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AGNOSIA FOR GLOBAL PATTERNS: WHEN THE CROSS-TALK BETWEEN GROUPING AND VISUAL SELECTIVE ATTENTION FAILS

Carolina Piccini, Rosapia Lauro-Grotto, Maria Michela Del Viva, and David Burr
University of Florence, Italy

We present a single case study of a 72-year-old mild AD patient, MC, with a highly specific deficit in deriving the global pattern of visual stimuli, in the absence of visuospatial neglect. MC shows a specific difficulty in segregating overlapping figures, in object decision, and in all neuropsychological tasks requiring perception of a global structure from local cues, such as the Street Completion Test and the perception of illusory contours and of the global level of hierarchical stimuli. The detailed neuropsychological assessment prompted a psychophysical experiment aiming to quantify the limits of perceptual grouping in MC. We measured the thresholds of integration for a closed chain of Gabor Patches as a function of background noise using stimuli with different values of the distance between the local elements. When compared to normal controls, the patient displays a statistically significant drop of performance for stimuli with the larger interelement distance. The data are interpreted in the context of the "association field" theory (Field, Hayes, & Hess, 1993). As MC presents with a marked atrophy of the right temporoparietal junction, we interpret our data as providing further evidence of a neuromodulatory role of the right temporoparietal junction over the occipital cortices, in line with recent functional evidence (Fink et al., 1997a). The study also highlights the benefits of complementing classical neuropsychological investigations with more quantitative psychophysical procedures.

INTRODUCTION

The huge amount of data on the functional segregation of visual processing collected in the last decades does not provide a conclusive account of the mechanisms that mediate the emergence of a unitary percept (Palmer, 1999; Van Essen, Anderson, & Felleman, 1992; Wandell, 1995). The Gestalt psychologists were the first to investigate more specifically the relationship between the perception of the whole and that of its constituent parts and pointed to the primacy of the former over the latter (Koffka, 1935). They proposed sensible rules such as good continuation, proximity, similarity, common fate, or closure, which represent a phenomenological basis for global perception, but still lack a proper neurophysiological counterpart (Polat, 1999).

Visual integration has been investigated either by studying contour integration and figure–ground segregation (Driver, Davis, Russel, Turatto, & Freeman, 2001; Field et al., 1993; Giersch , Humphreys, Boucart, & Kovacs, 2000; Saarineen, Levi, & Shen, 1997) or by addressing the related issue of the hierarchical organisation (local–global) of the visual scenes, the so-called "trees and forest" problem (Navon, 1977; Rafal & Robertson, 1995; Robertson & Delis, 1986; Robertson & Lamb, 1991).

Requests for reprints should be addressed to Carolina Piccini MD, Dept of Neurological and Psychiatric Sciences, University of Florence, Viale Morgagni 85, 50134, Florence, Italy (Tel/fax: 0039-55-415044; Email: carolina.piccini@unifi.it).

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More recent experimental studies directly addressed this issue by comparing reaction times (RTs) to the detection of the global or local level of hierarchical stimuli, such as letters made up of much smaller letters (Navon, 1977); these stimuli were used in order to reflect the perceptual organisation of a visual scene and to explore whether the perception of a visual array proceeds from a coarse to a fine-grained analysis or, vice versa, from basic units to the whole. A sophisticated chronometric analysis of the subjects' performance in similar tasks lead to the hypothesis of *global precedence*, that is, the putative advantage for the visual processing of the whole with respect to the constituent parts (Hughes, Nozawa, & Kitterle, 1996; Navon, 1977). However, global precedence is not a mandatory phenomenon; given the appropriate experimental manipulations it can be abolished if not reversed, giving rise to *local precedence* (Hughes et al., 1996; Kimchi, 1992; Polster & Rapcsak, 1994; Robertson & Lamb, 1991).

The experimental results on global precedence prompted the debate on two topics, among others, that are central to the present work: The first is the role of attentional versus purely perceptual factors in determining the pattern of results collected with hierarchical stimuli (Lamb, Robertson, & Knight, 1990; Robertson & Lamb, 1991; Robertson, Lamb, & Knight, 1988); the second is the differential role that the right and left hemisphere would have in the elaboration of the visual information presented at the global and the local level respectively (Lamb, Robertson, & Knight, 1989). A series of clinical observations on patients with unilateral cerebral lesions already pointed to a different style of the two hemispheres in processing information (Kaplan, 1976). In drawing hierarchical figures from memory, RH-damaged patients displayed a tendency to report the local elements and break the overall configuration, while LH-damaged patients correctly report the global pattern, losing the local details (Brown & Kosslyn, 1993; Delis, Robertson, & Efron, 1986). The anatomofunctional relationship among right and left lesions and the impairment of global and local processing was further investigated by shifting to a RT paradigm in the study of subjects with chronic, unilateral single lesions either of the temporoparietal junction (TPJ) or of the inferior parietal lobule (Robertson et al., 1988). Abnormal global and local bias in recognising hierarchical stimuli occurred only for the TPJ patients group, that is, right TPJ-damaged patients showed significantly longer RTs in processing global information, while left TPJ-damaged patients were significantly slower in identifying the local level (Rafal & Robertson, 1995).

An important source of evidence in this respect is constituted by the study of groups of patients with focal unilateral lesions at the level either of the temporoparietal junction or of the inferior parietal lobule (Lamb et al., 1989, 1990; Robertson et al., 1988). The acquired neuropsychological data have been considered as suggestive of specific anatomofunctional relationships and lead to the definition of a detailed cognitive model highlighting the central role of the interaction between attentional and perceptual mechanisms and providing elements for their localisation. The model postulates the existence of two neural subsystems located at the level of the temporoparietal junctions in the right and left hemispheres; the right subsystem would be preferentially involved in the elaboration of the global level while the left would focus on the local level. Furthermore the model assumes a control mechanism acting over the attentional resources, located in the inferoparietal cortex bilaterally, and finally it attributes to the callosal temporotemporal connections the mediation of the interaction, and of the interference, between the subsystems (Robertson & Lamb, 1991).

A different source of evidence on the issue of global/local processing comes from the study of patients with a specific deficit in integrating visual local information in a coherent whole. Already described as a form of fragmentary perception in some classical descriptions (Luria, 1966; Pick, 1908), this pattern of visual agnosia has been first identified as "integrative agnosia" by Humphreys and Riddoch in describing the patient HJA (Humphreys & Riddoch, 1987; Riddoch & Humphreys, 1987). The term integrative agnosia refers to a pattern of visual agnosia where the subject, who is able to recognise the component parts of an object, is incapable of putting them together in a unitary percept. Almost all the patients who have been described (Butter & Trobe, 1994; Grailet, Seron, Bruyer, Coyette, & Frederix, 1990; Kartsounis & Warrington, 1991; Riddoch & Humphreys, 1987; Thaiss & De Bleser, 1992) presented visual agnosia and prosopagnosia despite having preserved visual basic perception (as measured by judging line orientation, in size and shape discrimination tasks, etc.); the visual recognition impairment was mainly characterised by the adoption of a feature-by-feature naming strategy, by difficulties in segregating overlapping figures and in making object decision of real and chimaerical items, as well as by resorting to a slavish reproduction of drawings in the cases where constructional praxis was preserved. All these features point to a specific problem in grouping local form information. A few other cases, sharing some of the neuropsychological features of the integrative agnosic patients, present with a visual recognition impairment that is dependent on the size of the stimulus (Saffran, Fitzpatrick-DeSalme, & Coslett, 1990; Stark, Grafman, & Fertig, 1997). A reduction of the attentional spotlight (Eriksen & St. James, 1986; Eriksen & Yeh, 1985; Umiltà, 1988) has been proposed as an explanation for this type of deficit, which is frequently referred to as "agnosia for larger figures" (Saffran et al., 1990; Stark et al., 1997; Thaiss & De Bleser, 1992).

Recent functional neuroimaging studies have complemented data deriving from studies on groups of patients with unilateral lesions. In a recent series of PET studies Fink and coworkers attempted to provide a more detailed description of the areas involved in the elaboration of hierarchical stimuli of the Navon type (Fink et al., 1996, 1997a, 1997b, 1999). In a directed attention task they detected an activation asymmetry in early visual processing: Global processing corresponded to a significant increase of cerebral blood flow in the right lingual gyrus, while attending to local attributes exerted an increase in the left inferior occipital cortex (Fink et al., 1996, 1997a). Furthermore, shifting from a directed to a divided attention task, the authors found an activation of the right temporoparietal–occipital junction (Brodmann Areas 39–19) and of the left superior temporal gyrus (Brodmann Areas 22–39), which covaried with the attentional cost of the task, as measured by the number of target switches between the local and the global level required in the experimental procedure (Fink et al., 1997a). They suggested that "damage to the temporo-parietal cortex can accordingly impair either global or local processing because of the attentional control that these areas exert over the computations performed in prestriate cortex" (Fink et al., 1996, 1997a, 1999). Further research, using hierarchical object-based visual stimuli instead of letter-based, showed a reversal of hemispheric asymmetry in early visual cortex, depending on stimulus category; this finding has been interpreted as the result of a top-down effect due to the left hemisphere specialisation for language and the right hemisphere specialisation for object perception (Fink et al., 1997b). Among various investigated variables, greater attention has been paid to the role of spatial frequencies with respect to the issue of hemispheric specialisation in global and local processing (see Grabowska & Nowicka, 1996, for a review; Hughes et al., 1996). In the so-called spatial frequency account, the privileged access of the right hemisphere to global information is assumed to derive from its purported higher sensitivity to low spatial frequencies (Sergent, 1982, 1983; Shulman, Sullivan, Gish, & Sakoda, 1986; Shulman & Wilson, 1987). Subsequent studies have reported controversial results emphasising the relevance of methodological variables as the major source of such variability and reshuffling the idea that global processing and low spatial frequency processing are equivalent (Grabowska & Nowicka, 1996). In particular, asymmetries may emerge for complex stimuli (two overlapping gratings vs. simple gratings, see Kitterle, Christman, & Conesa, 1995) or more demanding tasks (identification vs. detection of simple gratings, see Kitterle, Christman, & Hellige, 1990).

Very recent neuroimaging studies devoted to exploring the relationship among hemispheric asymmetry and spatial frequencies showed a pattern of activation reversed with respect to the expected one (Fink et al., 1999). Fink et al. reported an activation of the right hemisphere for global processing of high spatial frequency stimuli in subjects reporting the orientation either of the global or the local level of hierarchical nonrepresentational stimuli at high or low spatial frequencies. In order to explain such results, the authors have further explored the perceptual characteristics of the stimuli and, following the results of a reaction-time study employing the same stimuli used in the PET experiment, have identified the relative spacing among the components of the stimuli as the characteristic that plays the major role in determining their visual salience, and hence the pattern of activation. In conclusion, neuroimaging studies have confirmed the presence of an asymmetric, although relative, involvement of the two hemispheres in global and local processing; more interestingly, they have shown that the activation, already present at the level of the prestriate cortices, is under the attentional control of the temporoparietal junctions; and finally, they suggest that the pattern of activation reflects both the top-down effects of hemispheric specialisation (stimulus category effect) as well as the effects of the perceptual salience of the stimuli (Fink et al., 1997b, 1999). In order to further explore this last issue, Fink and co-workers claim that the study of global processing needs to deploy stimuli derived from psychophysical experiments such as Gabor Patches (GPs)—sinusoidal luminance signals with a Gaussian envelope—aimed to model the receptive field structure of simple cells in V1 (Fink et al., 1999).

The psychophysical approach

Neurophysiological and psychophysical research approach the problem of global processing and that of perceptual organisation in terms of "perceptual grouping," that is, the emergence (pop out) of a meaningful stimulus from the segregation of a coherent set of local elements in an otherwise incoherent background (Palmer, 1999).

Given the assumption that simple cells in V1, behaving as localised spatial filters, are responsible for the first cortical representation of a visual scene, it is plausible to imagine the existence of lateral interactions among those filters in order to represent visual patterns extended over the visual field (Kovacs, 1996; Polat, 1999; Polat & Bonneh, 2000). This issue has been tackled by Polat and Sagi (1993, 1994) using a contrast masking paradigm where the contrast sensitivity for a foveal GP is measured as a function of the distance of two lateral "masking" GPs. In order to explain the pattern of the experimental results, different types of excitatory and inhibitory interactions have been postulated. Among these, long-range facilitatory interactions are supposed to subserve grouping and figure–ground segregation (Polat, 1999; Polat & Sagi, 1993, 1994). The anatomical substrate of such interactions could be constituted by the axonal collaterals of pyramidal cells, which form a plexus of horizontal connections within the visual cortex, connecting cells with similar physiological properties over a few millimetres of the cortex (Das & Gilbert, 1995; Gilbert & Wiesel, 1989).

Perceptual grouping has been further investigated in multiple-choice detection tasks in which a chain of GPs has to be segregated from a noisy background (Field et al., 1993). In this task there is no global cue—orientation, colour or texture—allowing for the segregation of the chain: The global patterns seem to emerge on the basis of local interactive processes, which are clearly influenced by local perceptual variables, such as relative orientation of nearby cues, relative position, and colinearity.

These experimental evidences lead Field and collaborators to postulate the existence of an *association field*, that is, a region of the visual space around any local cue over which the visual integration is thought to occur (Field et al., 1993).

Although Field et al. (1993) leave open the issue of the anatomical support for visual integration, and do not specify the level of visual processing at which the association field would be implemented, more recent data, derived within the lateral masking paradigm, suggest that the integration may be very early indeed (Polat & Sagi, 1993, 1994).

Now, if perceptual grouping does occur at such an early level of the visual stream, what is the role of the more anterior areas that have been called into question in the Robertson and Lamb model and, more recently, in the imaging literature? We will try to address this issue in a single case study of an early Alzheimer's Disease (AD) patient, MC, who presents with a specific deficit in the perception of global patterns and displays a marked zone of degeneration at the level of the right temporo-parietal junction in the context of a mild cortical atrophy. The cognitive deficit has been characterised in a detailed neuropsychological assessment, then it has been quantified in a psychophysical experiment aiming to measure the reduction in the integration thresholds for a closed chain of GP in the context of a noisy background.

Case report

MC, a right-handed woman with a primary school education (8 years), was 72 when referred in September 1998 to the Neurological Department of the University of Florence with a recent history of slowly progressive memory impairment. Her previous medical history included gastroresection in 1979 and bilateral hearing loss well corrected with aids. Widowed for 1 year, she has lead an almost independent life, continuing to live alone although in the neighbourhood of her daughter. The neurological examination was normal.

At the first observation, she complained of memory deficits over the last 3 years, having great difficulty in remembering recipes or the localisation of objects. She did not report any problem in recognising objects and people, although she complained about difficulties in remembering and imaging the faces of known people. She was first assessed on a range of standard neuropsychological tests included in a standardised protocol for the diagnosis of AD (Bracco et al., 1990) (see Table 1 for details). Alert and fully cooperative, she was substantially oriented in time and space. Her speech was fluent and well articulated, with no problems in verbal comprehension. Her ability to write and read was normal but she failed in 2-digit arithmetic. She scored 21/30 in the Mini Mental State Examination (Folstein, Folstein, & McHugh, 1975). She correctly reported the main autobiographical, historical, and current events. Her digit span was normal, while she was severely impaired in long-term memory tasks. On a Corsi block tapping task, her short-term memory spatial span was less than three. She had well-preserved general intellectual skills as measured by the Verbal Judgement Task (Spinnler & Tognoni, 1987), although her performance on the Raven Coloured Progressive Matrices was poor. She was able to perform easy concentration tasks such as counting backward whilst she was abnormally slow in the digit cancellation test and displayed an impaired performance on categorisation tasks. She was mildly impaired in category and letter fluency tests. In copying line drawings MC displayed a severe constructional apraxia, characterised by the presence of positional mislocations and loss of the global structure of the model (Figure 1), without spatial distortion. At an informal assessment she appeared to be able to reach adequately for a target and to estimate distances. She was formally tested for neglect with line bisection, digit cancellation, star cancellations, copying line drawings, and reading tasks; she showed no sign of neglect in any of these tests. Finally, in line with her

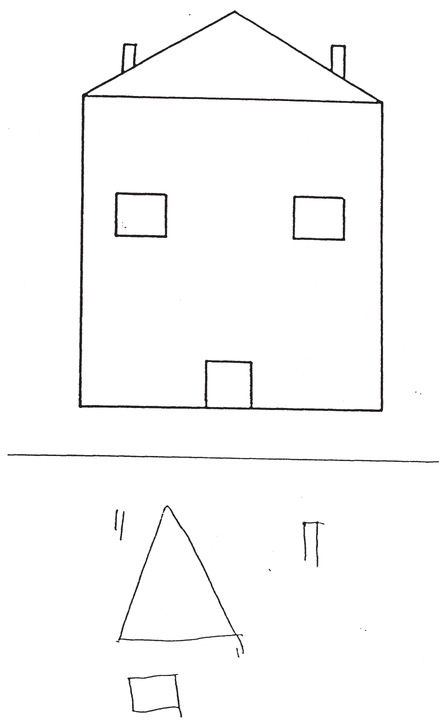

Figure 1. *Example of MC's performance in copying drawings.*

Table 1. *General neuropsychological assessment*[a]

	MC's score (max)	*Normal mean ± SD*	*Degree of deficit*
Mini Mental State Exam	21 (30)	>24[d]	Mild
Digit forward[b]	5	4.2 ± 1.2	Absent
Corsi Block Tapping Test[b]	1	4.2 ± 1.2	Severe
Randt Memory Test[b]			
5 words: acquisition	3 (15)	11.9 + 1.9	
5 words: after 10 min	10 (20)	17.6 + 1.9	Moderate
5 words: after 24 h	10 (20)	15.4+5.0	
Randt Memory Test[b]			
Paired-words: acquisition	6 (18)	13.3 + 2.5	
Paired-words: after 10 min	13 (24)	Moderate	
Paired-words: after 24 h	8 (24)	20.3 + 3.1	
Babcock Story[b]			
Acquisition[b]	5 (28)	9.1 ± 4.2	Moderate
After 10 min	0 (28)	11.2 ± 5.0	Severe
Category fluency[b]	35 (40)	38.5 ± 1.6	Mild
Token test[b]	27 (36)	33.1 ± 2.2	Mild
Copying drawings[b]	2 (16)	13.2 ± 1.9	Severe
Digit cancellation[c]	38.7 (60)	46.7 ± 8.2	Mild
Verbal judgement[c]	53 (60)	50.0 ± 6.8	Absent
Raven coloured matrices[d]	16 (36)	18.96[d]	Moderate
Letter fluency (P, F, L in 3 min)[d]	16	26.0 ± 9.3	Mild
Test of Facial Recognition (Benton)	38 (54)	40[e]	Moderate

[a]Performance of patient MC at the general neuropsychological assessment. MC's results are compared with normative data and her degree of impairment is classified as absent, mild, moderate, severe, and very severe. [b]These tasks are included in the Bracco protocol for dementia, which was standardised on a group of 146 normal elderly subjects (Bracco et al., 1990) and which explores short-term verbal and spatial memory, long-term verbal memory, semantic verbal fluency, language comprehension, and constructional praxis; for tests of attention, verbal and nonverbal reasoning, phonemic verbal fluency, and unknown facial recognition, normative data are derived from [c]Spinnler and Tognoni, 1987; [d]Carlesimo et al., 1996; [e]Novelli et al., 1986, and Benton et al., 1975, 1992, respectively; ([d,e] values expressed as cut-offs). All test scores are adjusted for MC's age and educational level.

complaints, she was found to be moderately impaired in the Benton Test for unknown face recognition—see Table 1 (Benton, Hamsher, Varney, & Spreen, 1975, 1992).

The standard work-up for the clinical diagnosis of dementia, including the instrumental investigations described below, pointed to a diagnosis of Alzheimer's Disease. The patient has been assessed over a period of 8 months. Two different general evaluations of cognitive performance, carried out at baseline and at a 6-month follow-up, showed a very slow progression of cognitive decline across the period spanned by the present experimental investigation.

Ophthalmological assessment and visual perimetry

MC's visual assessment revealed the presence of incipient mild cataracts prevalent in the right eye while visual acuity was normal in both eyes. Goldman perimetry as well as computerised perimetry (Humphreys 30.1) revealed an incomplete right homonymous hemianopia mainly affecting the upper quadrants of the visual field; an homonymous visual field defect that has been already described in other patients affected by degenerative dementia, with no evident lesions affecting the retrochiasmal visual pathways (Brazis, Lee, Graff-Radford, Desai, & Eggenberger, 2000; Kartsounis & Warrington, 1991; Thaiss & De Bleser, 1992; Trick, Trick, Morris, & Wolf, 1995).

Brain imaging

In September 1995, at the onset of symptoms, MC underwent a brain CT scan that was reported as being within the norm although, at a post hoc evaluation, the presence of a minimal enlargement of the Silvian fissures could be appreciated.

A first brain MRI, carried out in October 1998, showed a pattern of diffuse cerebral atrophy, markedly on the right hemisphere, where a region of greater enlargement of the cortical sulci was present at the level of the temporoparietal junction. In order both to verify the nature of this region and to follow the progression of cerebral atrophy, a second MRI scan of the brain was carried out in November 1999 on a 1.5 tesla superconductive magnet. We obtained Spin-Echo, sagittal, T1-weighted images (TR 612-TE 12.0, 5-mm slice thickness, 0.5-mm gap interslice); Fast Spin Echo, axial along the bicommissural plane, T2-weighted images (TR 6200-TE 90.0, 2-mm thickness, 0.5-mm gap interslice); Fluid Attenuated Inversion Recovery (FLAIR), axial, images (5-mm thickness, 1-mm gap interslice). The scan confirmed the presence of a generalised atrophy, prevalent on the right hemisphere and not substantially different from that revealed by the previous one. The FLAIR images allowed us to exclude the presence of white matter changes due to gliosis in the area of clear-cut, marked enlargement of the cortical sulci at the level of the right temporo-parietal junction; two skilled neuroradiologists judged the area to be located at the level of the right angular gyrus and to correspond to Brodmann Areas 39–40 (Figure 2). T2 weighted axial images showed minimal white matter lucencies.

THE NEUROPSYCHOLOGICAL INVESTIGATION

A preliminary assessment of semantic memory functions and object recognition

Semantic memory functions

The patient was submitted to a preliminary experimental investigation, which focused on semantic memory functions. These were evaluated with a set of formal tests including a battery of experimental tests (Lauro-Grotto, Piccini, & Shallice, 1997) derived from Hodges' Battery for Semantic Dementia (Hodges & Patterson, 1992), the Pyramids and Palm Trees Test (Howard, Patterson,

Figure 2. *Brain MRI scans: T2 axial sections, images along the bicommissural plane. On the right side (R) a marked enlargement of the sulci is evident at the level of the temporoparietal junction (BA 39/40) as localised by two independent neuroradiologists.*

Oxbury, & Funnell, 1992), the Semantic Judgement Type Test with real objects (Lauro-Grotto et al., 1997), and a tactile naming test. None of these tasks introduced any time limit.

Materials and methods. The Semantic Memory Battery includes five different tests employing as stimuli 24 living and 24 nonliving items from the Snodgrass and Vanderwart corpus of line drawings (Snodgrass & Vanderwart, 1990). The word–picture matching test presents a six-alternative forced-choice procedure in which the target item has to be selected from among semantically related distractors. The naming test requires the subject to name the 48 line drawings included in the battery. In the verbal definition test the subject is required to produce verbal definitions in response to the spoken names of the 24 living and 24 nonliving items. The visual sorting test requires the subject to sort the line drawings of the 48 stimuli according the following semantic dimensions: living (24) vs. man-made (24), household items (8) vs. vehicles (8) vs. musical instruments (8), birds (8) vs. land animals (8) vs. water animals (8). Finally the verbal sorting test only differs from the previous test in that written names are used as stimuli.

The Pyramids and Palm Tree Test (Howard & Patterson, 1992) is a two-alternative forced-choice task requiring the subject to match the stimulus (i.e., cheese) with a semantically associated item (i.e., mouse), which is presented together with a distractor (i.e., cat). In its original visual version the test uses 56 triplets of line drawings: The stimulus is presented at the top of an A4 page whose lower half contains both the target and the distractor. A verbal version of this task was devised by substituting the line drawings with the corresponding written names. The visual and the verbal versions of the task were administered in separate experimental sessions, around 10 days apart.

The Semantic Judgement Type Test is a three-alternative forced-choice test designed along the lines of the Pyramids and Palm Tree Test, but employing real manipulable objects as visual stimuli (Lauro-Grotto et al., 1997)

The stimulus is placed on a coloured card to highlight its role, while the three objects composing the response triplet are aligned on the table at about 30 cm from the stimulus; the target is presented in a randomised position with respect to the two distractors. The subject is not allowed to touch the objects and is asked to point to the selected item in the triplet. The test includes 60 trials. A few familiarisation trials precede the testing session. The verbal version of this task is obtained by substituting the real objects with the corresponding written names.

The visual version of the test was administered first; the verbal version followed a couple of weeks later.

Finally in the tactile naming task the subject is required to name an item that is manipulated out of view with both hands. The object employed are 13 common use artifacts such as a cork, a screw, and a pair of scissors.

Results. MC's performance in the Hodges' Battery for Semantic Dementia (Hodges & Patterson, 1992; Lauro-Grotto et al., 1997) was above 90% correct in all tasks except in the more demanding visual identification task, that is, Naming Line Drawings, where she showed a disproportionate deficit (54% correct), with a tendency to produce visual and visual-semantic errors. She performed 85% correct (11/13) in a tactile naming task using real objects as stimuli.

In the Pyramids and Palm Trees Test (Howard & Patterson, 1992) her performance (31/56, 55% correct) was at chance level (Binomial test, $p > .05$).

MC performed 85% (47/56) correct in the verbal counterpart of the Pyramids and Palm Trees Test, which is significantly better than in the original visual test (Sign Test, $p < .001$). In the verbal version of the Semantic Judgement Type Test she performed 85% correct (51/60; chance level 33%), that is not statistically different from the level of performance, 78% correct (47/60), that was obtained in the visual modality (Sign Test, $p > .1$). Finally, the set of real objects used in the Semantic Judgement Type Test was presented for naming; the patient named correctly all items ($n = 60$) except one (the *windscreen wiper*).

The gradient of performance obtained in going from real objects to line drawings, together with the lack of any effect of the semantic judgement type on performance, suggested that the semantic dimension was not crucial in determining the experimental outcomes, and that the main difficulty encountered by the patient was in the perceptual aspects of the tasks. We therefore submitted MC to the Birmingham Object Recognition Battery.

Object recognition: The Birmingham Object Recognition Battery

Material and methods. The Birmingham Object Recognition Battery (BORB) is a neuropsychological battery specifically designed to tap the level of processing at which a naming difficulty could emerge, in going from perception to semantics and name retrieval (Riddoch & Humphreys, 1993).

MC was submitted to the tests of the BORB, which do not overlap with those already administered within Hodges' battery.

Results. Table 2 shows the results that MC obtained in the various subsections, all of which have been classified as either "within the norm" or "outside the norm," according to the battery prescriptions.

Table 2. *The Birmingham Object Recognition Battery*[a]

	MC's score	
Tasks	*Within the norm*	*Outside the norm*
Copying (test 1)		0
Length match task (test 2)	23/30	
Size match task (test 3)	26/30	
Orientation match task (test 4)	22/30	
Position of gap match task (test 5)	29/40	
Overlapping line drawings (test 6)		
Single shapes (s)		160
Paired non overlapping (s)		160
Paired overlapping (s)		355
Minimal feature view task (test 7)	23/25	
Foreshortened view task (test 8)		17/25
Object decision task (test 10)		33/64

[a]MC's performance on a group of selected tasks from the BORB; scores have been classified as either "within the norm" or "outside the norm" according to the cut-offs of the battery. For the overlapping line drawing test MC's performance is rated in terms of time of execution.

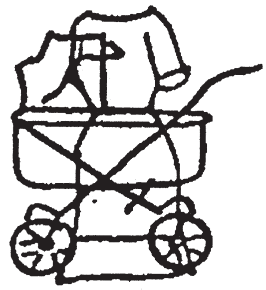

Figure 3. *Example of overlapping figures (BORB: Test 6).*

The patient's performance clearly demonstrated intact ability to achieve a pre-categorical analysis of objects properties such as size, length, orientation, and location, and confirmed the absence of neglect (Tests 2–5). She was impaired at the level of figure/ground segregation, as shown by the disproportionate time required to name paired overlapping line drawings (Figure 3) with respect to nonoverlapping ones (Test 6); in the nonoverlapping condition MC was able to identify both the elements of each pair and correctly name 85% of the items (typical errors were "lamp" for a glass, "cat" for a squirrel, and "flag" for a hatchet). She showed a mild impairment within one of the two subtests assessing the capacity to achieve object constancy, the Foreshortened View Match, in which, according to the authors, a critical local feature of the object has to be detected in order to perform the task.

Finally she was at chance level in the Object Decision task (Test 10), in which she invariantly accepted as "real" chimaerical items obtained by the junction of parts of real items (Figure 4).

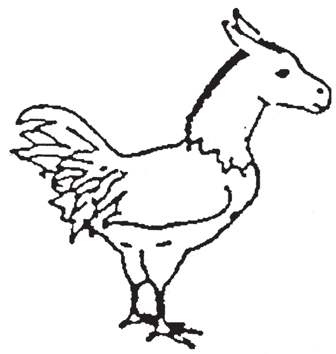

Figure 4. *Example of chimaerical stimuli (BORB: Test 10).*

According to the authors, the Object Decision task is aimed at measuring the integrity of stored knowledge about the visual aspect of the items; however, at an informal assessment, when asked to name the chimaerical items she had judged to be real animals, the patient invariantly switched back and forth from the names of the two animals composing the chimaera. This would suggest that the problem causing her failures in object decision may be linked to the emergence of a stable unitary percept and not only to a degradation in stored knowledge about the visual appearance of the items.

In conclusion, we can interpret the results at the BORB as pointing to a specific difficulty in segregating and integrating object parts in a unitary and coherent percept.

Exploring the perception of global patterns

Driven by the suggestion that MC's impairment in more demanding visuoperceptual and constructive tasks could result from a specific deficit in global processing, we asked the patient to describe two pictures of Arcimboldo—the "Rudolf" and the "Biblico"—where the figures are respectively represented by a composition of fruit and books, located in precise spatial relationships. MC promptly and carefully described the sets of fruit and books but she was unable to see the faces, even when prompted.

This anecdotal evidence of a deficit in global processing was further confirmed by her very poor performance on a standardised gestalt completion test that assesses the ability to recognise degraded pictures, the Street Completion Test. The task requires the subject to recognise degraded drawings (Figure 5). The first two items are presented as examples; then stimuli with an increasing level of perceptual difficulty are presented for naming. MC was only able to name the two easy examples, while age-matched controls recognise the first six items of the test (Spinnler & Tognoni, 1987).

In order to explore this issue more formally, the patient underwent a series of tasks tapping different aspects of global processing. The main purpose of this series of experimental assessments was to obtain both a cognitive profile of MC comparable to that of cases with integrative visual agnosia and a baseline for the psychophysical study.

Figure 5. *Example of degraded figures from the Street Completion Test.*

THE EXPERIMENTAL INVESTIGATION

Local and global processing of hierarchical stimuli

In order to investigate the ability to derive global structure from the spatial relationship of the local components we devised an experimental task employing hierarchical stimuli of the Navon type. Measures of RTs have been generally applied with this type of stimuli to evaluate whether the global level is perceived *before* the local one or vice versa (i.e., global or local precedence). In our case we focused on MC's capacity to perceive the two levels of the stimuli without measuring RTs, because the patient did not produce speeded responses.

The four neuropsychological experiments, described below, have been performed by five AD controls, matched for age and dementia severity. The control patients have been selected for the presence of a mild cognitive impairment mainly affecting memory and language abilities, in order to assess the effects of such deficits on the performance in the four tasks.

Experiment 1: Identification of the local and global level of hierarchical stimuli

Materials and methods. The test requires the subject to describe 12 hierarchical letters of the Navon type (Navon, 1977) printed in black on white cards. We applied two-level inconsistent stimuli (Figure 6a) where the local and global letters conflicted; some of the stimuli included neutral elements (stars) as local constituents (Figure 6b). The vertical dimension of the stimuli at the global level ranges between 2.2 and 6 cm. The horizontal dimension varies between 1.5 and 4.2 cm. The stimuli at the local level are Helvetica type characters; their height is 0.5 cm, 1.0 cm, or 1.3 cm. The stimuli are presented one at a time in free vision, without time limits, and without any constraint on the distance at which they have to be viewed.

In order to assess the effects of an attentional manipulation on MC's performance, the experiment is performed under three conditions, using the same letter pattern in separate sessions, at least 1 week apart. In the first condition (no-cue condition), the subject is required to describe the stimulus in as much detail as possible, without any further cue (Question: Can you please tell us in as much detail as you can what you see?). In the second condition (verbal-cue condition), the subject is explicitly required to say if the local elements form anything meaningful at the global level (Question: Can you please tell us if the local elements form something together?). In the third condition (perceptual-cue condition) a vertical black bar of the same dimension as the stimulus and 0.8 cm high is placed on the right side of the stimulus, at a distance of around 1 cm from it; the subject is required to describe the stimulus in as much details as possible (Question: The same as in the first condition).

Results. The patient promptly identified the local level of all the hierarchical stimuli (100% correct), although she was unable to spontaneously report the global level of any one of the stimuli (0% correct) (see Table 3).

Her ability to report on the global pattern improved only slightly in the verbal-cue condition (2/12; 17%); however, she performed significantly

Table 3. *Assessment of global perception*[a]

Tasks	*MC's performance*	*AD controls Mean + SD*
Street Completion test	0/14	8 ± 1 (n = 3)
Navon stimuli		
Local level	12/12	12 (n = 5)
Global level	0/12	12 (n = 5)
Object Decision: Silhouettes	17/32	26.7 ± 2.5 (n = 3)
Subjective contours	1/4	3.8 ± 0.5 (n = 5)
Illusory contours (Kanizsa figures)	0/8	8 (n = 5)

[a]MC's performance in the tasks devoted to assess global perception is compared to the mean performance of a control group of AD patients.

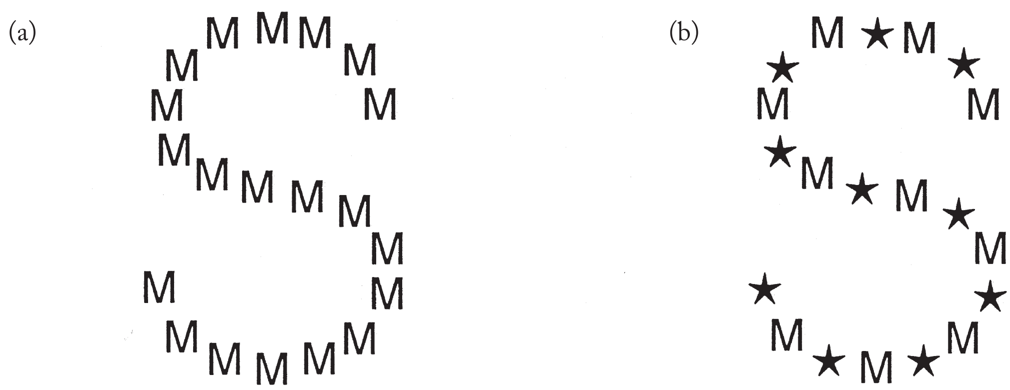

Figure 6. *Hierarchical stimuli of the Navon type. (a) Example of two-level inconsistent stimuli; (b) example of stimuli including neutral elements as local constituents.*

better in the perceptual-cue condition than in the no-cued condition, being able to identify the letter represented at the global level in half the trials (6/12; 50%; Sign test $p < .02$). Although the paucity of the trials does not allow us to draw firm conclusions on the nature of the deficits, the level of performance of MC on hierarchical stimuli identification on the three different procedural conditions (uncued vs. cued) suggested the possibility of affecting the patient's performance by means of attentional manipulations.

Global perception versus local integration: One or two processes?

Following an interpretation mainly based on psychophysical data (Kovacs, 1996), the identification of the global level of Navon stimuli is thought to represent a perceptual process grouping together the local elements. Other authors, however, have claimed that the perception of the global level of hierarchical stimuli is independent of perceptual grouping (Humphreys & Riddoch, 1987). In fact, patient HJA, a well-studied case with visual integrative agnosia, presents normal RTs in deriving the global level of hierarchical stimuli whilst showing responses significantly slower than those of controls in perceiving the local parts. Another way to explore the relationship between the grouping of local information and the perception of the global level, is by comparing the performance of the subject in a test of object decision using silhouettes of chimaeras (Figure 7) and real items instead of the line-drawings used, for example, in the BORB (Butter & Trobe, 1994; Riddoch & Humphreys, 1987). A better performance with silhouettes than with line drawings would support the independence of global processing from perceptual grouping, since it is assumed that line drawings are more demanding stimuli in terms of the perceptual load connected to the visual integration of the local details (Riddoch & Humphreys, 1987). An object-decision task with silhouettes derived from the chimaerical stimuli of the BORB was then applied to assess MC's ability to use global outline shape for object recognition.

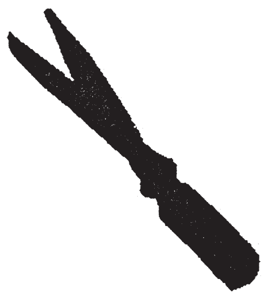

Figure 7. *Example of silhouette of a chimaerical item.*

Experiment 2: Object decision with silhouettes

Material and methods. The task is a two-alternative forced-choice test in which the subject is required to judge if the stimulus, presented in free vision and without any time limit, is the silhouette of a real item or not (Figure 7). The silhouettes are obtained by painting in black the items included in the Object Decision task of the BORB (Test 10—Figure 4): They therefore include the silhouettes of real objects, of real animals, and of chimaerical items obtained by joining two parts of objects or two parts of animals. The original items for which the recognition may be crucially influenced by internal details of the line drawing, for example, the tiger, have been excluded from the test. The overall number of stimuli is 32, half of which are chimaerical items.

Results. MC judged as real all the silhouettes, and therefore performed exactly at chance level (see Table 3), showing virtually no difference from the performance obtained in the line drawings version of the same task (Test 10), in contrast to HJA (Riddoch & Humphreys, 1987). Nevertheless, MC's findings, although not supportive of the independence between global and local processing, as suggested by an anonymous reviewer, cannot rule out the possibility of an association of two different deficits, one of grouping and one of poor attentional response to global form information.

Subjective and illusory contours

Finally, another aspect of global processing has been assessed by means of tests exploring subjective (Figure 8a) and illusory contours (Figure 8b) perception. Illusory contours such as Kanizsa figures represent a form of visual interpolation where the observer perceives an illusory white figure (i.e., a triangle) on a background of partly occluded circles. In the past, cognitive theories of visual perception emphasised the role of top-down processes, such as high-level cognitive inference, in perceiving illusory contours (Gregory, 1972). Recent neurophysiological data, however, show that illusory contours may actually be coded in the earlier step of visual processing (Grosof, Sharpley, & Hawken, 1993; Von der Heydt, 1995). For example, Von der Heydt, Peterhans, and Baumgartner (1984) reported that, in an experiment recording the responses of single cells from V2, 44% of the recorded cells appeared to be responsive to the orientation of the illusory contour. The authors support the idea that the response of orientation-specific cells in V2 could reflect the integration of inputs from simple and complex cells in V1, with similar orientation, as well as from end-stopped cells (Von der Heydt, 1995). Thus, the acquired data point to a dependency of illusory contour perception on low-level visual mechanisms and support a bottom-up model of their processing.

In the neuropsychological literature, illusory contours perception has been applied either in assessing integration of visual information relying on gestalt properties of the stimuli (Kartsounis & Warrington, 1991) or as a marker of integrity of early visual processing (Riddoch & Humphreys, 1987).

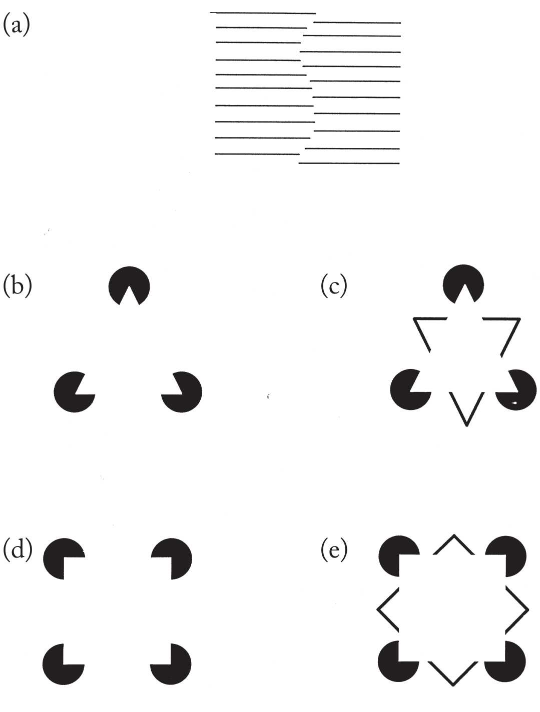

Figure 8. *Examples of subjective contours: (a) illusory contours; (b) (c) Kanizsa triangles; (d) (e) Kanizsa squares.*

Experiment 3: Subjective contours and illusory contours

Material and methods. The experimental material on subjective contours includes four subjective contour stimuli (Figure 8a), which are printed in black on white cards and presented one at a time in free vision, without any time limit and without any constraint on the distance at which they must be viewed. The subject is required to describe what he or she sees in as much detail as possible. In the subjective contours stimuli a vertical shift in the alignment of contiguous horizontal segments (inductors) induces the perception of a large S-shape (see Figure 8a). The distance between the inductors varies between 0.20 cm and 0.02 cm.

The printed illusory contours stimuli are four white Kanizsa triangles and four white Kanizsa squares obtained by inducers of various type (see Figure 8b–e); the radius of the circumferences in which the illusory contours are inscribed is 2 cm, while the radius of the circular inducers is 0.5 cm. The stimuli vary for presence or absence of supplementary linear inducers forming a black geometrical contour that is normally perceived as being "under" the illusory picture. The subject is required to verbally describe the stimulus.

Results. Although she was able to perceive one subjective contour out of four, MC did not identify any of the printed Kanizsa figures. The results have been further confirmed in a recognition two-alternative forced choice paradigm by means of an automatised presentation procedure on the computer screen (see below Illusory Contours, following).

MC's results in the assessment of global perception are summarised in Table 3, which compares her performance with that of five AD control patients, matched for age and degree of mental deterioration (mean age 70.6 + 6.6; MMSE 21.2 + 2.8; schooling 9.0 + 2.2 years). Her results in this set of experiments confirm the presence of a marked deficit in integrating local cues, in recognising the global shape of hierarchical stimuli, in identifying silhouettes, and in perceiving illusory contours. MC's performance was significantly impaired in all tasks except for the identification of the local level of hierarchical stimuli.

THE PSYCHOPHYSICAL INVESTIGATION

The evidence collected in the neuropsychological investigation of MC's impairment all points to a deficit in the visual integration of local elements into a unitary percept (perceptual grouping).

In the psychophysical approach perceptual grouping has been studied with different experimental paradigms (see the Introduction). In fact, most of the experimental investigations (Field et al., 1993; Kapadia, Minami, Gilbert, & Westheimer, 1995; Kovacs, 1996; Polat & Sagi, 1993, 1994; Saarinen, Levi, & Shen, 1997) and also the available computational models (Grossberg, Mingolla, & Ross, 1997; Neumann & Mingolla, 2001) have been produced under the assumption that grouping should occur quite early in the process of visual analysis, that is, already at the level of the primary visual areas V1 and/or V2.

Furthermore, there is evidence that the visual system of mammals is able to achieve visual integration at each scale of spatial frequency so that the use of spatial bandpass elements—GPs—as local stimuli has been considered a useful tool in psychophysical experiments exploring perceptual grouping with normal subjects (Field et al., 1993) as well as with patients (Giersch et al., 2000).

The present experimental investigation was designed in order to achieve the following goals: (1) to obtain a quantification of the integration deficit of our patient; (2) to define the role of perceptual variables, such as the distance between local cues and the global dimensions of the stimulus, in determining the patient's performance; (3) to provide evidence suggesting that in the present case it is possible to obtain an estimate of the contribution of the right temporoparietal modulatory top-down influence on the integration processes going on in the primary visual areas, which are assumed to be preserved in Alzheimer's disease (Haroutunian, Purohit, Perl, Marin, Khan, & Lantz, 1999; Mountjoy, Roth, Evans, & Evans, 1983; Yew et al., 1999).

Contrast sensitivity

Given the potential, although controversial, role of spatial frequency content in local and global processing (see Introduction), we measured contrast sensitivity as a preliminary assessment. Contrast sensitivity was evaluated by means of Vistech Consultant Inc. tables (see Methods), and MC's was within the normal range for low spatial frequencies (1.5–3 cycles/degree) while appearing to be decreased for high spatial frequencies. The pattern of performance was probably due to the presence of low-degree cataracts.

Illusory contours

In order to assess the ability of the subjects to detect illusory contours, beside using preliminary standard neuropsychological tests with cards (see Illusory Contours, above), we also designed a psychophysical test.

Experiment 4: Illusory contours—forced-choice task

Material and methods. The subject is required to detect a white "illusory" Kanizsa triangle in one of two patterns of inductors presented simultaneously on the two halves of a computer screen with a two-alternative forced-choice procedure. The inductors of the target pattern are disposed in the canonical configuration for the illusory perception to emerge (see Figure 8b), while in the distracting pattern the inductors have random orientations but are the same distance from the centre of the "supposed-to-be-there triangle."

The subject's task is to point the target on the screen. In order to make the recognition task unequivocal for the patient, a "nonillusory" template of the target, that is, a white triangle on a black card, was placed under the screen and continuously referred to by the experimenter as "the target to be found." Probability of success was computed as a function of inductor size, which was varied from trial to trial. Size of inductors was varied following an automatic staircase procedure (QUEST; Watson & Pelli, 1983).

The measure was repeated for two target dimensions, 4 degrees and 2 degrees, by varying the distance of the subject from the screen. Size of inductors ranged from a minimum of 0.16 degrees to a maximum of 3.2 degrees when size of target was 4 degrees and from 0.08 to 1.6 degrees when size of target was 2 degrees.

Total dimensions of the stimulus were 20 × 20 and 10 × 10 degrees respectively.

Stimulus duration was limited to 1 s to limit the influence of cognitive processes on perception.

Presentations were preceded by a sound to draw the attention of the subject on the screen.

Results. MC's performance was 25 correct from a total of 41 (61%) at 60 cm distance and 36 correct from a total of 57 (63%) at 120 cm distance from the screen—slightly above chance level (Binomial Test, $p < .05$). Moreover, performance seemed to be independent from the size of the inductors. There was no evidence that MC could also perceive illusory segments in conditions where they were evident for the experimenters and controls (an AD patient, matched for age, education, and severity of mental impairment performed flawlessly on the same task). Preliminary observations were therefore confirmed.

Visual integration of local stimuli into a global pattern

The sensitivity for the integration of local stimuli into a global pattern was measured by testing the

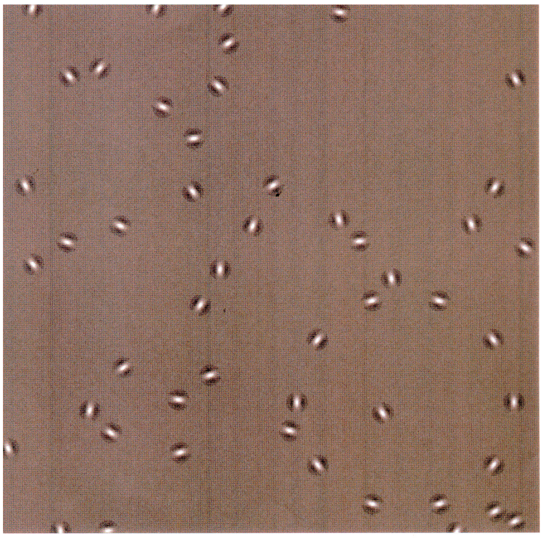

Figure 9. *Gabor patches: Example of stimulus used to explore visual integration ability. The circular feature is located in the centre of the lower right quadrant. Number of noise elements shown here are below threshold for all subjects.*

ability of the subject to detect a feature (circle) embedded in noise, where both the circle and noise elements were GPs of the same spatial frequency (see Figure 9 for a sample of the stimulus). This was quantified by measuring the threshold for detection of the circular feature as a function of background noise level. This measure was repeated by systematically varying the number of GPs aligned along the circle, i.e., by reducing the integration area around each element. In Experiment 5 the size of the circular feature was maintained constant with a radius of 4.3 degrees.

Experiment 5: Visual integration of local stimuli into a global pattern

Material and methods. We tested the ability of subjects to detect a feature (circle) embedded in noise as a function of the number of elements of the feature, where both the circle and noise elements were GPs of the same spatial frequency. We used a four-alternative forced-choice procedure for the detection task: From trial to trial the feature was presented randomly in a quadrant of the screen and the subject was asked to locate the target in one of four allowed positions, each centred in one of the four quadrants of the computer screen. The orientation of GPs in the circle was orthogonal to its radius while the orientation of noise elements was randomly distributed. Figure 9 shows an example of the stimulus used in this experiment. For each number of Gabor elements composing the feature we measured the probability of success in locating the target as a function of the background noise level, thus obtaining the psychometric curve related to this experiment. This curve is expected to range from 100% to 25% probability of success, which correspond to the chance level, as the noise level increases since it is a four-alternative forced choice. The noise level from trial to trial was varied according to a QUEST staircase procedure (Watson & Pelli, 1983). A maximum likelihood fit of each psychometric curve was performed with a monotone decreasing function. The threshold was then defined as the point where the probability of success was 80%. The quoted errors correspond to ±1 *SD* of the Gaussian curve estimated from the data obtained by the control group. We ran the experiment on MC and on a group of six naive age-matched control subjects (mean age 68 years, ranging from 59 to 72 years); all control subjects had normal or corrected-to-normal vision.

Stimulus duration was 1 s to limit the influence of cognitive processes on perception. Presentation was preceded by a sound to draw the attention of subject on the screen. Distance of subjects from the screen was 50 cm. Stimulus dimensions were 20 × 20 degrees. GPs were circular, with a wavelength λ of 0.57 degrees.

Results. Figure 10 shows the sensitivity (inverse of measured threshold) as a function of distance between elements composing the feature (inferior axis) and as a function of number of elements composing the feature (superior axis). It was evident that for all subjects the feature was more discernible as the number of its element increased: A feature constituted by 10 elements was perceptually much more salient than a 5-element one—it almost popped out from the background of GPs constituting the noise. MC performed significantly worse than the control group at 5 elements, that is at a distance between elements of 5.2 degrees or 9.1 λ ($p <$ .05, t Student's Test); she showed a borderline performance at 6 elements (4.3 degrees or 7.5 λ), falling 2 *SD*s below the mean of the control group. Finally, for 8 elements or more (3.4 degrees or 6 λ) her performance was not statistically different from the control group ($p > .05$, t Student's Test, for all comparisons).

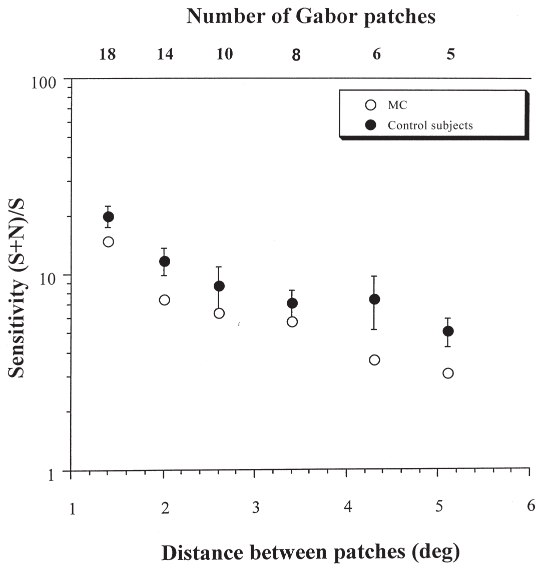

Figure 10. *Visual integration of Gabor patches. Sensitivity as a function of distance between elements (inferior axis) and as a function of the number of elements composing the circular feature (superior axis). The white circles represent MC's performance while the black ones refer to the mean performance of the control group ± 1 SD. MC performed significantly worse than the control group at five elements (*p < *.05,* t *Student's Test); she showed a borderline performance at six elements, falling 2* SDs *below the mean of the control group. All the other comparisons are not significant.*

Since the patient succeeded in the task for the smaller values of the interelement distance, the presence of a deficit of visual search or in distributing attentional resources could be ruled out (Saffran et al., 1990; Stark et al., 1997).

DISCUSSION

We present a single case study of a patient with a severe deficit in global processing in which we complement an extensive neuropsychological assessment with a psychophysical investigation of her ability to group local visual information in a coherent whole.

Although patients with cerebral localised lesions, such as stroke patients, have been considered the best target for cognitive research, the notion that dementia is a diffuse disorder affecting all cognitive domains is no longer tenable (Galton, Patterson, Xuereb, & Hodges, 2000), and as greater attention is paid to cases with a prevalent impairment of specific cognitive functions, the amount of neuropsychological investigations on patients affected by degenerative processes has also increased (De Renzi, 1986; Evans, Heggs, Antoun, & Hodges, 1995; Mesulam & Weintraub, 1992; Snowden, Neary, Mann, Goulding, & Testa, 1992; Tyrrel, Warrington, Frackowiak, & Rosser, 1990).

MC is a mild, slowly progressive, and very cooperative AD patient who presents a prevalent, severe impairment of visuoconstructive abilities as suggested by a specific deficit in visual naming of line drawings, by a significantly reduced spatial span and by a very severe constructional apraxia (Levine, Lee, & Fisher, 1993; Martin et al., 1985; Piccini et al., 1998). Her neuropsychological profile is highly consistent with the neuroradiological finding as she presents with a prevalent atrophy of the right hemisphere and with a significantly more marked and circumscribed enlargement of the sulci at the level of the right temporoparietal junction.

A deeper assessment of MC's visual and verbal semantics as well as of her visuoperceptual abilities in object and face recognition established the presence of apperceptive visual agnosia and prosopagnosia. As an interesting interaction between the deficit in perceiving either the global or the local level and visual neglect has been reported in the literature (Doricchi & Incoccia, 1998; Marshall & Halligan, 1995), we tested the patient for neglect; MC, however, showed no sign of neglect in reading, in line bisection, or in the star cancellation task. Despite having normal visual acuity as well as intact basic perceptual abilities—size, length, orientation, and shape discrimination are within the norm—MC displays a specific impairment in visual naming, in segregating overlapping figures, and in judging as unreal chimaeras of animals and objects presented both as line drawings and silhouettes. On the other hand, she is almost perfect in naming real objects. The patient presents with a severe constructional apraxia, characterised by positional mislocations of details and loss of the global structure of the model in copying drawings. Compared to AD cases matched for age and degree of mental deterioration, our patient was unable both to identify pictures of objects or animals that have been degraded and to perceive subjective and illusory contours such as Kanizsa figures. When asked to describe hierarchical stimuli of the Navon type, she consistently reported their local level, while she was unable to identify the global figure, excepted on a few occasions when cued by the presence of a black vertical bar beside the stimulus.

MC's cognitive profile fits well with the neuropsychological pattern of "visual integrative agnosia" (Riddoch & Humphreys, 1987), although she differs by lacking the typical feature-by-feature naming strategy and an overt agnosic disorder. The subclinical nature of the deficits, closely resembling those found in patients with an impairment of categorical perception (Farah, 1995; Warrington & James, 1988), is consistent with the gradient of performance observed in visual naming and in associative matching tasks (see Semantic Memory Functions earlier).

Overall, the data suggest the existence of "critical" perceptual conditions responsible for the emergence of the deficit. Nevertheless there is evidence that her integration deficit is not limited to static stimuli, as we demonstrate that she is also entirely unable to perceive biological motion (Del Viva, Lauro-Grotto, & Piccini, 2001).

In an attempt to provide a neurophysiological base for the impairment of global processing, and in line with the evidence of global precedence (see Introduction), some authors proposed an account of the global processing impairment based on a supposedly defective perception of the low-frequency content of the visual patterns (Sergent, 1982, 1983; Shulman, Sullivan, Gish, & Sakosa, 1986; Shulman & Wilson, 1987). A measure of contrast sensitivity failed to detect any abnormality in the perception of low spatial frequencies in the present case; in fact only sensitivity to high spatial frequencies was slightly reduced in MC. Nevertheless, this does not allow us to exclude the possibility that the information coded at the level of low spatial frequencies may be handled in a defective way in further steps of visual processing (Grabowska & Nowicka, 1996; Kitterle et al., 1990, 1995; Sergent, 1987). Although this may influence neuropsychological performance, an effect on the pattern of results with GPs is implausible, as the frequency content of these stimuli is strictly controlled.

Recent psychophysical data on perceptual grouping have been interpreted by considering perceptual grouping as the result of a series of local rules determined by the relative orientation, distance, and position of the local elements, which amount to the definition of the *association field* (Field et al., 1993; Kapadia et al., 1995; Kovacs 1996). We therefore applied a psychophysical approach to the study of perceptual grouping, which allowed us to measure the integration threshold for the detection of a closed chain of local stimuli over a noisy background, local elements consisting of sinusoidal luminance signals modelled on the receptive fields of simple cells in V1 (GPs). The linear dimension of the association field along the closed chain was estimated in a group of six normal subjects: For the employed feature it reached 9.1 λ, where λ is the wavelength of the GPs. MC performed significantly worse than the control group at five elements, that is at a distance between elements of 9.1 λ; she showed a borderline performance at six elements (7.5 λ). Finally for eight or more elements (6 λ) her performance was not statistically different from the control group. The results provide a quantitative measure of the integration deficit of our patient, which can be compared directly with psychophysical findings on perceptual grouping obtained with normal subjects: Overall the patient showed a 17% reduction in the linear dimension of the association field.

The "association field" describes a region of the visual space surrounding each local element, over which other local elements group together according to a set of specific rules such as alignment, coorientation, and relative position of the local cues along the path (Field et al., 1993). Long-range horizontal connections in the primary visual cortex (Das & Gilbert, 1995; Gilbert & Wiesel, 1989; Grinvald, Lieke, Frostig, & Hildesheim, 1994), which have been proposed as the functional and anatomical substrate of the facilitatory effects reported in the lateral masking experiments (Polat & Sagi, 1993, 1994), could in principle play a role in the dynamical "build-up" of the association field as well (Kovacs, 1996; Neumann & Mingolla, 2001).

A large amount of recent data suggest that perceptual mechanisms subserving global processing exist at an early phase of visual information analysis, under the attentional control of other cerebral areas (Fink et al., 1996, 1997a). In particular, for global processing, functional neuroimaging studies have located the source of such a modulatory activity in the right temporoparietal junction (BA 39–22) (Fink et al., 1996); a cerebral area broadly corresponding to the region of prevalent atrophy in MC (BA 39–40). The data obtained in imaging experiments using nonrepresentational stimuli have been explained by postulating an interaction between the level of processing and the stimulus characteristics, among which the local spacing plays a major role (Fink et al., 1999). In particular, the smaller "gaps" typical of high spatial frequencies stimuli are thought to increase the visual saliency of the global pattern, therefore determining a greater activation of the right early visual cortices (Fink et al., 1999).

In the early 1990s some functional neuroimaging studies complemented neurophysiological data (Moran & Desimone, 1985) by showing that the activation of different extrastriate areas was dependent on the kind of "attended" perceptual attributes. These results stressed the attribute specific nature of the attentional modulation (Corbetta, Miezin, Dobmeyer, Shulman, & Petersen, 1990, 1991). One of the most relevant claims from research on the anatomical substrate of attentional processes is that the degree of stimulus dependency decreases from early visual processing areas to areas putatively exerting a pure attentional control (Kastner, Pinsk, DeWeerd, Desimone, & Ungerleider, 1999); intermediate visual areas have been identified in the intraparietal sulcus, whose baseline activity due to stimulus expectation (attentional modulation) is highly increased after the onset of visual stimuli (Kastner et al., 1999). In this large set of experimental studies, activation of different cerebral areas appears to depend both on exogenous (bottom-up) and endogenous (top-down) processes (Fink et al., 1999; Kastner et al., 1999).

The role of top-down modulation in perception is especially controversial (Shulman, Corbetta, Buckner, Raichle, Fiez, & Miezin, 1997). The functional meaning of feedback connections still remains obscure despite their anatomical prominence (Mignard & Malpeli, 1991; Vanduffel, Payne, Lomber, & Orban, 1997). A neurophysiological approach to the study of top-down neuromodulation exploits inactivation by reversible cooling of higher-order visual areas while recording from single units or multiunits in the early visual cortices (V1, V2, V3) of the monkey. In a recent experiment (Hupé et al., 1998), area V5 was cooled and the activity of V3 neurons was recorded while the monkey performed a detection task with optimally oriented moving bars presented over a stationary background. The findings provide evidence for the existence of facilitatory effects due to the feedback connections; in fact, the response of neurons in early cortices decreases as a result of V5 inactivation and such a decrease is especially relevant for low-saliency stimuli. The authors argue that such facilitatory connections "serve to amplify and focus activity of neurons in lower-order areas and that they are important in the differentiation of figure–ground, particularly in the case of stimuli of low visibility" (Hupé et al., 1998). Although the role of feedback corticocortical connections is not clearly established, the neurophysiological findings suggest that they may improve the visibility of features and contribute to the "pop-out" phenomenon.

We cannot obtain evidence as direct as that obtained with cooling experiments; nevertheless we would like to put forward the hypothesis that MC's performance could be explained by postulating a defective top-down modulatory control of the right temporoparietal junction over the primary visual cortex, which is generally spared in AD (Haroutunian et al., 1999; Mountjoy et al., 1983; Yew, Wong, Li, Lai, & Yu, 1999) and rather unaffected in the present case (see Figure 2).

In line with this interpretation, MC's integration deficit was found to be highly sensitive to critical perceptual conditions. Additionally, in the grouping experiment her deficit emerged only for the larger interelement distance, that is, when the visual system was supposed to rely heavily on the "task related integration rules" in order to achieve the segregation of the target from background.

On the other hand, in the easier segregation conditions, and in real life, the local corticocortical connectivity would be able to support an adequate perception of global patterns even in the absence of the modulation from the damaged areas located in the right temporoparietal junction.

The picture emerging from our hypothesis could in principle be related to any condition in which the visual system is faced with a relevant perceptual effort under the pressure of a predetermined task. In particular, going back to our grouping experiment, we would like to speculate that a naive subject, uninformed about the nature of target to be detected on the screen would probably fail to perceive the circular pattern under the same conditions in which an informed subject, well aware of the type of stimulus to be detected, would still be able to perceive it. The role of the modulatory mechanism implemented by the temporoparietal junction would therefore be to translate the rules of the game, which are probably coded at the level of the frontal cortices, into operative instructions for the perceptual system.

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