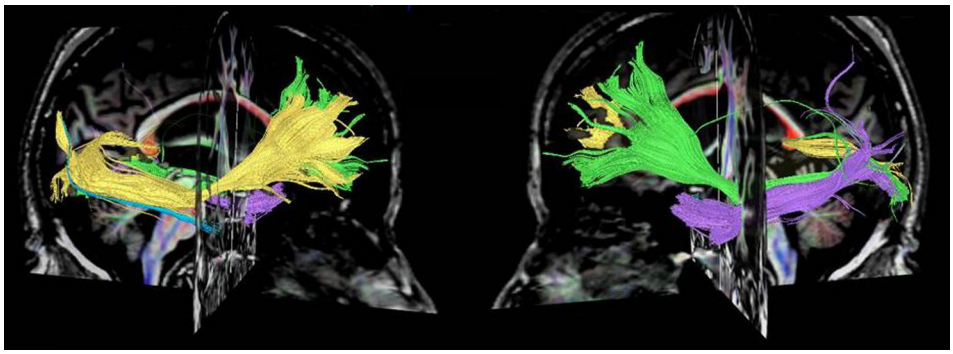

Fig. 3 – Left and right oblique sagittal sections. Colour-coding of fasciculi same as in Fig. 2. Clear asymmetry of ILFs can be appreciated, due to a severe atrophy of the right one.

Bayesian approach that is thought to be prudent, preventing overestimation of evidence in favour of an effect (Wetzels et al., 2011). We thus used a Bayesian inferential method (SingleBayes.exe; Crawford and Garthwaite, 2007) that allows to test if patient's values are significantly above (or below) the respective values of a small control sample.

In G.S., the number of lines of the rILF was far below the range of the values found in HC, but the wide variability of such values precluded to find a significant difference between G.S. and HC, associated with an ADC ratio above the range of HC. The relevant damage in rILF was denoted by the significantly higher ADC value in G.S. with respect to HC (see Table 4).

4. Discussion

In the present paper we observed a marked asymmetry in volume of ILF but not of IFOF in a patient with selective PP. Before examining possible theoretical implication of this finding, it is useful to discuss G.S.' clinical presentation in comparison to the few patients with PP described in literature.

Our patient G.S. presented with severe prosopagnosia, along with mild visual associative agnosia, with no relevant low-level visuospatial or semantic deficits. Previously reported cases of PP showed other visuoperceptual deficits or impairments in other cognitive domains (De Renzi, 1986; Tyrrell et al., 1990) or presented a multi-modal loss of person-based semantic knowledge not restricted to the visual modality (Evans et al., 1995; Barbarotto et al., 1995; Gentileschi et al., 1999, 2001; Gainotti, 2003). All these patients presented with anterior temporal lobe atrophy. Joubert et al. (2003) described a case of selective PP associated with mild visual agnosia that exhibited an atrophy of the posterior temporal lobe involving the fusiform gyrus. Although the neuroradiological study in G.S. revealed a widespread cortical atrophy, involving the right temporal lobe with relative sparing of the hippocampus, the clinical features of PP were suggestive for a prominently modality-specific disorder, that however might evolve towards more generalized defects of person-based semantic knowledge as in Evans et al.'s (1995) case. The follow-up assessment performed about 1 year after the first evaluation in the present patient could not demonstrate such an evolution of the clinical picture.

The association of modality-specific PP, mild object visual agnosia, and early behavioural changes with insidious onset and gradual progression, in presence of normal phosphorylated tau and beta-amyloid in CSF, might be consistent with a diagnosis of prosopagnosic variant of FTD (Neary et al., 1998), more recently defined as right-temporal variant of FTD (rtFTD; Chan et al., 2009; Josephs et al., 2009; Miller et al., 1993).

To our knowledge, there are no studies in literature that explore brain connectivity in PP or in rtFTD, whereas tractography studies in temporal variants of FTD showed bilateral reductions in ILF and IFOF, thus suggesting disrupted connectivity between the posterior occipital pole and the anterior temporal lobe (ILF), and between the inferolateral and dorsolateral frontal cortices and both the temporal and occipital cortices (IFOF; Borroni et al., 2007). Such data suggested that DTI measures can contribute to characterize patients with different variants of FTD and their clinical symptoms (Borroni et al., 2007).

On this basis, our finding that G.S. showed a selective marked reduction of ILF in the right hemisphere, whereas IFOF showed only a mild asymmetry, might explain the prominent cognitive disorder, i.e., modality-specific prosopagnosia, shown by our patient. Indeed, a reduction in the microstructural integrity of both ILF and IFOF bilaterally has been reported in congenital prosopagnosic subjects by Thomas et al. (2009). In DP, developmental hypotrophy of bilateral ILF and IFOF (Thomas et al., 2009) and of the anterior part of fusiform gyri (Behrmann et al., 2007; Garrido et al., 2009) would impair maturation of normal face processing skills, and preclude formation of any efficient compensatory pathway. In the present patient PP was related to the atrophy of the rILF, related to progressive neuronal loss, affecting both grey and white matter. This idea is compatible with a recent study in which Omar et al. (2011) investigated the neuroanatomical basis of face processing deficits in frontotemporal lobar degeneration (FTLD) by means of voxel based morphometry. Omar et al. (2011) observed that patients' performance on famous face identification was associated with reduced grey matter volume in a region of the right fusiform gyrus anterior to the fusiform face area (FFA), consistent with previously described evidence based on focal lesions and neuroimaging studies. On the basis of these observations and of the present findings, we could suggest that the disproportionate atrophy of the rILF can be the specific hallmark of the dysfunction in the neural circuit dedicated to face

processing in the ventral regions of the right hemisphere in our patient. These results are also compatible with the finding that white matter lesions in the ILF as a result of multiple sclerosis may induce symptoms of prosopagnosia and object agnosia (Yamasaki et al., 2004).

In recent years Fox et al. (2008) hypothesized that damage of ILF might be specifically related to associative prosopagnosia with relatively preserved perceptual abilities. In the present patient both the baseline evaluation and the follow-up assessment revealed a composite clinical picture in which minor defects of configurational face analysis were associated with an impairment to experience visual familiarity for well-known faces, and a substantial impairment to associate visually perceived faces to preserved semantic information about people. This is no room here to tackle the controversial distinction between associative and apperceptive forms of prosopagnosia (De Renzi et al., 1991; Duchaine and Weidenfeld, 2003; see Gainotti and Marra, 2011, for a recent review), but our data support the hypothesis that ILF is the most critical fibre pathway connecting regions of the core system of face processing (see Haxby et al., 2000; Catani and Thiebaut de Schotten, 2008), as proposed in the past (Benson et al., 1974; Habib, 1986; Kawahata and Nagata, 1989; Meadows, 1974; Takahashi et al., 1995). A damage of rILF would disconnect the occipital face area and the FFA from each other or from regions in the anterior temporal lobe and the precuneus (Catani et al., 2003), thus hampering modulation of right occipital lobe on temporal lobe activity. However, it remains to be explored the possible contribution of short U-shaped tracts connecting adjacent gyri that have been identified in human visual regions (Catani et al., 2003).

In conclusion, the selective damage of rILF in the present patient G.S. suggests possible underpinnings of early stages of PP, in line with previous DTI findings in DP. Longitudinal studies will clarify the clinico-anatomical correlates of evolution of PP and possible relationships with clinical diagnosis of different variants of neurodegenerative diseases.

REFERENCES

Alberici A, Geroldi C, Cotelli M, Adorni A, Calabria M, Rossi G, et al. The Frontal Behavioural Inventory (Italian version) differentiates frontotemporal lobar degeneration variants from Alzheimer's disease. *Neurological Sciences*, 28(2): 80–86, 2007.

Allison T. Electrophysiological studies of human face perception. I: Potentials generated in occipitotemporal cortex by face and non-face stimuli. *Cerebral Cortex*, 9(5): 415–430, 1999.

Allison T, Ginter H, McCarthy G, Nobre AC, Puce A, Luby M, et al. Face recognition in human extrastriate cortex. *Journal of Neurophysiology*, 71(2): 821–825, 1994a.

Allison T, McCarthy G, Nobre AC, Puce A, and Belger A. Human extrastriate visual cortex and the perception of faces, words, numbers and colors. *Cerebral Cortex*, 5: 544–554, 1994b.

Angelini R and Grossi D. *La terapia razionale dei disordini costruttivi*. S. Lucia: Centro di Riabilitazione, 1993.

Appollonio I, Leone M, Isella V, Piamarta F, Consoli T, Villa ML, et al. The Frontal Assessment Battery (FAB): Normative values in an Italian population sample. *Neurological Sciences*, 26(2): 108–116, 2005.

Barbarotto R, Capitani E, Spinnler H, and Trivelli C. Slowly progressive semantic impairment with category specificity. *Neurocase*, 1: 107–119, 1995.

Bartolomeo P. The quest for the "critical lesion site" in cognitive deficits: Problems and perspectives. *Cortex*, 47(8): 1010–1012, 2011.

Barton JJS. Structure and function in acquired prosopagnosia: Lessons from a series of 10 patients with brain damage. *Journal of Neuropsychology*, 2: 197–225, 2008.

Barton JJS, Press DZ, Keenan JP, and O'Connor M. Lesions of the fusiform face area impair perception of facial configuration in prosopagnosia. *Neurology*, 58(1): 71–78, 2002.

Behrmann M, Avidan G, Gao F, and Black S. Structural imaging reveals anatomical alterations in inferotemporal cortex in congenital prosopagnosia. *Cerebral Cortex*, 17(10): 2354–2363, 2007.

Benson DF, Segarra J, and Albert ML. Visual agnosia–prosopagnosia. *Archives of Neurology*, 30: 307–310, 1974.

Benton AL, Sivan AB, Hamsher K, Varney NR, and Spreen O. *Contributions to Neuropsychological Assessment*. New York: Oxford University Press, 1983.

Bodamer J. Die-Prosop-agnosie. *Archives of Psychiatric Nervenkrankh*, 179: 6–54, 1947.

Borroni B, Brambati SM, Agosti C, Gipponi S, Bellelli G, Gasparotti R, et al. Evidence of white matter changes on diffusion tensor imaging in frontotemporal dementia. *Archives of Neurology*, 64(2): 246–251, 2007.

Bruce V and Young A. Understanding face recognition. *British Journal of Psychology*, 77(3): 305–327, 1986.

Caffarra P, Vezzadini G, Dieci F, Zonato F, and Venneri A. Rey-Osterrieth complex figure: Normative values in an Italian population sample. *Neurological Sciences*, 22(6): 443–447, 2002.

Caltagirone C, Gainotti G, Carlesimo GA, and Parnetti L. Batteria per valutazione del deterioramento mentale (parte I): descrizione di uno strumento per la diagnosi neuropsicologica. *Archivio di Psicologia, Neurologia e Psichiatria*, 55: 461–470, 1995.

Catani M and ffytche DH. The rises and falls of disconnection syndromes. *Brain*, 128: 2224–2239, 2005.

Catani M and Thiebaut de Schotten M. A diffusion tensor tractography atlas for virtual dissections. *Cortex*, 44(8): 1105–1132, 2008.

Catani M, Jones DK, Donato R, and ffytche DH. Occipito-temporal connections in the human brain. *Brain*, 126: 2093–2107, 2003.

Chan D, Anderson V, Pijnenburg Y, Whitwell J, Barnes J, Scahill R, et al. The clinical profile of right temporal lobe atrophy. *Brain*, 132(Pt 5): 1287–1298, 2009.

Crawford JR and Garthwaite PH. Investigation of the single case in neuropsychology: Confidence limits on the abnormality of test scores and test score differences. *Neuropsychologia*, 40: 1196–1208, 2002.

Crawford JR and Garthwaite PH. Comparison of a single case to a control or normative sample in neuropsychology: Development of a Bayesian approach. *Cognitive Neuropsychology*, 24: 343–372, 2007.

Damasio AR, Damasio H, and Van Hoesen GW. Prosopagnosia: Anatomic basis and behavioral mechanisms. *Neurology*, 32(4): 331–341, 1982.

De Renzi E. Prosopagnosia in two patients with CT scan evidence of damage confined to the right hemisphere. *Neuropsychologia*, 24: 385–389, 1986.

De Renzi E, Faglioni P, Grossi D, and Nichelli P. Apperceptive and associative forms of prosopagnosia. *Cortex*, 27(2): 213–221, 1991.

Duchaine BC and Nakayama K. The Cambridge Face Memory Test: Results for neurologically intact individuals and an investigation of its validity using inverted face stimuli and prosopagnosic participants. *Neuropsychologia*, 44(4): 576–585, 2006.

Duchaine BC and Weidenfeld A. An evaluation of two commonly used tests of unfamiliar face recognition. *Neuropsychologia*, 41(6): 713–720, 2003.
Duchaine BC, Germine L, and Nakayama K. Family resemblance: Ten family members with prosopagnosia and within-class object agnosia. *Cognitive Neuropsychology*, 24(4): 419–430, 2007.
Duning T, Warnecke T, Mohammadi S, Lohmann H, Schiffbauer H, Kugel H, et al. Pattern and progression of white-matter changes in a case of posterior cortical atrophy using diffusion tensor imaging. *Journal of Neurology, Neurosurgery, and Psychiatry*, 80(4): 432–436, 2009.
Evans JJ, Heggs AJ, Antoun N, and Hodges JR. Progressive prosopagnosia associated with selective right temporal lobe atrophy. *Brain*, 118(1): 1–13, 1995.
Farah MJ, Levinson KL, and Klein KL. Face perception and within-category discrimination in prosopagnosia. *Neuropsychologia*, 33(6): 661–674, 1995a.
Farah MJ, Wilson K, Drain H, and Tanaka J. The inverted face inversion effect in prosopagnosia: Evidence for mandatory, face-specific perceptual mechanisms. *Vision Research*, 35: 2089–2093, 1995b.
Formisano E, Linden DEJ, Salle FD, Trojano L, Esposito F, Sack AT, et al. Tracking the mind's image in the brain: Time-resolved fMRI during visuospatial mental imagery. *Neuron*, 35: 185–194, 2002.
Fox CJ, Iaria G, and Barton JJS. Disconnection in prosopagnosia and face processing. *Cortex*, 44(8): 996–1009, 2008.
Gainotti G. Slowly progressive defect in recognition of familiar people in a patient with right anterior temporal atrophy. *Brain*, 126(4): 792–803, 2003.
Gainotti G and Marra C. Differential contribution of right and left temporo-occipital and anterior temporal lesions to face recognition disorders. *Frontiers in Human Neuroscience*, 5: 55, 2011.
Garrido L, Furl N, Draganski B, Weiskopf N, Stevens J, Chern-Yee Tan G, et al. Voxel-based morphometry reveals reduced grey matter volume in the temporal cortex of developmental prosopagnosics. *Brain*, 132: 3443–3455, 2009.
Gentileschi V, Sperber S, and Spinnler H. Progressive defective recognition of familiar people. *Neurocase*, 5(5): 407–424, 1999.
Gentileschi V, Sperber S, and Spinnler H. Crossmodal agnosia for familiar people as a consequence of right infero polar temporal atrophy. *Cognitive Neuropsychology*, 18(5): 439–463, 2001.
Grill-Spector K, Knouf N, and Kanwisher N. The fusiform face area subserves face perception, not generic within-category identification. *Nature Neuroscience*, 7(5): 555–562, 2004.
Grossi D and Trojano L. Constructional apraxia. In Denes G and Pizzamiglio L (Eds), *Handbook of Clinical and Experimental Neuropsychology*. Psychological Press Hove, 1999: 441–452.
Grossi D, Trojano L, Modafferi A, and Pelosi L. On different role of hemispheres in Mental Imagery. "O'clock Test" in two cases. *Brain and Cognition*, 10: 18–27, 1989.
Grossi D, Fragassi FA, Chiacchio L, Valoroso L, Tuccillo R, Perrotta C, et al. Do visuospatial and constructional disturbances differentiate frontal variant of frontotemporal dementia and Alzheimer's disease? An experimental study of a clinical belief. *International Journal of Geriatric Psychiatry*, 17: 641–648, 2002.
Habib M. Visual hypoemotionality and prosopagnosia associated with right temporal lobe isolation. *Neuropsychologia*, 24: 577–582, 1986.
Haxby JV, Hoffman EA, and Gobbini MI. The distributed human neural system for face perception. *Trends in Cognitive Sciences*, 4: 223–233, 2000.
Howard D and Patterson K. *Pyramids and Palm Trees*. Bury St. Edmunds, England: Thames Valley Test Company, 1992.
Huang H, Zhang JY, van Zijl PCM, and Mori S. Analysis of noise effects on DTI-based tractography using the brute-force and multi-ROI approach. *Magnetic Resonance in Medicine*, 52: 559–565, 2004.
Josephs KA, Whitwell JL, Knopman DS, Boeve BF, Vemuri P, Senjem ML, et al. Two distinct subtypes of right temporal variant frontotemporal dementia. *Neurology*, 73(18): 1443–1450, 2009.
Joubert S, Felician O, Barbeau E, Sontheimer A, Barton JJ, Ceccaldi M, et al. Impaired configurational processing in a case of progressive prosopagnosia associated with predominant right temporal lobe atrophy. *Brain*, 126(Pt 11): 2537–2550, 2003.
Joubert S, Felician O, Barbeau E, Sontheimer A, Guedj E, Ceccaldi M, et al. Progressive prosopagnosia: Clinical and neuroimaging results. *Neurology*, 63(10): 1962–1965, 2004.
Kanwisher N, McDermott J, and Chun MM. The fusiform face area: A module in human extrastriate cortex specialized for face perception. *Journal of Neuroscience*, 17(11): 4302–4311, 1997.
Kawahata N and Nagata K. A case of associative visual agnosia: Neuropsychological findings and theoretical considerations. *Journal of Clinical and Experimental Neuropsychology*, 11: 645–664, 1989.
Meadows JC. The anatomical basis of prosopagnosia. *Journal of Neurology, Neurosurgery, and Psychiatry*, 37: 489–501, 1974.
Measso G, Cavarzeran F, Zappala G, Lebowitz BD, Crook TH, Pirozzolo FJ, et al. The mini-mental state examination: Normative study of an Italian random sample. *Developmental Neuropsychology*, 9(2): 77–85, 1993.
Mesulam M. Defining neurocognitive networks in the BOLD new world of computed connectivity. *Neuron*, 62: 1–3, 2009.
Migliaccio R, Agosta F, Toba MN, Samri D, Corlier F, de Souza LC, et al. Brain networks in posterior cortical atrophy: A single case tractography study and literature review. *Cortex*, 48(10): 1298–1309, 2012.
Migliaccio R, Agosta F, Scola E, Magnani G, Cappa SF, Pagani E, et al. Ventral and dorsal visual streams in posterior cortical atrophy: A DT MRI study. *Neurobiology of Aging*, 33(11): 2572–2584, 2012.
Miller BL, Chang L, Mena I, Boone K, and Lesser IM. Progressive right frontotemporal degeneration: Clinical, neuropsychological and SPECT characteristics. *Dementia*, 4(3–4): 204–213, 1993.
Mori S, Kaufmann WE, Davatzikos C, Stieltjes B, Amodei L, Fredericksen K, et al. Imaging cortical association tracts in the human brain using diffusion tensor-based axonal tracking. *Magnetic Resonance in Medicine*, 47: 215–223, 2002.
Neary D, Snowden JS, Gustafson L, Passant U, Stuss D, Black S, et al. Frontotemporal lobar degeneration: A consensus on clinical diagnostic criteria. *Neurology*, 51(6): 1546–1554, 1998.
Novelli G, Papagno C, Capitani E, Laiacona M, Cappa SF, and Vallar G. Tre test clinici di ricerca e produzione lessicale. Taratura su soggetti normali. *Archivio di Psicologia, Neurologia e Psichiatria*, 47: 477–506, 1986.
Omar R, Rohrer JD, Hailstone JC, and Warren JD. Structural neuroanatomy of face processing in frontotemporal lobar degeneration. *Journal of Neurology, Neurosurgery, and Psychiatry*, 82(12): 1341–1343, 2011.
Orsini A, Grossi D, Capitani E, Laiacona M, Papagno C, and Vallar G. Verbal and spatial immediate memory span: Normative data from 1355 adults and 1112 children. *Italian Journal of Neurological Sciences*, 8(6): 537–548, 1987.
Paivio A. Comparisons of mental clocks. *Journal of Experimental Psychology*, 1: 61–71, 1978.
Pitcher D, Charles L, Devlin JT, Walsh V, and Duchaine BC. Triple dissociation of faces, bodies, and objects in extrastriate cortex. *Current Biology*, 19(4): 319–324, 2009.
Rajimehr R, Young JC, and Tootell R. An anterior temporal face patch in human cortex, predicted by macaque maps. *Proceedings of the National Academy of Sciences*, 106: 1995–2000, 2009.

Riddoch MJ and Humphreys GW. *BORB: The Birmingham Object Recognition Battery*. Hove, UK: Lawrence Erlbaum Associates, 1993.
Rizzo S, Venneri A, and Papagno C. Famous face recognition and naming test: A normative study. *Neurological Sciences*, 23(4): 153–159, 2002.
Rossion B, Caldara R, Seghier M, Schuller A-M, Lazeyras F, and Mayer E. A network of occipito-temporal face-sensitive areas besides the right middle fusiform gyrus is necessary for normal face processing. *Brain*, 126(Pt 11): 2381–2395, 2003.
Schmalzl L, Palermo R, Harris IM, and Coltheart M. Face inversion superiority in a case of prosopagnosia following congenital brain abnormalities: What can it tell us about the specificity and origin of face-processing mechanisms? *Cognitive Neuropsychology*, 26(3): 286–306, 2009.
Sergent J, Ohta S, and MacDonald B. Functional neuroanatomy of face and object processing. *Brain*, 115(1): 15–36, 1992.
Spinnler H and Tognoni G. Standardizzazione e taratura italiana di test neuropsicologici. *Italian Journal of Neurological Sciences*, 8(Suppl.): 1–12, 1987.
Takahashi N, Kawamura M, Hirayama K, Shiota J, and Isono O. Prosopagnosia: A clinical and anatomical study of four patients. *Cortex*, 31(2): 317–329, 1995.
Taylor MJ, Batty M, and Itier RJ. The faces of development: A review of early face processing over childhood. *Journal of Cognitive Neuroscience*, 16(8): 1426–1442, 2004.
Thomas C, Avidan G, Humphreys K, Jung KJ, Gao F, and Behrmann M. Reduced structural connectivity in ventral visual cortex in congenital prosopagnosia. *Nature Neuroscience*, 12(1): 29–31, 2009.
Trojano L, Grossi D, Linden DE, Formisano E, Hacker H, Zanella FE, et al. Matching two imagined clocks: The functional anatomy of spatial analysis in the absence of visual stimulation. *Cerebral Cortex*, 10: 473–481, 2000.
Trojano L, Fragassi NA, Chiacchio L, Izzo O, Izzo G, Di Cesare G, et al. Relationship between constructional and visuospatial abilities in normal subjects and in focal brain-damaged patients. *Journal of Clinical and Experimental Neuropsychology*, 26: 1103–1112, 2004.
Tsao D, Moeller S, and Freiwald W. Comparing face patch systems in macaques and humans. *Proceedings of the National Academy of Sciences*, 105: 19513–19518, 2008.
Tyrrell PJ, Warrington EK, Frackowiak RS, and Rossor MN. Heterogeneity in progressive aphasia due to focal cortical atrophy. A clinical and PET study. *Brain*, 113: 1321–1336, 1990.
van den Brink JS, Watanabe Y, Kuhl CK, Chung T, Muthupillai R, Van Cauteren M, et al. Implications of SENSE MR in routine clinical practice. *European Journal of Radiology*, 46: 3–27, 2003.
Wada Y and Yamamoto T. Selective impairment of facial recognition due to a haematoma restricted to the right fusiform and lateral occipital region. *Journal of Neurology, Neurosurgery, and Psychiatry*, 71(2): 254–257, 2001.
Wetzels R, Matzke D, Lee MD, Rouder JN, Iverson GJ, and Wagenmakers E-J. Statistical evidence in experimental psychology: An empirical comparison using 855 *t* tests. *Perspectives on Psychological Science*, 6(3): 291–298, 2011.
Yamasaki T, Taniwaki T, Tobimatsu S, Arakawa K, Kuba H, Maeda Y, et al. Electrophysiological correlates of associative visual agnosia lesioned in the ventral pathway. *Journal of Neurological Science*, 221(1–2): 53–60, 2004.
Yovel G and Duchaine B. Specialized face perception mechanisms extract both part and spacing information: Evidence from developmental prosopagnosia. *Journal of Cognitive Neuroscience*, 18(4): 580–593, 2006.