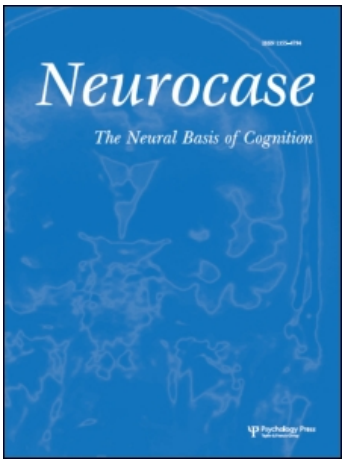

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Right anterior temporal lobe atrophy and person-based semantic defect: A detailed case study

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We report a new case of a right temporal pole variant of frontotemporal dementia (Rtv-FTLD), MD, who presented a slowly progressive deterioration of the recognition of familiar and famous people. We thoroughly investigated MD's face processing and semantic abilities, including a neuroimaging investigation. This analysis revealed a cross-modal person-based deficit together with a more general semantic alteration. However, there was no evidence of impairment in face perception, including holistic processing, or of an abnormal pattern of brain activation in face-sensitive cortical areas. We discuss the nature of face processing in the Rtv-FTLD and the context of a person-based semantic defect.

Keywords: Right temporal lobe atrophy; Progressive prosopagnosia; Semantic dementia; Face processing; Person-based semantic defect; FTLD.

INTRODUCTION

Focal cortical atrophies are degenerative processes that selectively affect one domain of mental functioning. In early stages these syndromes are characterized by relatively specific impairments of cerebral functions. Thus their study offers the opportunity to better understand the organization of cognitive processes in the human brain.

Focal cortical atrophies can selectively disrupt language, speech, episodic memory, vision, gesture and semantic memory. There are also multiple potential histological causes of these disruptions as demonstrated in non-specific atrophies, Lewy body disease, Pick's disease, Alzheimer's disease, etc. (Didic, Felician, Ceccaldi, & Poncet, 1999, Neary et al., 1998). Among the focal atrophies, frontotemporal lobar degeneration is the second most common cause of cortical dementia (Thompson, Patterson, & Hodges, 2003). Three prototypic neurobehavioral syndromes can be produced by frontotemporal lobar degeneration: frontotemporal dementia, progressive nonfluent aphasia and semantic dementia (Grossman, 2002; Neary et al., 1998; Snowden, Neary, & Mann, 1996). These three major clinical presentations reflect the predominant locus of the atrophy. When atrophy is localized predominantly in the anterior temporal lobe, the observed clinical pattern is semantic dementia (SD). SD is characterized by a severe

We are grateful to MD for her participation and her great patience during the experiments, to her husband and her family, and to all of our control participants. We also thank Dr Eric Mormont from the Cliniques Universitaires de Mont-Godinne for his collaboration, and Gwenaelle Feyers for having conducted the language assessment, Valerie Goffaux for the making of the stimuli used in the task testing perception of distances between face features, as well as two anonymous reviewers and the editor for precious comments on a previous version of this paper. This research was supported by the Belgian National Fund for Scientific Research (FNRS), mandat d'impulsion scientifique to BR.

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naming and word comprehension deficit, reflecting a profound loss of conceptual knowledge, while other cognitive abilities remain relatively preserved (Neary et al., 1998; Thompson et al., 2003). SD appears mainly in the context of an atrophy localized predominantly in the left anterior regions of the temporal lobe (Didic et al., 1999; Gorno-Tempini et al., 2004; Grossman, 2002; Knibb & Hodges, 2005; Simons, Graham, Galton, Patterson, & Hodges, 2001; Thompson et al., 2004). However, the nosology of semantic dementia has been complicated by the report of cases of cortical atrophies localized predominantly in the right anterior regions of the temporal lobe (right temporal pole variant of frontotemporal dementia, Rtv-FTLD). This right-lateralized anterior temporal lobe atrophy seems to present a particular symptomatic pattern, characterized by a progressive and selective inability to recognize and identify faces of familiar people. Such cases have been described in the literature for the past 20 years (Barbarotto, Capitani, Spinnler, & Trivelli, 1995; Evans, Heggs, Antoun, & Hodges, 1995; Kitchener & Hodges, 1999; Gainotti, Barbier, A., Marra, 2003; Gainotti, Ferraccioli, Quaranta, & Marra, 2008; Gentileschi, Sperber, & Spinnler, 1999, 2001; Gorno-Tempini et al., 2004; Joubert et al., 2003, 2004, 2006; Mendez & Ghajarnia, 2001; Thompson et al., 2004; Tyrrell, Warrington, Frackowiak, & Rossor, 1990; Verstichel, 2005; Williams, Savage, & Halmagyl, 2006; for a review, see Gainotti, 2007) and have been referred to by different labels: *progressive prosopagnosia* (Evans et al., 1995; Joubert et al., 2003, 2004; Mendez & Ghajarnia, 2001), *associative degenerative prosopagnosia* (Gentileschi et al., 1999), *cross-modal agnosia for familiar people* (Gentileschi et al., 2001; Joubert et al., 2006), *person-specific semantic defect* (Barbarotto et al., 1995; Thompson et al., 2004). Typically, these patients show slowly progressing difficulties in recognising and identifying familiar people in their surrounding (relatives and friends), and famous people.

Classically, prosopagnosia is defined as the inability to recognize faces of people known to the patient on the basis of visual perception, a difficulty that cannot be explained by low-level visual impairments or cognitive alterations such as mental confusion or amnesia (Bodamer, 1947). The ability to recognize people through other cues (voice or other visual traits), and access to semantic knowledge concerning people is preserved (for a recent review, see Mayer & Rossion, 2007). However, in most case studies of Rtv-FTLD the impairment does not concern only the recognition of faces, but also people's names (Barbarotto et al., 1995; Evans et al., 1995; Gainotti et al., 2003; Gorno-Tempini et al., 2004; Joubert et al., 2004, 2006; Kitchener & Hodges, 1999; Thompson et al., 2004) or voices (Gainotti et al., 2003, 2008; Gentileschi et al., 1999, 2001; Joubert et al., 2006). These observations have led several authors (e.g., Gainotti, 2007; Joubert et al., 2006) to suggest that Rtv-FTLD reflects less a form of associative prosopagnosia than a cross-modal person-based recognition defect, similar to the 'amnesic associative' prosopagnosia syndrome which can follow focal lesions to the anterior part of the temporal lobe (Damasio, Tranel, & Damasio, 1990). Moreover, in most cases, the person-based deficit is associated with a more extended semantic deficit, concerning famous places (Barbarotto et al., 1995; Gainotti et al., 2008; Gentileschi et al., 2001; Joubert et al., 2003), famous events (Barbarotto et al., 1995; Kitchener & Hodges, 1999; Joubert et al., 2003), flowers (Evans et al., 1995), food items (Gorno-Tempini et al., 2004) or odors (Mendez & Ghajarnia, 2001).

The question of whether face perception is entirely preserved in cases of Rtv-FTLD is still unclear. Do these patients present face recognition impairments, without any indication of visual impairments in processing faces? This question is of interest since several authors have cast doubts on the existence of a pure mnesic form of prosopagnosia (Davidoff & Landis, 1990; Delvenne, Seron, Coyette, & Rossion, 2004; Farah, 1990; but see Anaki, Kaufman, Freedman., & Moscovitch, 2007). That is, it is thought that so-called associative prosopagnosic patients should always present difficulties in perceiving the individuality of a face in full, and thus proceed by analysing faces feature-by-feature (Farah, 1990), taking usually more time than normal controls. However, this hypothesis has not been tested thoroughly in cases of acquired prosopagnosia clearly defined as of the associative form, as in the case of Rtv-FTLD. An in-depth investigation of a patient's face perceptual abilities is called for, including tests of integration of facial features into global individual face representation, and reports of response times measures.

In the present study, we present the detailed investigation of a new case of Rtv-FTLD. MD is a 71-year-old right-handed woman who has a focal atrophy of the anterior temporal lobe, predominant in the right hemisphere (Figure 1). In relation to this atrophy, she has been complaining of a slowly progressing deterioration of her ability to

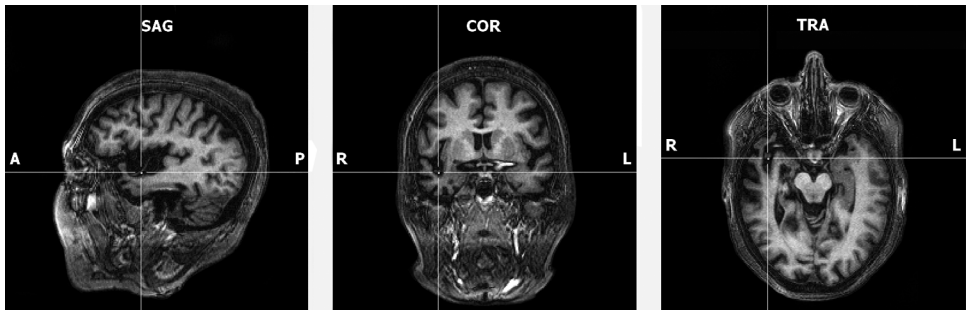

Figure 1. MRI data of MD obtained in May 2006. The images show a clear focal atrophy of the anterior temporal lobe, predominantly within the right hemisphere (right = left). Inferior and superior parts of anterior temporal regions are affected, both laterally and medially.

recognize personally familiar and famous people by their faces, which she first noted about 1 year before the start of this investigation (January 2004). The aim of this study is to extensively document this new case of Rtv-FTLD by emphasizing the investigations on person recognition processing, particularly the visuo-perceptive mechanisms involved in face processing. In the first part of the paper, we present the results of an extended behavioural investigation of the patient MD. This section consists of a set of face perception tasks, completed by a multimodal and multicategorical investigation, testing identification by means of faces, names and voices. Finally, we also assessed MD's semantic knowledge with respect to other specific domains. Our hypothesis was that MD would present a normal profile concerning all perceptual face tasks. In contrast, we expected to observe a multimodal impairment in person-based knowledge, including faces, names and voices. We also predicted a deficit extending to the recognition of other semantic categories. In the second section of the paper, and for the first time in a case of Rtv-FTLD, we localized face-preferential responses in MD's brain via functional magnetic resonance imaging (fMRI). This research was included to test for abnormalities in MD's ability to process faces at the neural level, and to extract information from a brain damaged case of prosopagnosia that could potentially refine our understanding of the cortical face network in normal observers (see Rossion, 2008a). In line with the hypothesis of an intact perceptual face system at the behavioural level, we hypothesized that MD would present a normal pattern of activation in the visual areas of the cortical face processing network (e.g., Haxby, Hoffman, & Gobbini, 2000). This was assessed by comparing the level of activation for faces to other object categories, and testing the sensitivity of areas of the cortical face network to individual faces through an fMR-adaptation paradigm (Grill-Spector & Malach, 2001; Grill-Spector, Henson, & Martin, 2006).

To our knowledge, this is the most complete investigation of a case of Rtv-FTLD reported in the literature, with a focus on face processing abilities, combining behavioral and functional neuroimaging investigations.

CASE DESCRIPTION

MD: Clinical history

MD is a 71-year-old right-handed woman and retired dressmaker who presented at a neurological unit of a Belgian hospital (Cliniques Universitaires de Mont-Godinne) with complaints of a slowly progressive deterioration of the recognition of familiar and famous persons trough their face (prosopagnosia), associated with difficulties in retrieving words (January 2005). At first, MD's complaints concerned the recognition of celebrities: she could no longer recognize several famous faces when seeing them on TV or in the press. Later, her recognition difficulties extended to family members (some nephews and cousins, particularly at family events such as weddings) and friends (former colleagues, neighbours, shopkeepers). According to her family, her face recognition impairment had never been present before, and had been gradually deteriorating over the past year. Moreover, MD was unable to recognize the faces of the neurologist, the neuropsychologist and the experimenter each time she saw them in the hospital, although she met them regularly over the course of several months.

As a second complaint, MD showed difficulties in finding and understanding names of persons and common objects. She had lost the feeling of

familiarity for several words, e.g., food or flowers. MD's spontaneous speech was still fluent and free of grammatical, syntactic or prosodic errors. She became more talkative and even presented with logorrhoea. However, her speech was characterized increasingly by frequent anomias, with recurrent *passe-partout* words and circumlocutions. Furthermore, in parallel with her cognitive impairments, MD experienced progressive changes in her general behaviour and personality. She showed an increasing tendency towards stereotypical and compulsive behaviours, narrowed preoccupations and irritability. MD had also become self-centred and unconcerned about other people's feelings and needs. Otherwise, MD presented with good performances of general memory and spatio-temporal orientation. She had no prior history of neurological or vascular disease, head injury or alcohol abuse, and she was completely independent in everyday life. MD was strongly aware of her deficit and was very insightful with regard to developing strategies that would allow her to cope with her problems. MD's ophthalmologic assessment showed normal visual acuity, colour perception and contrast sensitivity. Before testing, MD gave informed consent.

Throughout the assessment, which took place between January 2005 and June 2006, MD was well focused and conscientious. She easily understood the instructions and showed great flexibility over the different tests. We tested her over the course of about 1 year at regular intervals. This provided a large corpus of data and, to our knowledge, offered the most systematic and extensive neuropsychological investigation of a case of right temporal progressive cortical atrophy. Nevertheless, MD eventually decided to stop rehabilitation conducted in the hospital and likewise ended the experimental testing. Consequently, the longitudinal assessment was interrupted, resulting in the last investigation of the recognition of relatives remaining at the stage of temporary informal testing.

Neuroradiological findings

A set of neurological and neuroanatomical examinations were conducted with MD. There were no abnormalities detected on the electroencephalogram (EEG). A structural MRI obtained in May 2005 showed clear atrophy of the anterior parts of the temporal lobes with a right lateral dominance. These MRI findings were confirmed by a positron emission tomography examination which showed hypoperfusion restricted to the anterior parts of the right temporal lobe and to a lesser extent in the right frontal lobe, insula and parahippocampal gyrus.

A second MRI scan was conducted in May 2006. It confirmed a clear focal atrophy of the anterior temporal lobe, again predominantly within the right hemisphere. Inferior and superior parts of anterior temporal regions were affected, both laterally and medially (Figure 1).

General neuropsychological assessment

MD underwent a first general neuropsychological evaluation in January 2005, followed by complementary tests during the following months. A specific language assessment was also conducted in March 2005. MD underwent a second neuropsychological evaluation in January 2006. The results are summarized in Table 1.

The results of the first standard neuropsychological evaluation indicated that MD had an average full-scale IQ (global IQ = 96) (Weschler, 1989). She scored 30/30 in the Mini-Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975). Her praxic, executive functioning, attentional, visuo-perceptual and memory skills were generally normal (only two perceptual tasks below average, along with a low score in the Visual Memory Subtests of WMS-III (Weschler, 2001), presumably due to the fact that the score included the visual faces subtest). In contrast, MD presented severe impairments in language skills. Although repetition, reading, writing and fluency were preserved, oral production and comprehension along with written comprehension were severely impaired. MD failed some tests of naming, assigning and semantic matching (upon oral or written cues). Concerning face memory, two tasks revealed deficits in the memorization of new faces (WRMT, Warrington, 1984; face subtest of the WMS-III, Weschler, 2001). MD also failed two tasks involving the naming and designation of famous people (unpublished tests). Finally, perceptual processing of faces seemed to be preserved, as shown by the Benton Facial Recognition Test (Benton, Sivan, Hamsher, Varney, & Spreen, 1983).

The second neuropsychological assessment conducted in January 2006 confirmed these results, but also included the verbal episodic memory test of Grober and Buschke (1987). These results

TABLE 1
MD's and age-matched controls results on general neuropsychological assessments

	2005		*2006*	
	MD	*Age-matched controls*	*MD*	*Age-matched controls*
General				
MMSE	30/30		30/30	
WAIS-R				
Verbal IQ	91	[P27]		
Performance IQ	103	[P58]		
Full-scale IQ	96	[P39]		
Low level visual perception				
BORB				
(1) Copy of drawings	8/8	/		
(2) Length match task	27/30	26.9(1.6)		
(3) Size match task	28/30	27.3(2.4)		
(4) Orientation match task	25/30	24.8(2.6)		
(5) Position of gap match task	38/40	35.1(4)		
(6) Overlapping line drawings task	0 err, 61 s	0 err, <66.9 s		
High level visual perception				
BORB				
(7) Minimal feature view task	23/25	23.3(2)		
(8) Foreshortened match	23/25	21.6(2.6)		
(9) Drawing from memory	3/6*	/		
(10) Object decision task	19/32*; 16/32*	27(2.2); 30.5(1.4)		
(11) Item match task	32/32	30(2.2)		
(12) Associative match task	26/30	27.5(2.4)		
Executive functioning				
Phonological verbal fluency	15	19.9(6.3)	13	19.9(6.3)
Trail Making Test				
Part A	0 err – 49 s	0(0.2) – 83.1(34.4)	0 err – 62 s	0(0.2) – 83.1(34.4)
Part B	2 err – 128 s	0.9(1.5) – 157.7(56.6)	3 err – 160 s	0.9(1.5) – 157.7(56.6)
Stroop Test				
Naming	0 err – 58 s	1(1.2) – 71.9(13.8)	2 err – 64 s	1(1.2) – 71.9(13.8)
Reading	0 err – 40 s	0.1(0.5) – 49.5(11.7)	0 err – 37 s	0.1(0.5) – 49.5(11.7)
Interference	1 err – 147 s	3.8(4.9) – 150.4(39)	0 err – 101 s	3.8(4.9) – 150.4(39)
Incompatibility TEA	1 err – 537 ms	[P>82 – P14]		
Go/No go TEA	0 err – 529 ms	[P>46 – P86]		
Flexibility TEA	0 err – 686 ms	[P>99 – P99]		
Praxias				
Clock Drawing Test				
Oral order	9/10	/	9/10	/
Copy	9/10	/	10/10	/
CERAD	11/11	8.8(1.9)	10/11	8.8(1.9)
Attention				
Alertness TEA (without and with AS)	243 ms; 217 ms	[P79; P92]		
Divided attention TEA	0 err – 678 ms	[P>62 – P50]		
Memory				
Working memory				
WMS-III – Working Memory Subtest	108	[P70]		
Working memory TEA (updating)	3 err – 816 ms	[P<42 – P7]		
Forward span	5 numbers	5(1)		
Backward span	4 numbers	3.4(1)		
Spatial span (Block tapping)	6	[P75]		

(*Continued*)

TABLE 1
(*Continued*)

	2005		*2006*	
	MD	*Age-matched controls*	*MD*	*Age-matched controls*
Verbal episodic memory				
RL-RI 16 items				
Immediate recall	14	15.3(0.8)	10*	15.3(0.8)
Free recall (1; 2; 3; delayed)	6; 7; 8; 11	8.4(2.5); 9.2(2.4); 11.2(2.8); 11(2)	5; 8; 9; 9	8.4(2.5); 9.2(2.4); 11.2(2.8); 11(2)
Cued recall (1; 2; 3; delayed)	11; 12; 13*; 15	14.3(2.1); 14.8(1.8); 15.6(0.8); 15.2(1.4)	7*; 10*; 13*; 10*	14.3(2.1); 14.8(1.8); 15.6(0.8); 15.2(1.4)
Recognition	15	15.2(1.4)	16	15.2(1.4)
RLS 15 items				
Mean			10	9.6(1.6)
Delayed recall			11	11.6(2.1)
WMS-III – Verbal Memory Subtests				
Immediate	94	[P34]		
Delayed	82	[P12]		
Visual episodic memory				
Doors Test (Baddeley)				
Part A	10/12	[P25–50]	11/12	[P75]
Part B	4/12	[P10]	5/12	[P25]
WMS-III – Visual Memory Subtests				
Immediate	67*	[P1]		
Delayed	72*	[P3]		
Autobiographical memory				
Kopelman et al.	52/63; 27/27	50–52/63: low-average; 19–27/27: normal		
Language				
Oral production				
Automatic speech	10/10	/		
Repetitive speech	51/51	/		
Semantic verbal fluency	17	26.5(6.3)		
Lexis Naming 64 items	37/64*	57.9(4.9)		
Colored Snodgrass & Vanderwart naming (Rossion & Pourtois, 2004)	166/260*	241.8(2.4)		
Naming on oral definition	34/72*	/		
Oral comprehension				
Oral lexical decision	71/72	/		
General categorization	44/46	45.4(0.8)		
Specific categorization	41/46*	44.8(0.8)		
Semantic attributes checking	10/16*	14.1(1.4)		
Item-word match checking	8/16*	15.4(0.5)		
Lexis Assigning 64 items	56/64*	60.7(1.5)		
Pyramids and Palm Trees Test (visual)	35/52*	>47		
Written production				
Dictation	19/20	18.5(1.5)		
Spelling	7/12*	10.5(1.5)		
Written comprehension				
Reading	77/80	77.3(1.5)		
General categorization	44/46*	45.6(0.7)		
Specific categorization	42/46*	45.1(0.6)		
Semantic attributes checking	11/16*	14.3(1.6)		
Item-word match checking	12/16*	15.8(0.4)		
Pyramids and Palm Trees Test (verbal)	41/52*	>47		

(*Continued*)

TABLE 1
(*Continued*)

	2005		*2006*	
	MD	*Age-matched controls*	*MD*	*Age-matched controls*
Faces				
Faces perception				
Benton Facial Recognition Test	47/54 (age-corrected score)	Normal: 41–54	44/54 (age-corrected score)	Normal: 41–54
Memory of new faces				
RMT (Warrington)	33/50*	42.4(3.8)	30/50*	42.4(3.8)
WMS-III – facial subtest	25/48*; 26/48*	[NS4; NS5]		
Identification of famous people				
Naming	9/100*	47.2(16.6)		
Designation	52/100*	87.2(12.1)		

When they are available, the average scores and the standard deviations of the age-matched controls scores are provided. When they are note available, the percentiles or the standard notes are provided in brackets.
*Indicates impaired scores ($SD < -2$ or $p < 5$).

suggest a semantic, rather than a memory, impairment, given that MD obtained 16/16 on the recognition task and that she succeeded with the 15 items test of Buschke (1973) which is more demanding in terms of mnesic recruitment.

A more detailed analysis of perceptual and semantic treatment of faces was conducted in this study, as well as an extensive analysis of other verbal and visual categories, the exact experiments and results of which will be described below.

BEHAVIORAL EXPERIMENTS

MD was administered a set of 21 specific tasks. These tasks were conducted during a period of 6 months, using the same testing conditions. The stimuli were presented using E-prime 1.1 (Schneider, Eschman, & Zuccolotto, 2002), with the patient positioned 40 cm from the screen. She was asked to provide a binary response using the keyboard of the laptop computer. Percentages of correct responses and response times on correct trials were calculated.

As means of comparison for MD's results, four healthy control subjects were selected for participation in the study, taking into account to their socio-economic background and their age (mean: 69.75). None of them had a history of neurological or vascular disease, head injury or alcohol abuse, nor did they display cognitive complaints [MMSE: 30/30 (Folstein et al., 1975)].

For statistical analysis, rather than using *z*-scores, we used the modified *t*-test of Crawford and Howell (1998). Indeed, when the normative sample of control participants is small (less than 10), using *z*-scores may be misleading due to an underestimation of the variance. This bias provokes an overestimation of the *z*-score. As a consequence, there is a higher risk to erroneously conclude that the patient is impaired (type 1 error). To decrease the likelihood of this error, a more appropriate test is the modified *t*-test, as proposed by Crawford and Howell (1998). The principle of this method is to consider the control sample statistics as statistics rather than as parameters (in contrast with *z*-scores). This procedure decreases the probability of a type 1 error, as it tests whether a patient's score is significantly below controls by providing a point estimate of the abnormality of the score (a *p* value). Here we used a .05 *p* value within the framework of an unilateral hypothesis. Consequently, we will consider all comparisons leading to a *p* value under .05 as reflecting an abnormal result. We conducted analysis with a computerized version of the Crawford and Howell's method: *SINGLIMS.EXE: Point estimate and confidence limits on the abnormality of a test score* (Crawford & Garthwaite, 2002).

Perception of unfamiliar faces

In this section, we describe the tests aimed at assessing MD's perceptual face processing abilities. We began the assessment using pictures of unfamiliar faces. This allowed us to determine her

ability to merely discriminate two individual faces, and assess her response profile during tests which reflect the high-level processing of faces (face inversion effect, composite face effect, perception of relative distances between features, . . .).

Description

Faces and objects discrimination. The patient was presented with items from different categories of objects: birds, boats, cars, chairs and faces, in an experiment performed previously with a case of acquired prosopagnosia (see Schiltz et al., 2006). In a delayed two-alternative forced-choice decision task, MD was first presented, for one second, with a target stimulus belonging to one of the five categories. After an ISI (white screen) of the same duration, two probe stimuli (target and distractor) appeared, and she was asked to indicate which one had been previously presented. To encode her response, MD was asked to press a key corresponding to the position of the stimulus (i.e., right-key if right-stimulus; left-key if left-stimulus); no time constraints were applied. The distractor belonged to the same (intra-category discrimination) or to another category (inter-category discrimination). Photographs of faces were cropped (the external cues were removed). Twenty-four grey-scale pictures of each category were used in the two conditions (inter- and intra-category). The script was divided into four blocks of 60 randomized trials. The stimuli subtended approximately the following sizes, respectively in height and width: birds (6.4° × 9.9°), boats (8.5° × 9.9°), cars (5° × 9.9°), chairs (9.9° × 5.7°) and faces (9.2° × 7.1°). The pictures were displayed on a white background.

Matching faces in identical viewpoint and different viewpoint conditions. In the first experiment, we tested MD with a simultaneous matching task presenting faces in the same viewpoint. A given face picture appeared on the top of the screen with two faces located adjacently below. She was asked to choose which of the two was identical to the one on top (the two corresponding images were always different but represented the same person). Two color pictures of 16 individuals (8 females) were used. The experiment was divided into two blocks of 32 randomized trials.

The two following tests consisted of matching faces presented in different viewpoints (one full front and two ¾ profiles). MD was presented with a simultaneous as well as a delayed version of this task. In each task she was asked to match a full front target-face with one of two ¾ profile faces. Depending on task type the target was located either above both probe stimuli (simultaneous matching) or in the centre (delayed matching; 2-s presentation followed by 1s ISI). One full front and two ¾ profile colour photos cropped of external cues of 16 individuals (8 women) were used. Irrespective of task type the experiment was divided into two blocks of 32 randomly presented trials. The stimuli subtended approximately 7.1° in height and 5.7° in width, on a white background.

Face inversion effect. The face inversion effect (FIE) was originally defined as a larger decrease in recognition performance for faces than for other mono-oriented objects when they are presented upside down (Yin, 1969). The particularly large effect of inversion on the recognition of faces is thought to primarily reflect the disruption of holistic/configural face processes, i.e., the ability to integrate simultaneously the multiple features of a face into a single perceptual representation (see Farah, Wilson, Drain, & Tanaka, 1995; Rossion, 2008b). In this experiment, we tested MD's inversion effect as compared to controls. Pictures of faces or cars were presented either upright or inverted. In a simultaneous matching task (see above) a full front target-stimulus had to be matched to one of two profile stimuli, by indicating whether the left or right probe stimulus corresponded to the target (Figure 2). One full front and one ¾ profile grey-scale photo of 24 individuals (12 women) and 24 cars were used. The experiment was divided into two blocks of 72 randomized trials. The pictures of cars subtended approximately 5° in height and 7.8° in width, the pictures of faces 7.1° in height and 5.7° in width. The stimuli were displayed on a white background.

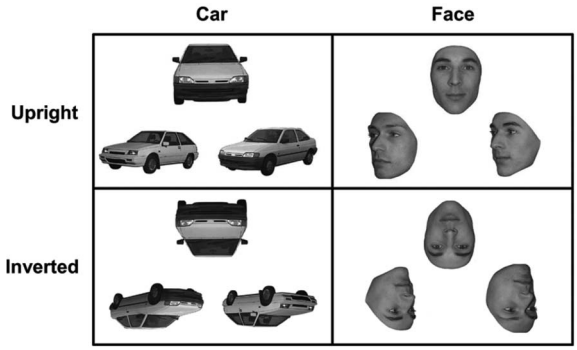

Figure 2. Example of trials used in the experiment of Face inversion effect.

Composite face effect. The composite face effect was originally described by Young, Hellawell, and Hay (1987). When unfamiliar faces are used (as in e.g., Hole, 1994; Michel, Rossion, Han, Chung, & Caldara, 2006), the effect corresponds to a visual illusion in which two identical top parts of a face are perceived as slightly different if their respective bottom parts belong to different identities (see Rossion & Boremanse, 2008). This perceptual illusion vanishes if the top and the bottom parts of the face are laterally misaligned. In the task implemented here, the composite faces were created by dividing faces into top and bottom segments by inserting a small horizontal gap in the middle of the nose and by aligning or misaligning the two parts (for further details about the making of these stimuli, see Michel et al., 2006). The small gap of 3 pixels in height (<0.1°) between top and bottom parts was used so that participants could identify the top parts to match/discriminate as easily in the aligned that in the misaligned condition.

MD completed a delayed matching task in which each trial began with the presentation of a 300-ms fixation cross at the center of the computer screen. The fixation cross was followed by a blank screen (200 ms) upon which a target face was presented for 600 ms. After a 300-ms ISI (blank screen), a second stimulus was presented for unlimited duration (Figure 3). In the first experiment (Top-part) MD was instructed to ignore the lower parts and to decide as accurately and quickly as possible whether the upper part of the second stimulus was the same or different from the upper part of the target. The same procedure was applied in a second experiment (Lower-part), in which MD was instructed to ignore the top of the faces and to judge merely the bottom face parts. Forty grey-scale photographs (20 women) were used to create the stimuli. The two experiments (Top-part and Lower-part) were divided into two blocks of 58 randomized trials each. In total, 80 trials required a 'same' decision, and the remaining 36 required a 'different' decision. This bias, equal for the aligned and misaligned conditions, was introduced because only same trials were of interest for the purposes of our study, the composite effect being assessed by the difference in performance between the misaligned and the aligned conditions for same trials (see Le Grand, Mondloch, Maurer, & Brent, 2004; Michel et al., 2006). Half of the trials were aligned, the other half misaligned. The aligned stimuli subtended approximately 9.9° in height and 7.8° in width, and the misaligned stimuli 9.9° in height and 11.3° in width. The stimuli were displayed on a gray background (128,128,128).

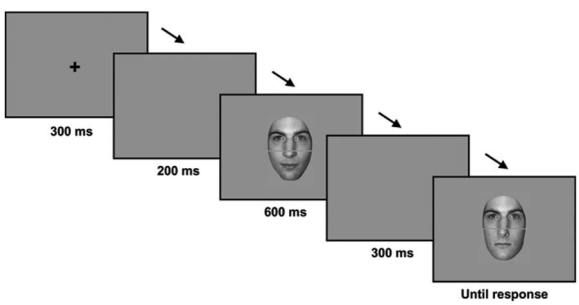

Figure 3. Illustration of time course and stimuli used in the experiment of Composite face effect.

Perception of relative distances between features in faces. This task was extracted from the work of Goffaux and Rossion (2007) to evaluate the perception of relative distances between features of faces, which are thought to provide diagnostic cues for individualizing human faces (Haig, 1984; Rhodes, 1988), in addition to local features. In the experiment, there were four randomly interleaved stimulus conditions (eyes featural, eyes vertical, eyes horizontal, and 'nose–mouth'). As usual, face stimuli were free of facial hair, glasses and hairline in order to remove any external cues to face recognition. The inner features of each face (eyes, nose and mouth in their original spatial relations) were pasted on a generic face shape. Then each stimulus was modified at the level of a feature (eyes were exchanged with those of another face and contrast-adjusted), at the level of vertical distances between features (i.e., eyes moved upward or downward), at the level of horizontal relatives distances (i.e., smaller or larger inter-ocular distance), and at the level of the nose and the mouth (nose and mouth were exchanged with those of another face) (see Goffaux & Rossion, 2007). The task involved simultaneous matching in which a target-stimulus presented in the top of the screen had to be matched with one of two probe stimuli located adjacently below (the target and one of the four modified faces of this target-face). MD indicated whether the left or right probe stimulus corresponded to the target. Twenty full-front grey-scale pictures of faces (half males) with a neutral expression were used. Each trial was repeated twice, leading to 40 trials per condition. The experiment was divided into two blocks of 80 randomized trials. The stimuli subtended

approximately 9.2° in height and 7.1° in width, on a gray background (128,128,128).

Results

Faces and objects discrimination. For the inter-category discrimination, performance was at ceiling for all participants in accuracy (mean: 98%, MD: 98%) and participants were quite fast to perform the task (mean: 832 ms, MD: 829 ms). In the intra-category discrimination, MD also showed performance within the normal range. The accuracy and the response times of MD were similar to the control participants for all conditions, including the category of faces (Figure 4).

Matching faces in identical viewpoint and different viewpoint conditions. MD obtained results comparable with the previous experiment in the three tasks requiring face matching (simultaneous matching faces in identical viewpoint, simultaneous matching faces in different viewpoints, and delayed matching faces in different viewpoints). She obtained high scores on accuracy (respectively 98, 95 and 84%), that were similar to the control participants (respectively, mean: 95, 94 and 85%). MD's response times were also in the normal range (respectively 3672, 3461 and 1537 ms) and she was sometimes even faster than the control participants (respectively, mean: 6615, 3161 and 2834 ms) (Figure 5).

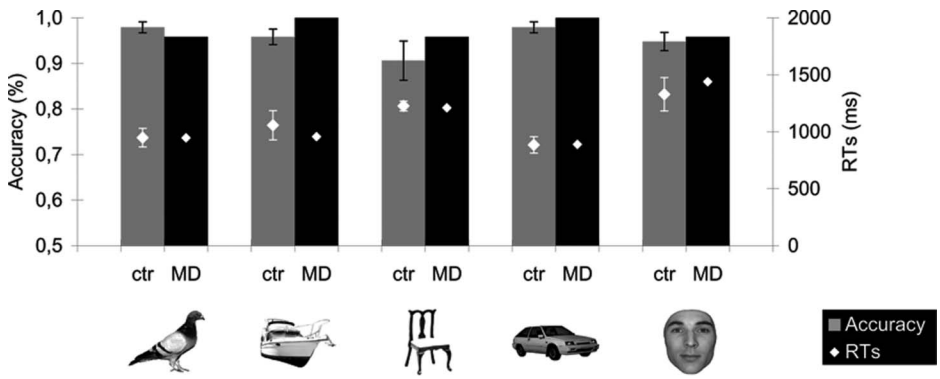

Figure 4. Results of MD and control participants ('ctr') in the faces and objects discrimination task for the intra-category condition. Accuracy and response time of MD are within the normal range in each condition (birds, boats, chairs, cars, faces). Bars represent the standard errors.

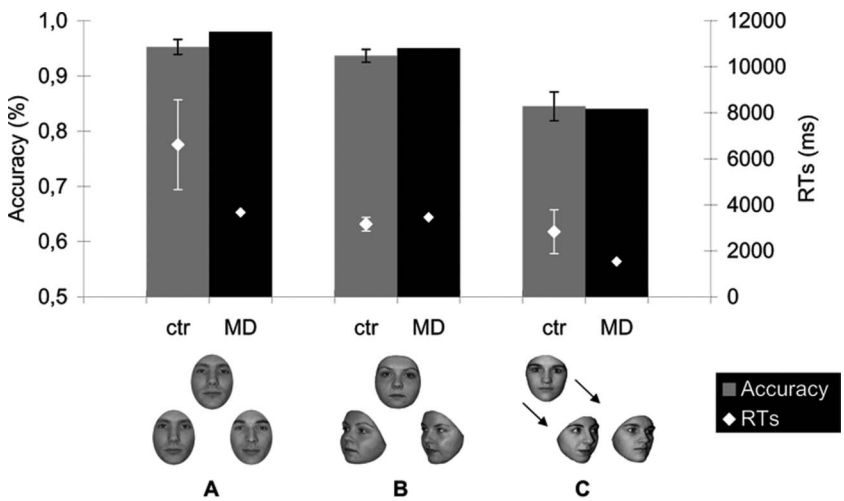

Figure 5. Results of MD and control participants ('ctr') in the three tasks of matching faces. (A) Simultaneous matching faces in identical viewpoint. (B) Simultaneous matching faces in different viewpoints. (C) Delayed matching faces in different viewpoints. Accuracy and response times of MD are similar to the control participants in the three tasks. Bars represent the standard errors.

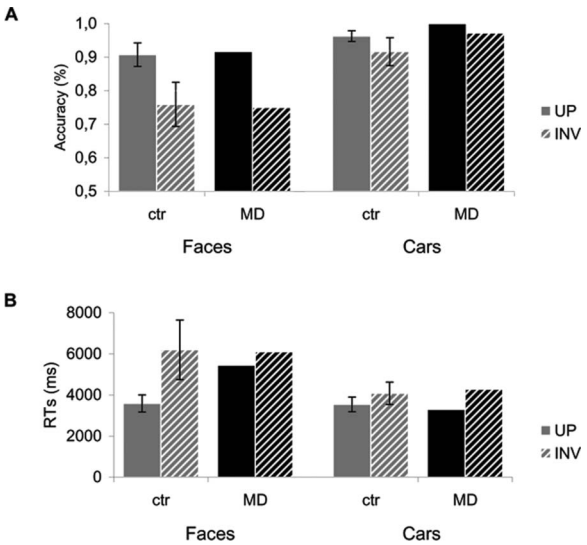

Figure 6. Results of MD and control participants ('ctr') in the task of face inversion effect. (A) Accuracy. (B) Average response times on correct trials. MD obtained similar results to the controls participants concerning accuracy and response times. Furthermore, her inversion effects (for faces and cars) are within the normal range. Bars represent the standard errors.

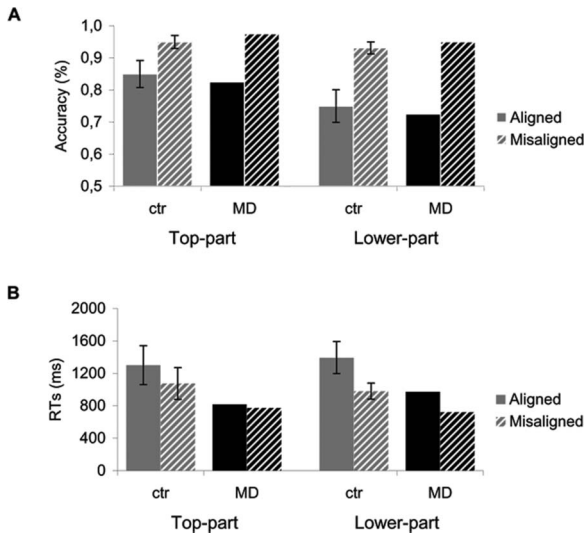

Figure 7. Results of MD and control participants ('ctr') in the task of composite face effect. (A) Accuracy. (B) Average response times on correct trials. The results of MD on accuracy and response times are within the range of the control participants. The composite effects obtained by MD in the Top-part and in the Lower-part conditions are also comparable to the controls. Bars represent the standard errors.

Face inversion effect. Concerning faces, MD obtained a profile virtually identical to that of the control participants on accuracy. In the upright condition she succeeded with 92% (mean: 91%) and in the inverted condition, her accuracy was 75% (mean: 76%) (Figure 6A). In total, her index of inversion for faces[1] revealed a 10% decrease. This index was similar to the normal participants' index (9.3%; $t = 0.065$, $p = .476$). Concerning response times, MD also responded in the normal range for speed (Figure 6B). In the upright condition, MD was slightly slower than the average of controls but this difference was not significant (MD: 5453 ms, mean: 3590 ms; $t = 1.981$, $p = .071$). In the inverted condition, she was as fast as the controls (MD: 6104 ms, mean: 6202 ms). In total, MD's index of face inversion on response time was lower than the controls but remained in the normal range, given the high variance between normal controls on this task (MD: 5.6%, mean: 22.6%; $t = -0.889$, $p = .220$).

Next, concerning pictures of cars, MD's performance was comparable to the control participants (Figures 6A&B). On accuracy, she obtained 100% in the upright condition (mean: 96%), and 97% in the inverted condition (mean: 92%). Her index of car inversion was 1.4%, which was comparable to the controls (mean: 2.6%; $t = -0.325$, $p = .383$). Regarding response times, MD was as fast as the control participants in the upright condition (MD: 3298 ms, mean: 3547 ms) as well as the inverted condition (MD: 4283 ms, mean: 4084 ms). Her index of car inversion was in the normal range (MD: 13%, mean: 6.4%; $t = 1.157$, $p = .165$).

In conclusion, we can reasonably claim that MD has a profile comparable to the controls concerning her abilities to perceive and match pictures of cars and faces. She also showed good results overall, and inversion effects that were similar in magnitude to the control participants.

Composite face effect. In the first experiment (Top-part), MD obtained normal results. On accuracy, she obtained 97.5% in the misaligned condition and 82.5% in the aligned condition, which was similar to the control participants (respectively, 95 and 85%) (Figure 7A). The indexes of the composite effect[2]

[1]Index of inversion effect was calculated by using the following formula: (Face upright – Face inverted)/(Face upright + Face inverted)

[2]Index of composite effect was calculated by using the following formula: (Misaligned – Aligned)/(Misaligned + Aligned)

were similar for MD (8.3%) and the controls (mean: 5.7%; $t = 0.447$, $p = .334$). Concerning response times, MD was faster than the control participants both for the misaligned (MD: 775 ms, mean: 1075 ms) and aligned conditions (MD: 819 ms, mean: 1302 ms) (Figure 7B). Consequently, her composite effect (2.7%) was a bit lower than the controls but did not significantly differ from the average (mean: 9%; $t = –0.687$, $p = .271$).

The results obtained by MD in the second experiment (Lower-part) are comparable to those from the previous experiment. The composite effects of MD and the controls were similar for accuracy (MD: 13.4%, mean: 11%; $t = 0.268$, $p = .403$) and response times (MD: 14.9%, mean: 16.8%; $t = –0.340$, $p = .378$) (Figures 7A,B).

In conclusion, MD presents a profile similar to the control participants and shows normal composite effects in both tasks.

Perception of distances between features. For accuracy, MD's results were within the normal range for three types of modifications (eyes featural, eyes horizontal, and nose-mouth featural) (Figure 8). For response times, she also obtained results in the normal range for all conditions. However, surprisingly, MD's performance was below the normal range in the eyes-vertical condition (MD: 71.3%, mean: 92.1%; $t = –2.297$, $p = .05$). This was the only impaired score of MD amongst all the face perception tasks. In all likelihood, these results in themselves do not reflect a perceptual face processing impairment and need to be interpreted with caution. Unfortunately we were not able to replicate these results due to MD's decision to withdraw participation in the study.

To summarize, the results showed normal global performances of MD in all tests. In comparison to the control participants, MD obtained good qualitative and quantitative results: she presented high accuracy rates and was quite fast in all tests. MD was able to discriminate faces from other objects and to match faces from same or different viewpoints, whether all items were presented simultaneously or with a delay. Furthermore, she presented face inversion and composite face effects that were in the normal range of the population, even though her effects in response times were in the lower range. These results indicate preserved holistic perception of faces. Finally, MD was able to perceive relative distances between features in faces, except for the vertical transformations for which MD obtained a poor score in comparison to the control participants. However, this was the only score which fell under the threshold. This condition, which requires estimating relative distances between features across the whole face, can be more difficult than other manipulations for ageing participants (Ramon & Rossion, in press), so that it would be difficult to argue that MD has a specific impairment of perceiving vertical distances between features.

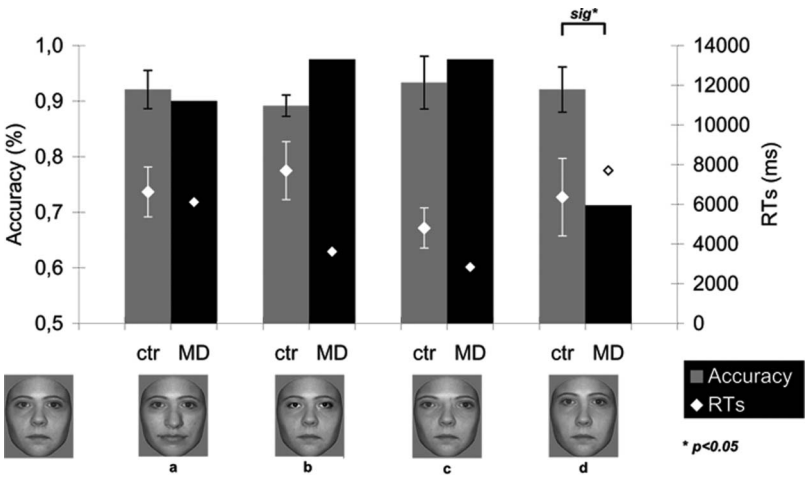

Figure 8. Results of MD and control participants ('ctr') in the task of perception of relative distances between features in faces. The performance (accuracy and RTs) of MD are within the normal range for three types of modification (A, Nose–mouth featural. B, Eyes featural. C, Eyes horizontal). MD's accuracy for the fourth condition (D, Eyes vertical) is impaired in comparison with the controls. Bars represent the standard errors.

Overall, it can be concluded that perceptive aspects of face processing seem to be globally preserved for the patient MD.

Facial expression analysis

Description

In this task, MD was presented with a set of photographs taken from the Ekman and Friesen (1975) series. Each photograph displayed one of seven possible emotional expressions (fear, anger, disgust, sadness, happiness, surprise and neutrality) (Figure 9). MD was instructed to match each face presented at the center of the screen with the best corresponding facial emotion. The answers were encoded by the experimenter with seven different keys on the keyboard. Fifteen grey-scale items of each category were repeated twice. The experiment was divided into two blocks of 105 randomized trials. The stimuli subtended 12.7° in height and 8.5° in width, on a gray background (128,128,128).

Results

MD was largely impaired in the judgment of three expressions: anger (MD: 3%, mean: 78.9%; $t = -4.041$, $p < .05$), fear (MD: 13%, mean: 81.1%; $t = -5.972$, $p < .01$), and disgust (MD: 50%, mean: 96.7%; $t = -12.657$, $p < .01$) (Figure 9). The error analysis showed that MD has a tendency to attribute the expression of anger to disgust (27% of the responses) and fear (23% of the responses) and to categorize fear as surprise (73% of the responses). The four other facial expressions (happiness, surprise, sadness and neutrality) were well recognized, her scores falling within the normal range.

Famous people recognition

Description

Yes/no familiarity task from photographs. To make a famous person recognition test for MD, we selected 100 celebrities that MD had easily recognized in the past (actors, singers, politicians, sportsmen and star presenters from the 1950–2000s), following her husband's recommendations. In the familiarity task, these 100 famous faces were paired with 100 unknown persons (of the same gender and approximately the same age that the famous persons). The photographs were selected from the web. These 200 faces were randomly presented in the center of the screen. The stimuli subtended 10.6° in height and 8.5° in width, and were displayed on a white background. MD was asked to determine whether each face was familiar or not by pressing a corresponding key (right key if familiar; left key if unfamiliar).

Identification of famous people from photographs. In this task, we again presented the 100 famous previously selected faces. MD was instructed to name the person, or, failing that, to provide as much information as possible about each famous person. If not named, a famous person was considered to be correctly identified if at least three semantic attributes were accurately provided without any errors (e.g., nationality, profession and another specific element).

Yes/no familiarity task from name. For this experiment, the names of the same 100 celebrities were selected and paired with 100 unknown names (respecting the composition and the sonority of the famous name). These 200 names were successively

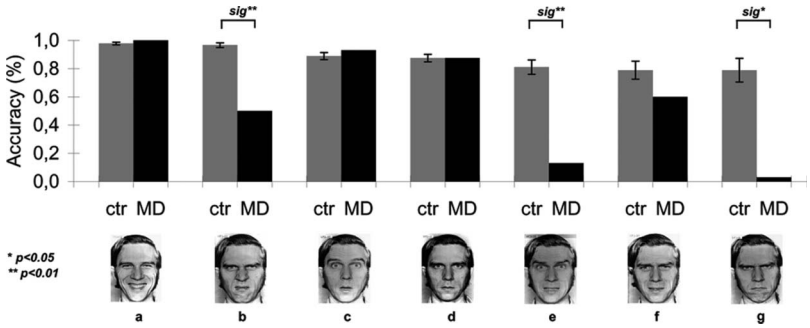

Figure 9. Results of MD and control participants ('ctr') in the facial expression analysis task. The results of MD are impaired in three conditions (B, Disgust. E, Fear. G, Anger). The performance of MD for the four other emotions is within the normal range (A, Happiness. C, Surprise. D, Neutrality. F, Sadness). Bars represent the standard errors.

presented in the center of the screen and were read aloud at the same time by the experimenter. MD was asked to determine whether each name was familiar or not by pressing the same keys than in the previous task of familiarity judgment.

Identification of famous people from name. Finally, in this fourth experiment, the names of the 100 celebrities previously selected were again presented in the center of the screen and were simultaneously read aloud by the experimenter. MD was asked to give as much information as possible about each person. The criteria for correct responses were the same as previously used.

These four tasks were proposed at different times, with a 1-week delay between each task. Furthermore, no feedback was provided to MD in order to avoid a learning effect.

Results

MD's results illustrated a massive global impairment, with poor performance on all four tasks (Figure 10). MD failed the first task in which she had to judge the face familiarity. (MD: 65%, mean: 93.8%; $t = -11.200$, $p < .01$). She was also unable to recognize the set of famous faces in the identification task (18%) whereas the control participants performed very well (mean: 94.7%; $t = -11.828$, $p < .01$). MD was also below normal range in the two tasks in which the name was provided. She failed both the familiarity task (MD: 85%, mean: 96.7%; $t = -4.186$, $p < .05$) and the identification task (MD: 37%, mean: 91%, $t = -5.682$, $p < .01$) with names. Although MD performed slightly better when the persons' names were provided, the abnormal results reveal a multimodal defect in the recognition of famous people.

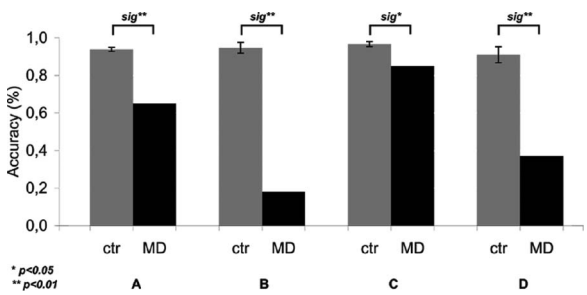

Figure 10. Results of MD and control participants ('ctr') in the famous people recognition tasks. (A) Yes/no familiarity task from photographs. (B) Identification of famous people from photographs. (C) Yes/no familiarity task from names. (D) Identification of famous people from names. The results obtained by MD are impaired in the four tasks. Bars represent the standard errors.

Processing of other visually complex entities

Description

Object decision. For this experiment, we selected 88 black and white drawings of real objects taken from the Snodgrass and Vanderwart (1980) battery, and 88 black and white drawings of non-objects taken from the Kroll and Potter (1984) battery. The stimuli were displayed in random order on a white background, and subtended approximately 7.1° × 7.1°. MD had to decide whether the stimulus represented a real object or not by pressing a corresponding key (right key if real object; left key if no-real object).

Identification of famous places from photographs. As for the famous persons test, with the help of MD's husband we selected with 30 famous places previously well-recognized by the patient (e.g., Eiffel Tower, Atomium). The colored photos were selected from the web and they were presented one-by-one in the same size in the center of the screen. MD was asked to name the 30 monuments and places, or, failing that, to provide as much information as possible about each famous place. A famous place was considered to be correctly identified if it was named or if at least two correct semantic attributes were provided (among them at least the country where the place is situated). The stimuli subtended 12° × 16° on a white background.

Identification of flowers from photographs. This test was constructed in the same way as the previous test. We selected 30 colored photographs of flowers previously easily recognized by MD and we presented them one-by-one. Again, MD was instructed to name each flower or to provide precise information about this flower. A response was considered correct if either the correct name or two semantic attributes were provided (flowering time and habitual place where it can be found). The stimuli subtended 14° × 18.6° on a white background.

Results

First, and contrary to the object decision task of the BORB (Riddoch & Humphreys, 1993) (see Table 1), MD obtained good results for the

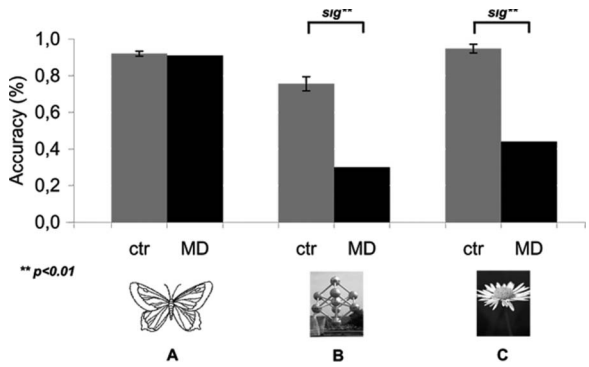

Figure 11. Results of MD and control participants ('ctr') in the tasks of processing of other visually complex entities. (A) Object decision. (B) Identification of famous places from photographs. (C) Identification of flowers from photographs. The results obtained by MD are impaired in the two last tasks. Bars represent the standard errors.

judgment of real objects and non-objects (MD: 91%, mean: 92%) (Figure 11). However, this task consisted in a basic yes/no judgment, involving fewer resources than an identification task. Concerning the two other tasks, which were naming tasks, MD obtained much poorer results. She had extremely low accuracy rates for both the famous place identification (MD: 30%, mean: 75.6%, $t = -5.297$, $p < .01$) and the flower identification (MD: 44%, mean: 94.8%, $t = -9.466$, $p < .01$) tasks.

Verbal semantic memory

Description

Identification of famous places from names. For this experiment we selected the 30 famous places that were used in the photograph identification task. We presented the names of these 30 places in the center of the screen, one at a time, while simultaneously reading them aloud. MD was asked to give as much information as possible about each monument and place. The criteria for a correct response were the same as previously used: an item was considered to be correctly identified if at least two correct semantic attributes were provided.

Identification of famous events from names. In another verbal semantic memory task we selected 30 significant and memorable events from the 1930 to 2000s. The events concerned Belgium history (e.g., the death of 40 football fans in the Heysel stadium in 1985) as well as international episodes (e.g., the Gulf War). The names of these events were presented visually and simultaneously read aloud by the experimenter. MD was asked to provide as much semantic information as possible about each event. A response was considered correct if the accurate decade was provided and if the patient was able to tell roughly what had happened.

All the tests in which the assignment of a correct required a subjective evaluation (identification of celebrities, places, flowers and events) were submitted to an inter-judge agreement between two independent persons.

Results

Regarding identification from visual inputs, MD obtained poor scores in these two tasks (Figure 12). In the identification of famous places from names, she obtained an accuracy of 43%, which was below the normal range of performance (mean: 76.7%, $t = -3.546$, $p < .05$). She also failed to identify famous events (MD: 47%, mean: 81%, $t = -3.578$, $p < .05$).

Recognition of relatives: informal testing

Description

Yes/no familiarity task from photographs. Similarly to the famous faces recognition task, we constructed new tests using MD's relatives. We collected 24 standardized photos of members of her family (children, grandchildren, daughter-in-law, son-in-law, . . .) We paired each photograph with a photograph of a person with the same gender, the same age and the same general visual characteristic (e.g., with glasses and a beard). The pictures were presented randomly in the center of the screen, subtended 10.6° × 8.5° and were displayed on a white

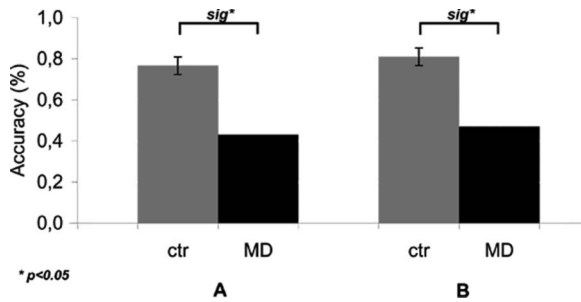

Figure 12. Results of MD and control participants ('ctr') in the verbal semantic memory tasks. (A) Identification of famous places from name. (B) Identification of famous events from name. MD obtained impaired scores in the two tasks. Bars represent the standard errors.

background. MD was asked to decide whether each person was a relative or not by pressing a corresponding key (right key if familiar; left key if unfamiliar).

Identification of relatives from photographs. The same 48 photographs collected in the previous task were also in this task. Here, MD was asked to try to identify each person. We specified that some of the people were unknown and that MD had to first choose whether the face was familiar, and then give the name of the person, or, failing that, provide as much information as possible with regard to this person. An item was considered correct if the name of the person was produced or if the right position in the family tree was given.

Yes/no familiarity task from voice. Finally, we collected voices samples from 14 of MD's relatives. We asked each person to read a short sentence, which we recorded. The 14 excerpts were paired with 14 others of unknown people (of the same gender and age). MD was presented with the 28 random excerpts and was asked to decide whether each person was a relative or not by pressing the same keys as in the previous familiarity task.

Identification of relatives from voice. In this last test, MD was again presented with the 28 previously presented voice excerpts and was asked to try to identify the person who was talking. Again, MD was informed that some of the voices were of unknown persons. The correction criteria were the same as previously used: an item was considered correct if the name of the person was produced or if the right position in the family tree was given.

For these last four tests, our objective was to test MD's husband as a control participant. Unfortunately, MD decided to end the experimental assessment before we were able to test her husband, so no control data can be provided here. Consequently, the results must be considered as qualitative indications.

Results

This last series of tests illustrates further deficits in recognition of relatives (Table 2). Although MD globally succeeded in judging the familiarity of photos of her real relatives (92%), she produced 10 false alarms. Also, in the photograph identification task, she produced 7 false alarms. These results most likely reflect abnormal functioning. Furthermore, when MD had to judge the familiarity and identify the voices of her relatives, she obtained very poor scores. In the familiarity task and in the identification task, she obtained 43 and 14%, respectively. These scores are quite striking. Even her husband's voice was not recognized. Although we cannot report any control data, these results probably reflect a dysfunction in the recognition of people from voice cues.

TABLE 2
MD's results on recognition of relatives tests

	Photo	*Voice*
Yes/no familiarity		
Relatives	0.92	0.43
unknowns	0.58	0.43
Identification		
Relatives	0.83	0.14
unknowns	0.71	0.43

FUNCTIONAL LOCALIZATION AND DESCRIPTION OF FACE-SENSITIVE AREAS

Stimuli and procedure

In addition to anatomical scans (see Figure 1), MR images of brain activity during face processing were collected from MD using a 3T Siemens Allegra headscanner. We covered most of the brain including the lower part of the anterior lobe (lowest Talairach point in the right temporal lobe: 37, –2, –31). The goal of this investigation was 2-fold. First, we aimed to test whether the areas that respond preferentially to faces in the visual cortex (Sergent, Otha, & MacDonald, 1992) had a normal level of activation. These areas concern mainly the lateral part of the middle fusiform gyrus ('fusiform face area', 'FFA', Kanwisher, McDermott, & Chun, 1997) and the inferior occipital gyrus ('occipital face area', 'OFA') (for a review see Haxby et al., 2000). They are usually activated bilaterally, but with a right hemispheric advantage in the normal brain. Second, we tested whether these areas were sensitive to individual faces using an identity face adaptation paradigm (Grill-Spector & Malach, 2001): if one face is repeated, the signal is lower in this region as compared to the presentation of a different face, revealing sensitivity to individual face representations in these areas. Using such paradigms, we previously demonstrated abnormal sensitivity to face identity in the right 'FFA' of an acquired prosopagnosic

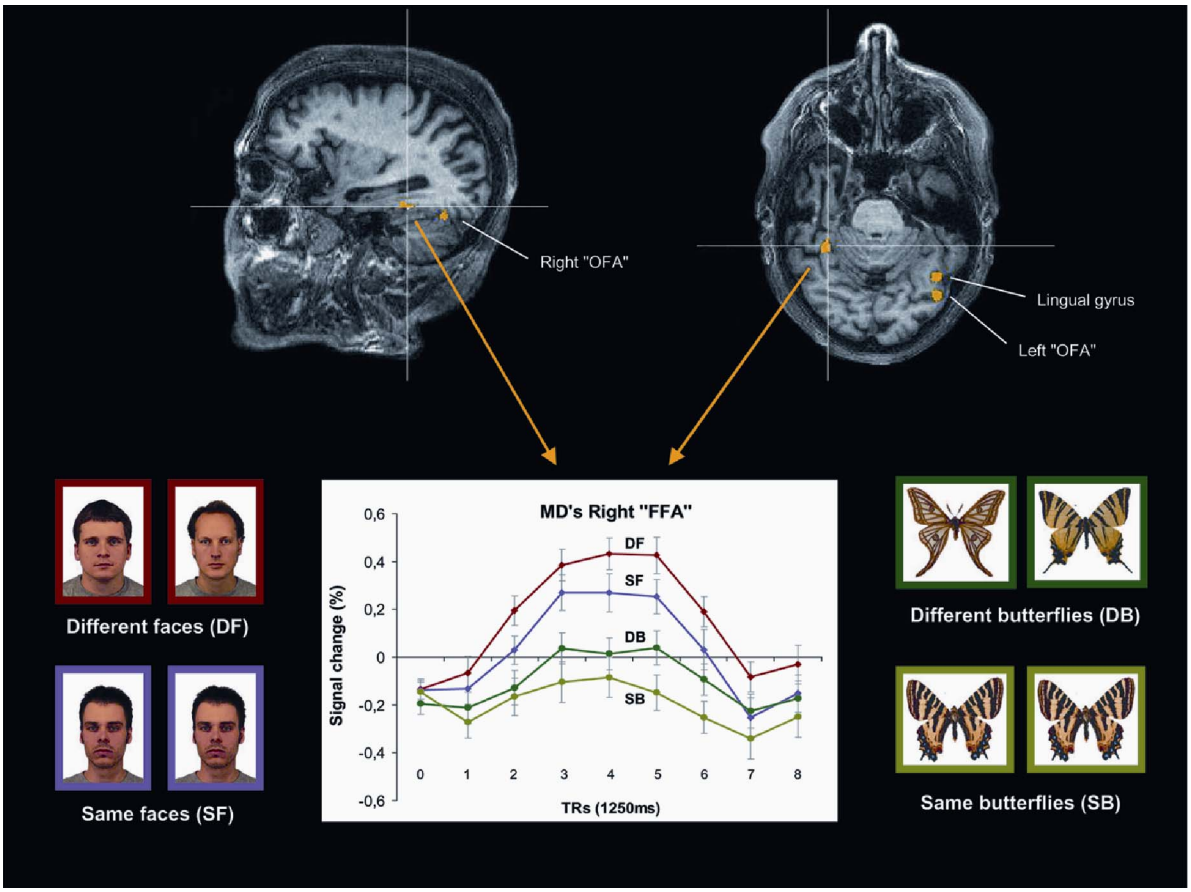

Figure 13. First, we show activations of the conjunction of the two contrast faces minus butterflies. Clusters (right 'FFA', right 'OFA', left posterior part of the lingual gyrus and probably left 'OFA'), see in the native space at p(uncorrected)<.001. The cursor indicates the location of the right 'FFA'. The third cluster (right lingual gyrus) is not visible on this figure. Next, we illustrate MD's time-course in the right 'FFA' for the 4 different conditions of the adaptation experiment. Similar to normal observers, the BOLD response was larger when pairs of different faces were presented than when the same face was repeated. This result indicates that the right 'FFA' of the patient is sensitive to individual faces. To view this figure in colour, please visit the online version of this issue.

patient (Schiltz et al., 2006; Dricot, Sorger, Schiltz, Goebel, & Rossion, 2008).

In the scanner, MD performed two runs following the protocol described by Dricot et al. (2008, Experiment 2). The two runs consisted of 80 pairs of stimuli displayed in random order in an event-related adaptation design. The stimuli were pictures of butterflies (42) and faces (38) with external features as shown in Figure 13. All images were presented in colour, and sustained a size of roughly 4° of visual angle. The stimuli were jittered in location by 40 pixels in X (5%, 1.2° visual angle) and 40 pixels in Y (7%, 1.2°) from trial-to-trial. There were four conditions of interest: two different face identities, two identical face identities, two different butterflies, two identical butterflies in the pair. A fifth condition of a butterfly followed by a face image (or the opposite order for half of the trials) was used. To be sure that MD paid attention to the stimuli, she was asked to press the response key for this latter condition – that is, to detect face-object pair trials. By collecting a response only for this condition, the conditions of interest would not be contaminated by any decisional and/or motor processes. There were 16 trials/condition/run, for a total of 80 trials in each run, and 32 trials/condition over two runs. Within a trial, the first stimulus of a pair was presented for 1000 ms following by a blank of 500 ms and thereafter by the second stimulus of the pair, which was presented for 1000 ms. The pairs were separated by a fixation cross with a duration 5000, 6250 or 7500 ms (4–6 TRs), and these ISI durations were also fully randomized. This timing ensured that the onsets of distinct events were separated by at least 6–8 TRs (7500–10000 ms) to avoid the overlapping of hemodynamic responses.

Randomization of trial order and of ISI duration further reduced any potential top–down effects of anticipation of the stimuli. Stimuli were displayed with a PC running E-prime 1.1 (PST Inc.) through a projector surface located over the head of the subject and viewed with an angled mirror.

Images of brain activity during face processing were collected from MD using a 3T head scanner (Siemens Allegra, Siemens AG, Erlangen, Germany), with repeated single-shot echo-planar imaging: repetition time (TR) = 1250 ms, 21 slices, slice thickness = 3.5 mm echo time (TE) = 50 ms, flip angle (FA) = 90°, matrix size = 64 × 64, field of view (FOV) = 224 × 224 mm^2, slice order descending and interleaved. A three-dimensional (3D) T1-weighted data set encompassing the whole brain was acquired to provide detailed anatomy (1 mm^3) thanks to a MDEFT sequence (TR = 7.92 ms, TE = 2.4 ms, FA = 15°, matrix size = 256 × 256, FOV = 256 × 256 mm^2, 176 slices, slice thickness = 1 mm, no gap, total scan time = 13 min 43 s).

The fMRI signal in the different conditions was compared using BrainVoyager QX (Version 1.9, Brain Innovation, Maastricht, The Netherlands) applying a regression analysis. Prior to analysis, the functional data sets were subjected to a series of pre-processing operations. Pre-processing consisted of a linear trend removal for excluding scanner-related signal, a temporal high-pass filtering applied to remove temporal frequencies lower than 3 cycles per run, and a correction for small inter-scan head movements by a rigid body algorithm rotating and translating each functional volume in 3D space.

Analysis

The areas responding preferentially to faces were first defined for MD: the conjunction of the contrast (faces-butterflies) between the two runs was computed in order to localize face preferential activations [notably in the right fusiform gyrus ('FFA')]; this procedure ensuring that larger activations to faces than objects identified were those consistent across the two runs. Second, the above-defined regions of interest (ROIs) were tested for fMRI-adaptation to identity in the event-related design with repeated-measures ANOVA using the contrast (different *vs.* same) for each category. The interaction between the fMRI-adaptation to butterflies and to faces was computed by the contrast: [(faces different – faces repeated) –(butterflies different – butterflies repeated)]. fMRI signals averages were also extracted and percent signal change was computed using the baseline epochs as reference for each condition. An adaptation index using the beta weights of the GLM analysis [(different – same)/(different + same)] allowing a comparison between MD and the control group, as described in Dricot et al. (2008), was computed for each category.

Conventionally, in order to be able to compare an activated brain region with the same region from previous subjects, all anatomical as well as the functional volumes are spatially normalized [Talairach-transformation; (Talairach & Tournoux, 1988)] and the statistical maps computed are overlaid to the 3D T1-weighted scans in view to calculate Talairach coordinates for all relevant activation clusters. Here we analysed first MD's results in her own native space to avoid the risk of 'brain inflation' with that Talairach transformation due to the large atrophy of her brain (see results). Nevertheless, we also performed the Talairach transformation in order to be able to compare the coordinates of the analysed regions of MD's brain to the reported coordinates in the literature.

Results

Anatomical scan

As mentioned in the description of the patient, a large atrophy of the (predominantly right) anterior temporal lobe, and to a lesser extent of the frontal lobe, was found. Also, when a comparison of the anterior (AP), posterior (PP), superior (SP), inferior (IP), right (RP) and left (LP) most extreme localizations of MD's brain was made with the same localizations of 10 subjects (age range: 25–64), a significant difference was found [modified *t*-test (Crawford & Garthwaite, 2002)] for the AP ($p < .043$), SP ($p < .044$), IP ($p < .015$) and RP (0.04) confirming again the cortical atrophy. It may be interesting to note that the same data collected in the acquired prosopagnosic patient PS (Rossion et al., 2003) are not significantly different than those of the same 10 subjects.

Functional scan

MD performed the behavioural task of indicating across-category trials at ceiling: 100%, no false alarm [control means: 94 ± 3.5% correct detection, no false alarm; (Dricot et al., 2008)]. She

responded with comparable response latencies to control subjects [controls: 599 ± 147 ms; (Dricot et al., 2008); MD: 493 ms; $t = -0.658$, $p = .273$; modified t-test (Crawford & Garthwaite, 2002)].

At q(FDR)<0.5, compared to butterflies, pictures of faces activated five bilateral regions of temporo-occipital regions (Figure 13): one region in the right internal part of the middle fusiform gyrus (region corresponding to the 'fusiform face area', 'FFA', cluster 1, 21 mm^3, 36 –54 –17 after talairach transformation), one between the right posterior part of the lingual gyrus and the right inferior occipital gyrus (cluster 2, 8 mm^3, corresponding to the 'OFA', 33 –66 –23), one between the right external part of the fusiform gyrus and the right lingual gyrus (cluster 3, 9 mm^3, 33 –42 –21), one on the left posterior part of the lingual gyrus (cluster 4, 93 mm^3, –41 –62 –16) and the last one in the left inferior occipital gyrus (cluster 5, 29 mm^3, left 'OFA' most probably, –40 –74 –14). All these activations were posterior to the damaged anterior temporal lobe. Interestingly, there was a left hemispheric dominance for the size of the activations but that activation was quite posterior.

The five above-defined regions of interest (ROIs) were tested for fMRI-adaptation to identity using the contrast (different *vs.* same) for each category. A significant adaptation ($t = 2.747$, $p < .006$) effect was found in cluster one ('FFA') (Figure 13). An almost significant adaptation effect for pictures of butterflies[3] ($t = 1.664$, $p < .096$) was also found in that cluster (without interaction). Calculating an adaptation index using the beta weights of the GLM analysis [(different – same)/(different + same)] we did not find any difference (see also note 1) between MD (Face Index = 0.111 and Object Index = 0.156) and the control group described in Dricot et al. (2008): [$t = -0.836$, $p = .221$ and respectively $t = -1.651$, $p = .080$; modified t-test (Crawford & Garthwaite, 2002)].

GENERAL DISCUSSION

Face processing in Rtv-FTLD

We report the case of a patient with right anterior temporal lobe atrophy who complains mainly of face recognition problems. How does this case study contribute to our understanding of face processing in Rtv-FTLD and its neural basis?

The initial question to ask is whether or not this case actually presents a deficit in visuo-perceptive mechanisms involved in face processing. First, when considering MD's visual face processing skills, we observed normal functioning. MD was able to discriminate faces from objects, and also to perform inter-individual face discrimination. Precisely, MD was able to make fine-grained discriminations between exemplars of different classes of objects (including faces), and to match faces, even when they were presented in different viewpoints. We also showed that MD has preserved holistic face processing abilities, unlike many reported cases of acquired prosopagnosia (e.g., Boutsen & Humphreys, 2002; Delvenne et al., 2004; Sergent & Signoret, 1992), including the progressive case of prosopagnosia reported by Joubert et al. (2003). This preserved holistic processing was illustrated by the presence of both the face inversion and composite face effects (see Rossion, 2008b). A slight deficit was observed in detecting vertical changes of eye positions (relatives distances task in faces), but this task was the hardest in all our experiments, and can be performed less well by ageing normal observers. Overall, it is difficult to claim the presence of a visual face processing deficit which can explain MD's entire profile. These observations are compatible with the view that the right anterior temporal pole is not critical for the perceptual analysis of faces (Damasio et al., 1990). In this context, we note that two Rtv-FTLD patients were described in the literature as presenting with an impairment in holistic face processing (Joubert et al., 2003; Williams et al., 2006). However, the first case, FG (Joubert et al., 2003), presents a bilateral atrophy of the posterior temporal lobe (including the fusiform gyrus), consisting of a more posterior damage than that of MD and the majority of the Rtv-FTLD patients. The site of the atrophy could, in the case of FG, explain a deficit of the perceptual aspects of face processing. The data reported on the other case, BD (Williams et al., 2006), are more surprising. This patient showed a severe anterior temporal atrophy particularly in the right hemisphere, and a marked hypometabolism in the anterior temporal poles. By means of a configural face task, the authors found a deficit in the ability to perceptually process the faces via configural information. However, this conclusion could be reinterpreted. First, the task used in the experiment was an unusual task employed to

[3]At q(FDR)<0.05, we found one cluster in the inferior occipital gyrus showing more activity for different butterflies than same butterflies but it is not a face region ($p = .251$).

evaluate configural face processing in prosopagnosia (see Boutsen & Humphreys, 2002; Saumier, Arguin, & Lassonde, 2001; Sergent & Vilemure, 1989). In the study of BD, the authors used a face masked priming paradigm in which the participants had to decide if the eyes or the mouth of a face were open or closed, measuring the influence of a primed face (congruent or incongruent) presented very briefly previously. In particular, using a priming task with short presentation times (50 ms) could be too demanding for a patient. Next, the authors omitted any mention of the accuracy obtained in the task, which is important to rule out an explanation in terms of trade-off effects. Finally, in that study, no information was available about face-preferential responses in face selective areas of BD's brain, prohibiting the exclusion of the possibility of functional defects extending to high-level visual areas.

In conclusion, the extended behavioral assessment of MD brings, for the first time, strong and replicated data revealing a case of Rtv-FTLD with preserved visual face perception processing. This observation allows us to conclude that holistic/configural face abilities can be preserved in Rtv-FTLD. Moreover, this conclusion is reinforced by a normal pattern of activation in the posterior face-sensitive areas (FFA).

Functional localization of face-sensitive areas

In addition to the behavioral experiments providing an in depth investigation of our patient's perception of individual faces, we report for the first time, to our knowledge, in such a case a localization of the regions sensitive to faces in the visual cortex. Previous studies had only reported either abnormal (e.g., Joubert et al., 2003) or normal anatomical data, for instance in the fusiform gyrus, but had not tested for functional activations. Our results demonstrate a normal sensitivity to face stimuli in both the fusiform gyrus ('FFA') and inferior occipital cortex ('OFA'). This is in line with the patient's normal face processing abilities, at least at the level of perception (of unfamiliar faces). Moreover, the right 'FFA' showed normal sensitivity to individual representations of faces, unlike what has been observed in cases of prosopagnosia with posterior lesions (Dricot et al., 2008; Schiltz et al., 2006). Since these areas are known to subtend individual face processing, and represent these faces holistically (Schiltz & Rossion, 2006), this observation is also in line with the behavior of the patient. Thus, we can safely exclude abnormal face perception abilities, from both behavioral and neural evidence, for the patient MD. Nevertheless, these visual areas may be sensitive to long-term familiar representations of faces in certain situations, showing decreases or increases to familiar faces (see Gobbini & Haxby, 2006), modulations of adaptation effects by familiarity (Henson, Shallice, & Dolan, 2000) or of holistic face processing (Harris & Aguirre, 2008). Thus, even though both our behavioral and neural observations exclude a perceptual defect for face processing in our patient, we cannot exclude that these visual areas would show abnormal profiles of activation when they depend on inputs from more anterior regions such as the right anterior temporal pole, where familiar representations would be stored (Damasio et al., 1990; Olson, Plotzker, & Ezzyat, 2007).

Cross-modal person-based semantic defect

Across this study, we showed that MD is impaired at judging familiarity and recognizing famous and personally familiar faces. However, we also showed that MD fails to judge familiarity and to recognize famous people from their names and she seems to present a deficit at identifying her relatives by their voices. Considering these observations we have to consider this case as presenting a defect that is not restricted to a prosopagnosia. We note that Damasio et al. (1990) described a form of 'amnesic associative prosopagnosia' with damage to anterior temporal lobes (bilateral, but see Sergent & Signoret, 1992 for right unilateral evidence), as patients who have preserved face perception abilities but impaired access to memory representations of faces. However, in these cases, the deficit of the patients extends to non-face recognition cues such as voice and gait, as in our patient.

On this basis, we can therefore, as Joubert et al. (2006) and Gainotti (2007), consider our patient as presenting a cross-modal person-based semantic defect. Indeed, we identified a multimodal deficit concerning individual recognition. However, we also uncovered multi-categorical difficulties. MD does not only fail to identify people, but she is also impaired across other semantic categories (identification of famous places, famous events and flowers). These deficits were shown both using visual inputs as well as verbal cues. Consequently, we probably have to consider that the cross-modal

person-based semantic defect of MD is part of a semantic dementia that is progressing. First, the neuropsychological evaluation has shown that MD presents severe semantic deficits in oral production, as well as oral comprehension and written comprehension. More specific evaluations revealed profound semantic defects for famous people and famous places (on visual and oral inputs), for famous events and for flowers. Finally, MD also presents behavioral changes, as often found in SD (Bozeat, Gregory, Lambon Ralph, & Hodges, 2000; Snowden et al., 2001). In total, MD presents nearly all of the symptoms of semantic dementia (Neary et al., 1998): insidious onset and gradual progression; language disorder characterized by fluent speech but impaired naming and comprehension; preserved visuo-perceptive abilities, single-word repetition, reading and writing; logorrhea; loss of sympathy and empathy; narrowed preoccupation; and finally predominant anterior temporal abnormality.

A reason why the profile of MD could seem less specific than previous cases (e.g., Gainotti, 2003) is that MD was seen at a stage of her disease where her cognitive symptoms were advanced enough to meet most of the clinical diagnostic criteria for semantic dementia. Moreover, based on the clinical description, the patient's person recognition deficits still seem to predominate, and MD could consequently be referred as a case of cross-modal person-based semantic defect that is progressing to a semantic dementia. Some previous well documented cases of Rtv-FTLD (e.g., Evans et al., 1995; Gainotti et al., 2003; Joubert et al., 2003, 2004, 2006; Kitchener & Hodges, 1999) bring evidence of an evolutionary progression of the symptoms in Rtv-FTLD from a relatively specific impairment to a cross-modal and multicategorial deficit. In 2003, Gainotti et al. proposed a three stage progression of Rtv-FTLD. In the very first stage of the atrophy in the right temporal pole, the deficit would be restricted to a selective form of associative prosopagnosia. Next, the second stage would be characterized by cross-modal inability to access the person-specific knowledge. The third and final stage would consist of complete disruption of person-specific knowledge and impairment of other specific categories (Gainotti et al., 2003, 2008). MD may have followed the same progression to reach the stage of her semantic dementia. In addition, a careful look at the neuroradiological data in the literature indicates that, as in the case of MD, in almost all the cases of Rtv-FTLD, the atrophy is actually bilateral, though predominant in the right hemisphere (e.g., Barbarotto et al., 1995; Gainotti et al., 2003; Gentileschi et al., 1999, 2001; Gorno-Tempini et al., 2004). One hypothesis is that these atrophies could have initiated first in the right hemisphere, and then spread to both hemispheres. Recently, Brambati et al. (2009) published a study on the progression of the atrophy in semantic dementia with asymmetric temporal involvement. They discovered that both Ltv-FTLD and Rtv-FTLD show significant progression of gray matter atrophy not only within the temporal lobe most affected at presentation, but also in the controlateral temporal regions. These results confirm a previous study of Seeley et al. (2005) that shows that within an average of 3 years, the syndromes of Ltv-FTLD and Rtv-FTLD patients begin to overlap. Concerning the Rtv-FTLD patients, the deficit progresses to semantic and language impairments. Brambati et al. conclude that Ltv-FTLD and Rtv-FTLD actually represent a unique 'merged' clinical syndrome that is finally characterized by semantic and behavioral deficits and a bilateral temporal atrophy.

CONCLUSION

This study provided a detailed analysis of a new case of Rtv-FTLD, with a focus on face processing abilities. We demonstrated that MD suffers from a cross-modal person-based semantic defect. More specifically, the body of observations presented in this study demonstrate an absence of perceptual impairment with person and object recognition in the context of a Rtv-FTLD. These findings were confirmed by fMRI data that showed a normal pattern of activation for individual faces in the case of MD that are in line with the patient's normal face processing abilities. Finally, our results are congruent with previous cases of Rtv-FTLD and seem to fall within the framework of a person-specific deficit that leads to a multi-categorical semantic impairment. The clinical interest of such an observation is obvious: the emergence of a progressive deterioration in the face-based recognition of familiar and famous people in the context of a right anterior temporal degeneration can be indicative of the slow development of a semantic dementia.

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REFERENCES

Anaki, D., Kaufman, Y., Freedman., M., & Moscovitch, M. (2007). Associative (prosop)agnosia without (apparent) perceptual deficits: A case-study. *Neuropsychologia, 45*, 1658–1671.

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

Benton, A. L., Sivan, A. B., Hamsher, K., Varney, N. R., & Spreen, O. (1983). *Benton facial recognition: Stimulus and multiple choice pictures*. Lutz: Psychological Assessment Resources Inc.

Bodamer, J. (1947). Die prosopagnosie. *Archiv für Psychiatrie und Nervenkrankheiten, 179*, 6–54. Partial English translation by Ellis, H. D., & Florence, M. (1990). *Cognitive Neuropsychology*, *7*, 81–105.

Boutsen, L., & Humphreys, G. W. (2002). Face context interferes with local part processing in a prosopagnosic patient. *Neuropsychologia, 40*, 2305–2313.

Bozeat, S., Gregory, C. A., Lambon Ralph, M. A., & Hodges, J. R. (2000). Which neuropsychiatric and behavioural features distinguish frontal and temporal variants of frontotemporal dementia from Alzheimer's disease? *Journal of Neurology, Neurosurgery, and Psychiatry, 69*, 178–186.

Brambati, S. M., Rankin, K. P., Narvid, J., Seeley, W. W., Dean, D., Rosen, H. J., Miller, B. L., Ashburner, J., & Gorno-Tempini, M. L. (2009). Atrophy progression in semantic dementia with asymmetric temporal involvement: A tensor-based morphometry study. *Neurobiology of aging, 30*, 103–111.

Buschke, H. (1973). Selective reminding for analysis of memory and learning. *Journal of Verbal Learning and Verbal Behaviour, 12*, 543–550.

Crawford, J. R., & Garthwaite, P. H. (2002). Investigation of the single case in neuropsychology: Confidence limits on the abnormality of test scores and test score differences. *Neuropsychologia, 40*, 1196–1208.

Crawford, J. R., & Howell, D. C. (1998). Comparing an individual's test score against norms derived from small samples. *The Clinical Neuropsychologist, 12*(4), 482–486.

Damasio, A. R., Tranel, D., & Damasio, H. (1990). Face agnosia and the neural substrates of memory. *Annual Review of Neuroscience, 13*, 89–109.

Davidoff, J., & Landis, T. (1990). Recognition of unfamiliar faces in prosopagnosia. *Neuropsychologia, 28*(11), 1143–1161.

Delvenne, J.-F., Seron, X., Coyette, F., & Rossion, B. (2004). Evidence for perceptual deficits in associative visual (prosop)agnosia: A single-case study. *Neuropsychologia, 42*, 597–612.

Didic, M., Felician, O., Ceccaldi, M., & Poncet, M. (1999). Les atrophies corticales focales progressives. *Revue Neurologique, 155*(4S), 73–82.

Dricot, L., Sorger, B., Schiltz, C., Goebel, R., & Rossion, B. (2008). The roles of 'face' and 'non-face' areas during individual face perception: evidence by fMRI adaptation in a brain-damaged prosopagnosic patient. *NeuroImage, 40*, 318–332.

Ekman, P., & Friesen, W. V. (1975). *Pictures of facial affect*. Palo Alto, CA: Consulting Psychologists Press.

Evans, J. J., Heggs, A. J., Antoun, N., & Hodges, J. R. (1995). Progressive prosopagnosia associated with selective right temporal lobe atrophy. *Brain, 118*, 1–13.

Farah, M. J. (1990). *Visual agnosia: Disorders of object recognition and what they tell us about normal vision*. Cambridge, MA: MIT Press.

Farah, M. J., Wilson, K. D., Drain, H. M., & Tanaka, J. R. (1995). The inverted face inversion effect in prosopagnosia: Evidence for mandatory, face-specific perceptual mechanisms. *Vision Research, 35*(14), 2089–2093.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). Mini-Mental State: A practical method for grading the state of patients for the clinician. *Journal of Psychiatric Research, 12*, 189–198.

Gainotti, G. (2007). Different patterns of famous people recognition disorders in patients with right and left anterior temporal lesions: A systematic review. *Neuropsychologia, 45*, 1591–1607.

Gainotti, G., Barbier, A., & Marra, C. (2003). Slowly progressive defect in recognition of familiar people in a patient with right anterior temporal atrophy. *Brain, 126*, 792–803.

Gainotti, G., Ferraccioli, M., Quaranta, D., & Marra, C. (2008). Cross-modal recognition disorders for persons and other unique entities in a patient with right fronto-temporal degeneration. *Cortex, 44*, 238–248.

Gentileschi, V., Sperber, S., & Spinnler, H. (1999). Progressive defective recognition of familiar people. *Neurocase, 5*, 407–424.

Gentileschi, V., Sperber, S., & Spinnler, H. (2001). Crossmodal agnosia for familiar people as a consequence of right infero-polar temporal atrophy. *Cognitive Neuropsychology, 18*(5), 439–463.

Gobbini, M. I., & Haxby, J. V. (2007). Neural systems for recognition of familiar faces. *Neuropsychologia, 45*(1), 32–41.

Goffaux, V., & Rossion, B. (2007). Face inversion disproportionately impairs the perception of vertical but not horizontal relations between features. *Journal of Experimental Psychology: Human Perception and Performance, 33*, 995–1002.

Gorno-Tempini, M. L., Rankin, K. P., Woolley, J. D., Rosen, H. J., Phengrasamy, L., & Miller, B. L. (2004). Cognitive and behavioural profile in a case of right anterior temporal lobe neurodegeneration. *Cortex, 40*, 631–644.

Grill-Spector, K., & Malach, R. (2001). fMR-adaptation: A tool for studying the functional properties of human cortical neurons. *Acta Psychologica, 107*(1–3), 293–321.

Grill-Spector, K., Henson, R., & Martin, A. (2006). Repetition and the brain: Neural models of stimulus-specific effects. *Trends in Cognitive Sciences, 10*(1), 14–23.

Grober, E., & Buschke, H. (1987). Genuine memory deficits in dementia. *Developmental Neuropsychology, 3*, 13–36.

Grossman, M. (2002). Frontotemporal dementia: A review. *Journal of the International Neuropsychological Society, 8*, 566–583.

Haig, N. D. (1984). The effect of feature displacement on face recognition. *Perception, 13*(5), 505–512.

Harris, A., & Aguirre, G. K. (2008). The representation of parts and wholes in face-selective cortex. *Journal of Cognitive Neuroscience, 20*(5), 863–878.

Haxby, J. V., Hoffman, E. A., & Gobbini, M. I. (2000). The distributed human neural system for face perception. *Trends in Cognitive Sciences, 4*(6), 223–233.

Henson, R., Shallice, T., & Dolan, R. (2000). Neuroimaging evidence for dissociable forms of repetition priming. *Science, 287*(5456), 1269–1272.

Hole, G. J. (1994). Configural factors in the perception of unfamiliar faces. *Perception, 23*(1), 65–74.

Joubert, S., Felician, O., Barbeau, E., Sontheimer, A., Barton, J. J., Ceccaldi, M., & Poncet, M. (2003). Impaired configurational processing in a case of progressive prosopagnosia associated with predominant right temporal lobe atrophy. *Brain, 126*, 2537–2550.

Joubert, S., Felician, O., Barbeau, E., Sontheimer, A., Guedj, E., Ceccaldi, M., & Poncet, M. (2004). Progressive prosopagnosia. Clinical and neuroimaging results. *Neurology, 63*, 1962–1965.

Joubert, S., Felician, O., Barbeau, E., Ranjeva J. P., Christophe, M., Didic, M., Poncet, M., & Ceccaldi, M. (2006). The right temporal lobe variant of frontotemporal dementia: Cognitive and neuroanatomical profile of three patients. *Journal of Neurology, 253*(11), 1447–1458.

Kanwisher, N., McDermott, J., & Chun, M. (1997). The fusiform face area: A module in human extrastriate cortex specialized for face perception. *The Journal of Neuroscience, 17*, 4302–4311.

Kitchener, E. G., & Hodges, J. R. (1999). Impaired knowledge of famous people end events with intact autobiographical memory in a case of progressive right temporal degeneration: Implications for the organisation of remote memory. *Cognitive Neuropsychology, 16*(6), 589–607.

Knibb, J. A., & Hodges, J. R. (2005). Semantic dementia: Losing the meaning of everything. *Practical Neurology, 5*, 236–239.

Kroll, J. F., & Potter, M. C. (1984). Recognising words, pictures and concepts: A comparison of lexical, object and reality decisions. *Journal of Verbal Learning and Verbal Behaviour, 23*, 39–66.

Le Grand, R., Mondloch, C. J., Maurer, D., & Brent, H. P. (2004). Impairment in holistic face processing following early visual deprivation. *Psychological Science, 15*, 762–768.

Mayer, E., & Rossion, B. (2007). Prosopagnosia. In O. Godefroy & J. Bogousslavsky (Eds), *The Behavioral and Cognitive Neurology of Stroke* (pp. 315–334). Cambridge University Press.

Mendez, M. F., & Ghajarnia, M. (2001). Agnosia for familiar faces and odors in a patient with right temporal lobe dysfunction. *Neurology, 57*, 519–521.

Michel, C., Rossion, B., Han, J., Chung, C.-S., & Caldara, R. (2006). Holistic processing is finely tuned for faces of our own race. *Psychological Science, 17*, 608–615.

Neary, D., Snowden, J. S., Gustafson, L., Passant, U., Stuss, D., Black, S., Freedman, M., Kertesz, A., Robert, P. H., Albert, M., Boone, K., Miller, B. L., Cummings, J., & Benson, D. F. (1998). Frontotemporal lobar degeneration: A consensus on clinical diagnostic criteria. *Neurology, 51*, 1546–1554.

Olson, I. R., Plotzker, A., & Ezzyat, Y. (2007). The enigmatic temporal pole: A review of findings on social and emotional processing. *Brain, 130*, 1718–1731.

Ramon, M., & Rossion, B. (in press). Is prosopagnosia associated with a particular impairment at processing relative distances between features, or of the eye region? A matter of knowledge. *Visual Cognition.*

Rhodes, G. (1988). Looking at faces: First-order and second-order features as determinants of facial appearance. *Perception, 17*(1), 43–63.

Riddoch, M. J., & Humphreys, G. W. (1993). *Birmingham Object Recognition Battery (BORB)*. Hove, UK: Lawrence Erlbaum.

Rossion, B. (2008a). Constraining the cortical face network by neuroimaging studies of acquired prosopagnosia. *NeuroImage, 40*, 423–426.

Rossion, B. (2008b). Picture-plane inversion leads to qualitative changes of face perception. *Acta Psychologica, 128*, 274–289.

Rossion, B., & Boremanse, A. (2008). Nonlinear relationship between holistic processing of individual faces and picture-plane rotation: Evidence from the face composite illusion. *Journal of Vision, 8*, 1–13.

Rossion, B., & Pourtois, G. (2004). Revisiting Snodgrass and Vanderwart's object databank: The role of surface detail in basic level object recognition. *Perception, 33*, 217–236.

Rossion, B., Caldara, R., Seghier, M., Schuller A.-M., Lazeyras, F., & Mayer, E. (2003). A network of occipito-temporal face-sensitive areas besides the right middle fusiform gyrus is necessary for normal face processing. *Brain, 126*, 2381–2395.

Saumier, D., Arguin, M., & Lassonde, M. (2001). Prosopagnosia: A case study involving problems in processing configural information. *Brain and Cognition, 46*, 255–316.

Schiltz, C., & Rossion, B. (2006). Faces are represented holistically in the human occipito-temporal cortex. *Neuroimage, 32*(3), 1385–1394.

Schiltz, C., Sorger, B., Caldara, R., Ahmed F., Mayer, E., Goebel, R., & Rossion, B. (2006). Impaired face discrimination in acquired prosopagnosia is associated with abnormal response to individual faces in the right middle fusiform gyrus. *Cerebral Cortex, 16*, 574–586.

Schneider, W., Eschman, A., & Zuccolotto, A. (2002). *E-Prime Reference Guide*. Pittsburgh, PA: Psychology Software Tools Inc.

Seeley, W. W., Bauer, A. M., Miller, B. L., Gorno-Tempini, M. L., Kramer, J. H., Weiner, D. M., & Rosen, H. J. (2005). The natural history of temporal variant frontotemporal dementia. *Neurology, 64*(8), 1384–1390.

Sergent, J., & Signoret, J.-L. (1992). Varieties of functional deficits in prosopagnosia. *Cerebral Cortex, 2*, 375–388.

Sergent, J., & Villemure, J. G. (1989). Prosopagnosia in a right hemispherectomized patient. *Brain, 112*(4), 975–995.

Sergent, J., Otha, S., & MacDonald, B. (1992). Functional neuroanatomy of face and object processing.

A positron emission tomography study. *Brain, 115*, 15–36.

Simons, J. S., Graham, K. S., Galton, C. J., Patterson, K., & Hodges, J. R. (2001). Semantic knowledge and episodic memory for faces in semantic dementia. *Neuropsychology, 15*(1), 101–114.

Snodgrass, J. G., & Vanderwart, M. (1980). A standardised set of 260 pictures: Norms for name agreement, familiarity and visual complexity. *Journal of Experimental Psychology: Human Perception and Performance, 6*, 174–215.

Snowden, J. S., Neary, D., & Mann, D. M. A. (1996). *Frontemporal lobar degeneration: Frontotemporal dementia, progressive aphasia, semantic dementia*. London: Churchill Livingstone.

Snowden, J. S., Bathgate, D., Varma, A., Blackshaw, A., Gibbons, Z. C., & Neary, D. (2001). Distinct behavioural profiles in frontotemporal dementia and semantic dementia. *Journal of Neurology, Neurosurgery, and Psychiatry, 70*, 323–332.

Talairach G., & Tournoux, P. (1988) *Co-planar stereotaxic atlas of the human brain*. New York: Thieme Verlag.

Thompson, S. A., Patterson, K., & Hodges, J. R. (2003). Left/right asymmetry of atrophy in semantic dementia. Behavioral-cognitive implications. *Neurology, 61*, 1196–1203.

Thompson, S. A., Graham, K. S., Williams, G., Patterson, K., Kapur, N., & Hodges, J. R. (2004). Dissociating person-specific from general semantic knowledge: Roles of the left and right temporal lobes. *Neuropsychologia, 42*, 359–370.

Tyrrell, P. J., Warrington, E. K., Frackowiak, R. S. J., & Rossor, M. N. (1990). Progressive degeneration of the right temporal lobe studied with positron emission tomography. *Journal of Neurology, Neurosurgery, and Psychiatry, 53*, 1046–1050.

Verstichel, P. (2005). Hyperfamiliarité stéréotypée pour les visages au cours d'une démence fronto-temporale avec prosopagnosie. *Revue Neurologique, 161*(8–9), 804–816.

Warrington, E. K. (1984). *Recognition Memory Test*. Windsor, Berkshire: NFER.

Weschler, D. (1989). *Echelle d'intelligence de Weschler pour adulte, forme révisée*. Paris: Les éditions du Centre de Psychologie appliquée.

Weschler, D. (2001). *Echelle clinique de mémoire de Weschler MEM III (WMS-III)*. Paris: Les éditions du Centre de Psychologie appliquée.

Williams, M. A., Savage, G., & Halmagyl, M. (2006). Abnormal configural face perception in a patient with right anterior temporal lobe atrophy. *Neurocase, 12*, 286–291.

Yin, R. K. (1969). Looking at upside-down faces. *Journal of Experimental Psychology, 81*, 41–145.

Young, A. W., Hellawell, D., & Hay, D. C. (1987). Configural information in face perception. *Perception, 16*, 747–759.