Progressive prosopagnosia

Clinical and neuroimaging results

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Abstract—The authors report the longitudinal case study of a patient with the right temporal variant of frontotemporal lobar degeneration. His deficit, initially limited to visuoperceptual disturbances, progressed 2 years later to a severe semantic breakdown. Neuroimaging data indicate that the underlying degenerative process, initially confined to unimodal visual associative cortices, progressed along the ventral pathways to multimodal areas in charge of integrating knowledge from various modalities (the anterior temporal lobes).

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Progressive prosopagnosia is a clinical syndrome that is characterized by a progressive and selective inability to recognize and identify faces of familiar persons. In aperceptive prosopagnosia, functional damage may occur at various levels of visuoperceptual processing, while associative prosopagnosia is characterized by an inability to access the stored semantic representations of known persons.[1] In most case reports of patients who presented with a progressive inability to recognize familiar faces, the deficit reflected a multi-modal loss of person-based knowledge,[2-5] thus not only limited to the visual modality. In all these studies, this distinctive clinical syndrome was associated with a locus of atrophy that predominated in the anterior and inferior portion of the right temporal lobe. This progressive condition, which affects selectively one domain of semantic knowledge, was considered by some authors to reflect a right hemisphere variant of semantic dementia,[2,5,6] a syndrome that affects largely similar regions of the left temporal lobe.[7,8]

Recently, we reported the case of a patient with progressive prosopagnosia whose deficit was limited to the recognition of familiar faces, but was not semantic (cross-modal) in nature.[9] His inability to recognize familiar and newly learned faces was found to result from an inability to build a global configurational representation of visually complex entities. A more in-depth evaluation had shown that his perceptual deficit extended to other classes of visually complex patterns such as certain biologic entities or monuments. Volumetric measurements of his temporal lobe structures (structural MRI) showed that the regions found to be most affected by the underlying atrophic process were located in the right posterior temporal lobe regions.[9] This led us to suggest that the right temporal variant of frontotemporal lobar degeneration (RtvFTLD) may be characterized during several years, at least in some patients, by a selective high-level visuoperceptual deficit resulting in prosopagnosia and mild visual agnosia.

In the present article, we report the longitudinal neuropsychological follow-up study of the same patient, 2 years later, along with new volumetric measurements of his cortical atrophy.

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Case study. The patient, a right-handed man, first came to the Service de Neurologie et de Neuropsychologie (Marseille, France) in 2001, at the age of 71, because he had been encountering increasing difficulties over the past 5 years in recognizing the faces of relatives, friends, and famous people he saw on television and magazines. Although his deficit had remained relatively stable in 2002, his face recognition deficit had worsened when he returned to the Service in 2003. He could not recognize at this stage close family members and was unable to recognize a photograph of his own face taken the day before and presented to him on three separate occasions. Furthermore, the patient had also lost considerable knowledge about familiar persons and famous celebrities. He did not remember the neurologist or the neuropsychologist with whom he had spent much time over the past 2 years, and could not recollect information regarding many of his friends and acquaintances. There was no behavioral change. Speech was fluent and well-structured, without any word-finding difficulties or paraphasias. Speech and behavior were not self-centered and stereotypical, as is typically found in semantic dementia. To this day, he is very aware and insightful of his difficulties.

General neuropsychological evaluation. The general neuropsychological evaluation undertaken in 2003 is summarized in table 1 and supplementary table E-1 (available on the *Neurology* Web site at www.neurology.org). When compared with the initial evaluation carried out 2 years before,[9] the patient's general intellectual and cognitive abilities had worsened noticeably: his global IQ score had fallen by more than 40 points. Furthermore, his global MQ score had fallen below 50 (<1st percentile), thus high-

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Table 1 *Neuropsychological profile over a period of 2 years*

	2001/2002	2003
Mini-Mental State Examination (30)	28	28
WAIS-R		
Verbal IQ	127 (96th percentile)	99 (47th percentile)
Performance IQ	122 (93rd percentile)	73 (4th percentile)
Full scale IQ	128 (97th percentile)	86 (18th percentile)
Executive functioning (WCST, Stroop test, TMT A and B)	Normal	Normal
Language (text comprehension, naming, reading)	Normal	Impaired picture naming
Visual perception		
Visual Object and Space Perception Battery	Impaired object perception Normal space perception	Impaired object perception Normal space perception
Episodic memory		
WMS-R	MQ	MQ
Verbal memory	90	63*
Visual memory	92	54*
Global memory	84	<50*
Attention/concentration	123	101
Delayed recall	75	50*
Semantic memory		
Pyramids and Palm Trees Test—visual	40*	37*
Test of famous persons		
Naming photographs	4/40*	1/40* Mean control = 36/40
Identification from photographs	7/40*	1/40* Mean control = 38/40
Identification from name	38/40	17/40* Mean control = 37.5/40

The test of famous persons was developed in the Service.

* Impaired scores.

WAIS-R = Wechsler Adult Intelligence Scale–Revised; WCST = Wisconsin Card Sorting Test; TMT = Trail Making Test; WMS-R = Wechsler Memory Scale–Revised.

lighting the severity and the aggravation of his memory impairment. Language, praxis, and executive functions, however, remained unaffected overall.

Semantic memory. The patient underwent a detailed examination of his general semantic memory. In order to test specifically his semantic knowledge of famous persons, he underwent a test in which he was asked to name and identify 40 famous celebrities from their photographs (visual modality) and from their names (verbal modality). In order to test other domains of knowledge, he underwent a detailed semantic memory battery. Results show that he was impaired in all domains of semantic memory, although his deficit was remarkably more pronounced for people. Results are presented in table 1 and table E-1 (available at www.neurology.org).

MR imaging. Results of a previous study showed that the patient's atrophy predominated in the right fusiform gyrus and right parahippocampal cortex, while anterior temporopolar regions remained relatively spared.[9] The patient underwent new volumetric measurements of his temporal lobe structures in 2003. Images were acquired on a 1.5 T Symphony system (Siemens, Erlangen) using a standard head coil and a tilted axial three-dimensional gradient echo sequence (magnetization-prepared rapid gradient echo: repetition time 2,160 msec, echo time 4.88 msec, inversion time 1,100 msec, flip angle 15°, field of view 256, matrix 230 × 256, slice number 144, slice thickness 1.5 mm) resulting in contiguous T1-weighted axial images parallel to the long axis of both hippocampi. Results are presented in table 2. Structural MRI analyses show that the extent of atrophy in posterior temporal lobe structures has remained relatively stable since the initial volumetric analyses. The main finding, in contrast, is that the anterior temporal regions have undergone extensive damage since the initial evaluation. The patient's widespread bilateral temporopolar atrophy is illustrated in the figure, A.

SPECT. Subtraction of SPECT data between 2001 and 2003 (2001–2003) indicates that significant changes in cortical perfusion during this time period include the right temporopolar region and the right posterior and inferior temporal lobe. Clearly, the regions most affected in this patient are located along the ventral visual pathway. Results are presented in the figure, B.

Discussion. We report the longitudinal neuropsychological, neuroimaging, and SPECT follow-up

Table 2 *Structural MRI results of the patient's temporal lobe structures in 2002 and 2003*

	Normalized volumes (expressed in mm^3)		% Volume loss 2003–2002
	2002	2003	
Left temporopolar cortex	3,976	2,283	43
Right temporopolar cortex	2,727	1,963	28
Left fusiform gyrus	2,892	2,518	13
Right fusiform gyrus	1,259	1,259	0
Left parahippocampal cortex	992	886	11
Right parahippocampal cortex	406	357	12
Left hippocampus	2,035	1,535	25
Right hippocampus	1,438	1,168	19

The right column expresses the percentage of volume loss in these structures over this given period of time. Results indicate that the anterior temporopolar region has experienced the most damage, while posterior temporal regions remained relatively unchanged. Volumetric analyses presented below were carried out on the same MRI in 2002 and 2003, while the MRI used in our previous study was different (differences in volumes differ by less than 2% between the two MRIs).

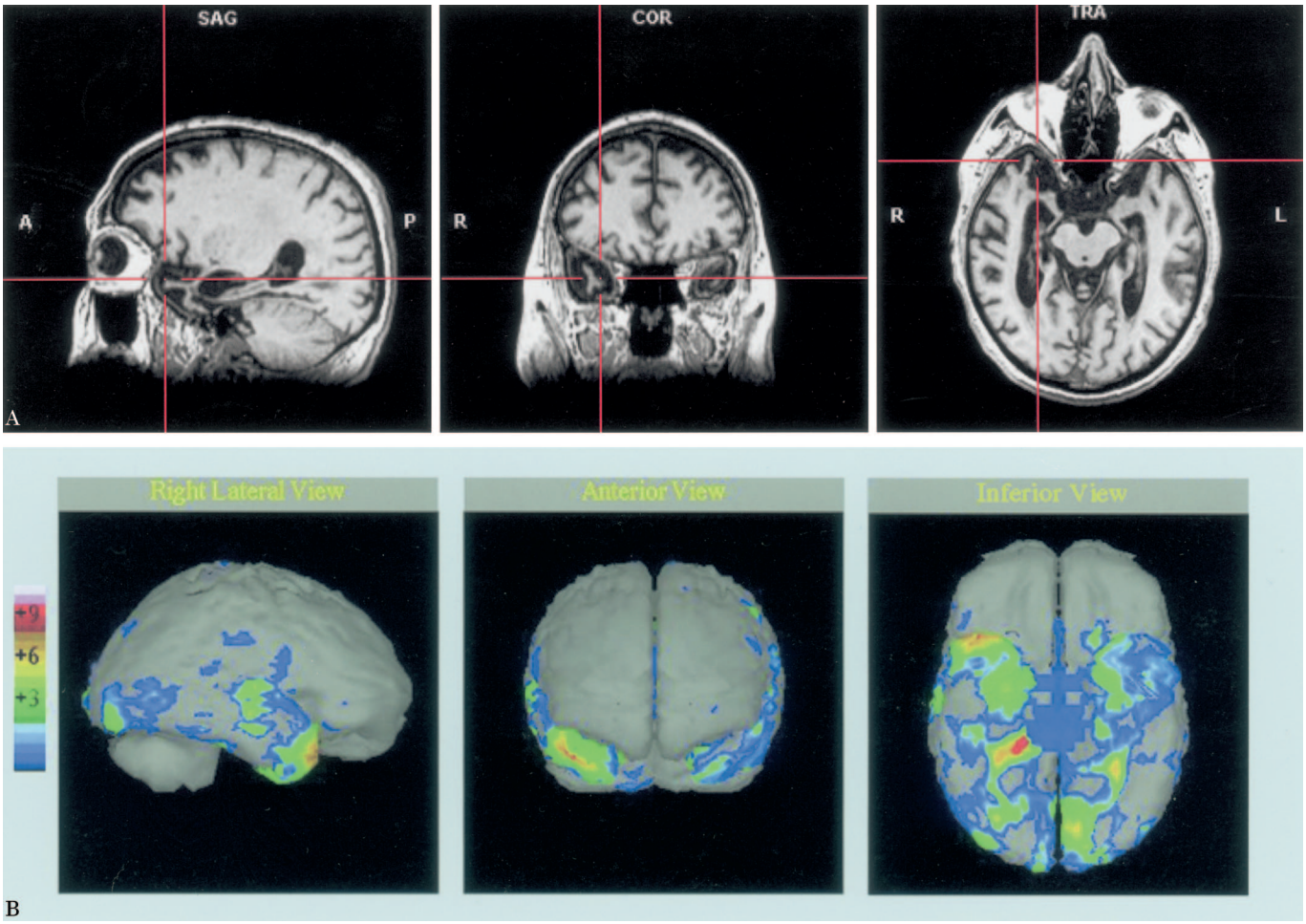

Figure. (A) Three-dimensional MRI carried out at the time of the last neuropsychological evaluation (2003). Significant atrophy of the right and left temporal poles is clearly visible on the sections. The patient's brain was imaged with a 1.5 T Magnetom (Siemens, Erlangen, Germany) using a standard head coil and tilted coronal gradient echo sequence. The sagittal section presented above is in the right hemisphere. (B) SPECT was performed in a double-head gamma camera (DST; Sopha Medical Vision International) equipped with fan-beam collimators. SPECT was performed 1 hour after IV injection of 740 MBq ^{99m}Tc-ethylcysteinate dimer (ECD). SPECT images presented above show a year 2001 minus year 2003 three-dimensional subtraction after normalization to the Talairach Space performed by NEUROGAM (SEGAMI). Areas most affected include the right temporopolar region and the right posterior temporal region. Right is left (radiologic convention).

study of a patient presenting with the RtvFTLD. During the initial stages of his disease, the patient presented with aperceptive prosopagnosia, associated with a pattern of atrophy that involved primarily the right fusiform gyrus and parahippocampal cortex.[9]

A subsequent neuropsychological evaluation carried out 2 years later indicates that his general cognitive and intellectual abilities have declined considerably. His prosopagnosia, which was initially confined to the visual modality, developed into a cross-modal, person-based, recognition deficit. Thus, in addition to not recognizing the faces of familiar persons, he does not remember them. In addition, the same categories of objects that were initially affected by his visuoperceptual disturbances (animals and biologic entities, famous public events, and famous monuments) were concerned 2 years later by his semantic deficit, to a greater extent than other categories, thus highlighting a consistent progression of breakdown along a perceptual to semantic continuum. The evolution could also be interpreted as reflecting a progression of damage from a unimodal system devoted to visual semantics to a multimodal semantics system.

Volumetric MRI and SPECT results are in agreement with the neuropsychological data. The cognitive decline from perceptual to semantic deficits is associated with a posterior to anterior progression of temporal lobe atrophy and cortical perfusion. Furthermore, results of this study support the view that the right anterior and inferior temporal polar region seems to play a role in the integration of person-based semantic knowledge and that the left and right temporal poles contribute together to more general semantic knowledge, including knowledge about biologic entities. This study corroborates previously reported cases in the literature, where progressive associative prosopagnosia was associated with predominantly right anterior temporal lobe atrophy.[2-6,10]

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