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# Combination of attentional and spatial working memory deficits in Bálint–Holmes syndrome

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This study aims to investigate whether attention and spatiotemporal integration deficits are dissociated in patients with bilateral posterior cortical atrophy (PCA), and whether it is their combination that leads to a severe clinical handicap. We recorded performance and ocular behavior of four PCA patients and four age-matched controls in visual search and counting tasks. We measured the percentage of targets detected and the mean detection time in a “pop-out” search. We also compared counting ability when a set of dots is presented briefly (in healthy individuals, the automatic deployment of attention over space allows a fast estimation of quantity) or for unlimited duration (favoring sequential counting, hence spatiotemporal integration). All patients showed reduced deployment of attention over space (simultanagnosia), resulting in increased visual search times and underestimations of the number of briefly presented dots. Only two patients showed ocular revisiting behavior that caused frequent omissions in visual search and overestimations of the number of dots presented for unlimited duration. The impairment to deploy attention is considered here as a bilateral covert attention deficit. Disorganized ocular exploration appears to be independent and is hypothesized to result from processes maintaining a salience map over time (spatial working memory) and especially across saccades.

**Keywords:** parietal neuropsychology; simultanagnosia; ocular search; counting; revisiting behavior; constructional apraxia; posterior cortical atrophy

## Introduction

Posterior cortical atrophy (PCA) is a rare and devastating neurodegenerative disease, characterized by a progressive impairment of higher-order visuospatial functions, earlier and much more prominent than other cognitive disabilities like memory and execution capacities.<sup>1</sup> PCA patients present bilateral occipitoparietal damage<sup>2</sup> and consistently develop Bálint–Holmes syndrome, a heterogeneous clinical entity which comprises a set of complex spatial behavior disorders characteristic of bilateral damage to the posterior parietal cortex (PPC).

On the one hand, Bálint<sup>3</sup> described his patient’s symptoms as a triad composed of (1) optic ataxia, a visually guided hand movement deficit characterized by spatial errors when the patient attempts to

reach objects in peripheral vision;<sup>4</sup> (2) a lateralized spatial attention disorder in which attention is oriented to the right of the body midline and stimuli lying to the left of fixation are neglected—corresponding to what is now called unilateral neglect; and (3) an extreme restriction of visual attention such that only one object is seen at a time. Bálint’s description and label of the third symptom (*seelenlähmung des Schauens*, often translated as *psychic paralysis of gaze*) highlighted that, while the patient exhibited no oculomotor paralysis, he/she did manifest lack of attention for visual events appearing in peripheral vision. Husain and Stein’s interpretation<sup>5</sup> corresponds to a restriction of the patient’s “psychic field of vision;” Michel and Hénaff<sup>6</sup> proposed a peripheral “shrinkage of the attentional field.” Another interpretation is that of

increased attentional competition between objects, a “disorder of simultaneous perception”<sup>7</sup> following the term *simultanagnosia* coined by Wolpert,<sup>8</sup> which is currently used to label this third symptom of the Bálint’s triad.

On the other hand, Holmes<sup>9</sup> described a visual disorientation syndrome in soldier patients with bilateral PPC lesions highlighting, in addition to a complete deficit for visually guided reach-to-grasp movements (optic ataxia), a wandering of gaze in search for peripheral objects and a difficulty maintaining fixation. This eye movement disorganization was later labeled *gaze apraxia* (reviewed in Ref. 10) and interpreted to be a particular oculomotor disorder. Holmes considered all symptoms to result from a retinal or extraocular muscle position sense deficit. However, primary visual or proprioceptive deficits are usually absent in the Bálint–Holmes syndrome.

A modern approach of the “wandering of gaze” symptom may be inspired by the literature about “revisiting behavior” recently described in patients exhibiting severe neglect during tasks involving ocular scanning (visual search tasks). This revisiting behavior has been ascribed to a deficit of spatial working memory (SWM), that is, misjudging old locations as new ones<sup>11–14</sup> and/or transsaccadic remapping<sup>15–18</sup> consecutive to the damage of the right inferior parietal lobule. To account for the full, severe, and chronic clinical expression of the neglect syndrome, the combination of rightward-lateralized attentional bias and spatiotemporal-integration deficit following damage to the right hemisphere has been postulated.<sup>17</sup> Similar to how severe neglect has been considered to result from more than a rightward attentional bias following unilateral right hemispheric damage, severe simultanagnosia following bilateral posterior cortical damage is often considered to be more than a local/foveal attentional bias, including reduced visual working memory storage capacity.<sup>19,20</sup> Clavagnier *et al.*<sup>21</sup> recorded ocular exploration that covered the whole space despite partial report performance in a simultanagnosic patient, suggesting that the lack of global report was owing to a deficit of high-level integration of different parts of the image that were explored by the eyes, rather than ocular exploration of a reduced part of the visual scene. Such a spatiotemporal integration deficit could result from an impaired maintenance of spatial

representation over time and across saccades, as revealed by disorganized ocular scanning and revisiting behavior.

A major difference between Bálint and Holmes is thus the description of attentional (lateralized or unlateralized) deficits (for Bálint) or of wandering of gaze (for Holmes). Attentional and eye movement deficits can be considered as two sides (perceptual/motor) of the same coin along this line, a reduction of the attentional field (foveal bias in simultanagnosic patients) would systematically induce a spatial disorganization of ocular exploration as an oculomotor consequence of the attentional deficit. However, in neglect there is converging evidence that the lateralized rightward attentional bias and the SWM deficit across saccades are anatomically dissociated because SWM deficits (1) can be observed without any lateralized bias of attention, for example, in a patient with constructional apraxia without neglect;<sup>22,23</sup> and (2) can be expressed in the entire space following right posterior parietal damage<sup>24,25</sup> or following transcranial magnetic stimulation over the right PPC,<sup>26,27</sup> hence they are considered to be nonspatial.

Here, we aimed to investigate whether attention and spatiotemporal integration deficits in patients with bilateral posterior cortical damage are dissociated, and whether it is the combination of simultanagnosia and revisiting behavior that leads to a severe clinical handicap, as assessed by Mini Mental State Examination (MMSE) and Clinical Dementia Rating (CDR) scales. We studied four PCA patients with simultanagnosia (assessed by the test of overlapping figures identification) and other features of Bálint–Holmes syndrome, with no primary visual field defect that would be characteristic of more focal occipital presentation of the syndrome (Table 1). We tested whether revisiting behavior (disorganization of ocular exploration) is systematically observed when spatial attention is reduced, which would argue in favor of either a common mechanism or two distinct mechanisms, respectively. The severity of simultanagnosia (i.e., a deficit of the fast and large spatial deployment of attention) was evaluated by underestimations in a counting task in which dots are presented briefly and longer detection time in a “pop-out” visual search task. The presence of spatiotemporal integration deficit across saccades was assessed by a possible disorganization of ocular exploration during visual search

**Table 1.** Neuropsychological and neurological assessment of the four PCA patients

Patient ID	Sex	Age (years)	Symptom duration (years)	Paraclinical profiles
MT	F	63	3	<p>Neuropsychological assessment: MMSE:14. CDR = 1. Impaired episodic and visual memories (California Verbal Learning Test 25/80, DMS48:62%). Visual spatial and constructional apraxia, unstructured clock-drawing test. Unable to perform the VOSP examination. Left visual extinction. Gerstmann syndrome and bilateral optic ataxia.</p> <p>Brain MRI revealed a diffuse bilateral cortical atrophy. Automated visual fields perimetry only displayed nonlateralized hyposensitivity related to attentional loss.</p> <p>CSF examination: profile of Alzheimer's disease.</p>
RG	M	76	4	<p>Neuropsychological assessment: MMSE: 14. CDR = 1. Global cognitive dysfunction with impaired memory and dysexecutive syndrome (RLRI16:7/48; DMS 48:92%, 83%). Severe ideomotor apraxia and bilateral optic ataxia. Visual spatial and constructional apraxia. Clock-drawing test: impossible to perform. Unable to perform the VOSP examination.</p> <p>Brain MRI: Despite obvious neurological and neuropsychological signs of posterior dysfunction, first MRI in 2007 was considered normal. Two years later, MRI revealed bilateral parieto-occipital atrophy. Automated visual fields perimetry only displayed nonlateralized hyposensitivity related to diffuse attentional loss.</p> <p>CSF examination: profile of Alzheimer's disease.</p>
MC	F	68	2	<p>Neuropsychological assessment: MMSE:29. CDR = 0.5. Bilateral optic ataxia. Visual spatial, perceptive, and memory dysfunction (RLRI16:43/48; VOSP: silhouettes 15/30, object decision 10/20, position discrimination 16/20, cube analysis 6/10, number location 6/10)</p> <p>Brain MRI revealed focal left parieto-occipital atrophy. Brain scintigraphy demonstrated bilateral parieto-occipital hypometabolism. Automated visual fields perimetry only displayed nonlateralized hyposensitivity related to attentional loss.</p> <p>The patient did not consent to the CSF examination; the clinical follow-up suggested a profile of Alzheimer's disease.</p>
MO	F	63	4	<p>Neuropsychological assessment: MMSE: 26. CDR = 0.5. Mild bilateral optic ataxia. Ideomotor apraxia. Slowdown and disturbances of mental flexibility. Mild perceptual agnosia and visual spatial dysfunction (RLRI16:48/48; VOSP: silhouettes 15/30, object decision 9/20, position discrimination 13/20, cube analysis 6/10, number location 5/10; BORB: 55/76).</p> <p>Brain MRI: discrete bilateral enlargement of the intraparietal sulci. Brain SPECT: parieto-occipital hypometabolism. Automated visual fields perimetry was normal.</p> <p>The patient did not consent to the CSF examination.</p>

or sequential counting with unlimited presentation of dots (revisiting behavior) that induced inefficient search and overestimations of the number of dots.

## Methods

### Patients

Patients (Table 1) were recruited from departments specializing in degenerative diseases and/or in the neuroophthalmology unit (civil university hospitals of Lyon) from November 1, 2009 to October 31, 2010. Both types of units enable a more comprehensive recruitment of these patients by including those diagnosed early with isolated neurovisual symptoms as well as those of retrospective diagnosis seen for the etiological investigation of an early demential syndrome.

Exclusion criteria were the presence of a severe dementia compromising the understanding and implementation of a simple order, and the presence of any other neurological affliction or of any oculomotor or ocular disease.

### Diagnosis of PCA

The diagnosis was determined by neurological, neuroophthalmological, and neuropsychological examination (Table 1). This included tests evaluating the presence of simultanagnosia (overlapping figures identification), bilateral optic ataxia,<sup>28</sup> global cognitive functioning (MMSE Folstein, CDR scale, and instrumental activities of daily living (EIADL)), memory (RL/RI-16 and Delayed Matching-to-Sample 48 (DMS48)), executive functions and attention (Trail Making Test (TMT)), verbal and categorical fluency similarities of the Wechsler Adult Intelligence Scale (WAIS), language (Bachy-Langedock, spelling and writing five regular and irregular words, identifying letters, reading sentences), apraxia, and, finally, visual-spatial and perceptual abilities (Visual Object and Space Perception Battery (VOSP), line bisection, protocol for evaluating visual agnosia (PEGV), Birmingham Object Recognition Battery (BORB)). Brain MRI scans were available and complemented by more sensitive brain scintigraphy scans when necessary. Lumbar puncture was proposed with measurement in the cerebrospinal fluid (CSF) of tau protein, phospho-tau, amyloid beta-proteins, and 14.3.3 protein. Automated visual field perimetry, visual acuity, and funduscopy were systematically checked.

### Age-matched controls

Control subjects were recruited among spouses of patients matched for age and level of education and who were free of any neurological or ophthalmological history. The spouses of MC (MDo), MO (MDa), RG (RA), and MT (DG) gave their informed consent and composed a control group of four individuals (77, 68, 63, and 67 years old). The tasks were made easy in order to allow all patients to perform them so that enough quantifiable data could be gathered. The performance of the control individuals thus provided the percentage of errors that cannot be considered pathological in the patients, for example, button press or casual inattention errors, as well as the mean speed of performance and standard deviation in healthy aged individuals to be compared with patients.

### Materials

Subjects sat in front of a custom experimental device, comprising a high speed cathode-ray tube (CRT) screen (frequency: 160 Hz) and a 21-in screen (ViSaGe, Cambridge Research Systems, Rochester, UK). A High Speed Video Eyetracker<sup>TM</sup>, attached to a head and chin rest (Cambridge Research Systems, Rochester, UK), registered eye movements with infrared camera (sampling frequency: 250 Hz; resolution: 0.05°). The eyetracker, the ViSaGe, and the screen were synchronized using a custom software interface. The head was supported by forehead and chin rests at 57 cm from the screen.

### Task design and recorded parameters

**Counting task.** Subjects were asked to count the number of square targets (2, 3, or 4 black) presented simultaneously in the central 14° area (7° around the central fixation cross). A total of 84 trials were presented randomly. Each trial began with a central fixation cross. After eye fixation was detected on the cross, two, three, or four dots were presented simultaneously for an unlimited duration in one condition and for 200 ms in another. The order of the condition was random across subjects. A push button was used to respond (subjects pressed the button as many times as they detected different targets with their right hand). They were then instructed to press another exit button with the left hand to end the trial and start the next trial. When the presentation was 200 ms, the response was given after the targets disappeared. Here, detection rather than

**Table 2.** Control subjects' button-press error percentages in the counting tasks

	Brief presentation (200 ms) condition		Unlimited presentation condition	
	Overestimations	Underestimations	Overestimations	Underestimations
Two dots	0% (SD = 0)	3.5% (SD = 2.1)	0% (SD = 0)	0% (SD = 0)
Three dots	1.8% (SD = 1.0)	8.4% (SD = 5.8)	5.6% (SD = 3.9)	0% (SD = 0)
Four dots	4.3% (SD = 1.5)	10.2% (SD = 5.7)	4.8% (SD = 2.2%)	3.8% (SD = 2.8)

active exploration is tested. In the unlimited condition, serial counting with oculomotor exploration is engaged and recorded, especially in trials with larger set sizes, because of the serial response mode in the presence of the stimuli. We calculated the percentage of correct responses, erroneous responses with overestimations, and erroneous responses with underestimations of the number of dots actually presented on the screen.

**Visual search task.** Once eye fixation was detected on a large central dot, a full-size visual array was displayed on the computer screen for an unlimited duration. This visual array consisted of a red disk (the visual target) among 12, 24, or 48 red squares (distractors) on a white background. There were 36 trials with the red disk presented in each the five horizontal segments of the display (far-left (from  $-17.5^\circ$  to  $-10.5^\circ$ ), near-left (from  $-10.5^\circ$  to  $-3.5^\circ$ ), center (from  $-3.5^\circ$  to  $3.5^\circ$ ), near-right (from  $3.5^\circ$  to  $10.5^\circ$ ), far-right (from  $10.5^\circ$  to  $17.5^\circ$ )). There were also three target-absent displays in which only distractors (12, 24, or 48) were presented. Subjects searched for the presence of the red disk and pressed a button as soon as they detected it. For controls and in patients MO and MC, the instruction was to press a different button if they did not detect a target. For patients RG and MT, it was the experimenter who pressed the *no-target* button when the patient struggled to find the target and then said that they did not see one. The reaction time was measured for each array in which a target was detected and then averaged separately for each of the five horizontal segments. The percentage of hits (trials in which the target was found) was also recorded for each of the five horizontal segments.

**Statistical analyses.** In the visual search task, detection time for each individual patient and age-matched control subject was submitted to factorial analysis of variances (ANOVA) with visual field (left–right) and target eccentricity (near: target

presented at  $7^\circ$ ; far: target presented at  $14^\circ$  or  $21^\circ$ ) as factors.

Each patient's performance (mean detection time and omission rate for each of the five horizontal segments in the visual search task, and percentages of underestimation and overestimation in the counting task) was compared against the control group using modified *t*-tests; these are designed specifically to test whether single-subject's (patient) data fall within the range of control data, using the control group's mean and standard deviation. They provide a robust comparison of a single data point against a small group of controls for single case studies.<sup>29</sup>

## Results

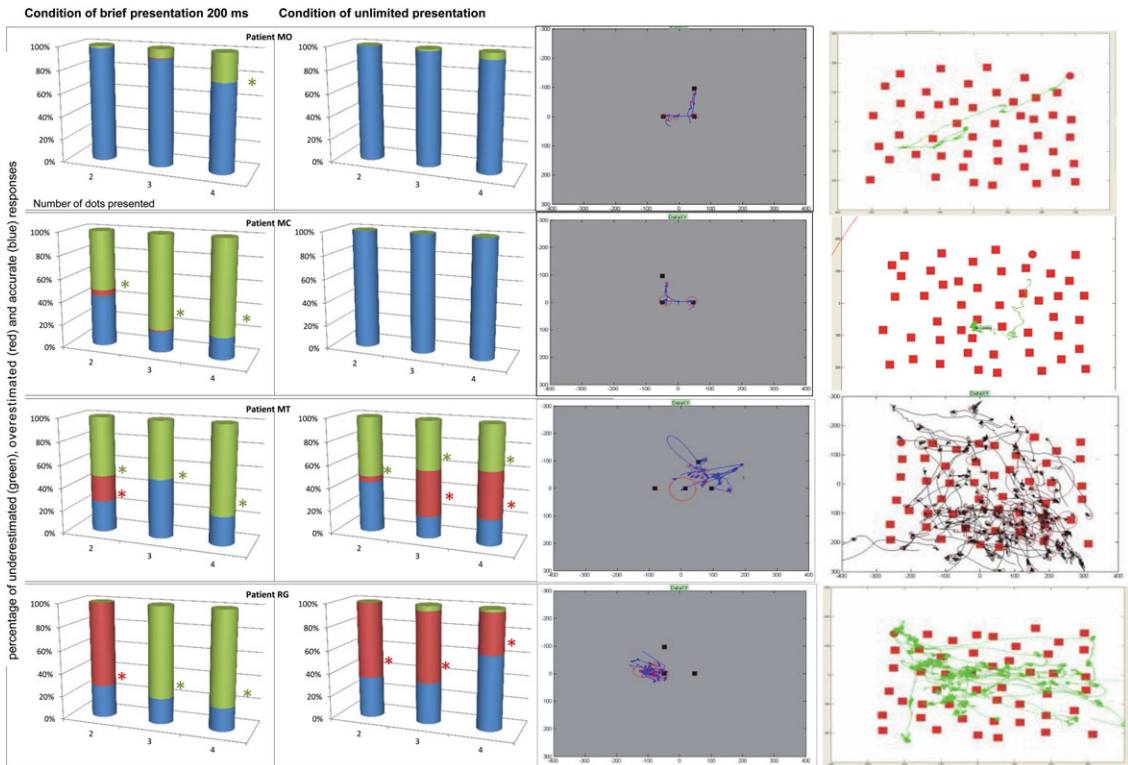
### Summary of results in control subjects

Control subjects performed the counting task with button-press errors that were not rare because of the serial response mode (Table 2). These percentages of errors indicate false-positive error rates (that cannot be considered as pathological) to be compared with the performance of the patients (Fig. 1).

In the pop-out visual search task, the control subjects typically detected all the targets (as can be seen in Fig. 2, the percentage of target omissions was close to zero, corresponding to rare button-press errors), and performed the task with only one saccade, with a constant mean detection time irrespective of the position of the target on the visual display (as can be seen in Fig. 3) and of the number of distractors. Individual ANOVAs indeed showed no significant effect of visual field or eccentricity on target detection time in any of the control subjects (all *P*s > 0.05).

### Summary of results in patients

**Counting errors.** The brief presentation condition revealed that all four patients produced significantly more underestimations (in green) than controls, even if the respective comparison was significant only for four dots in patient MO (Crawford

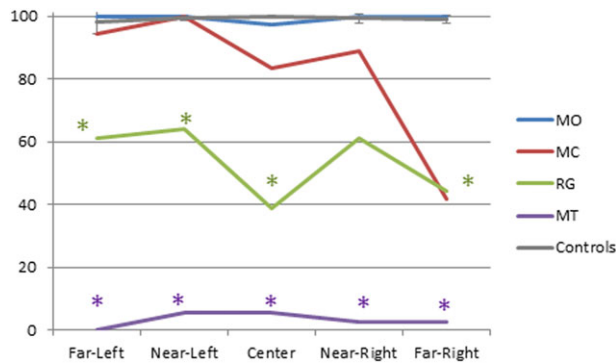


**Figure 1.** Performance of patient MO, MC, RG, and MT in the counting tasks. The left panels show the percentages of correct responses (in blue), underestimations (in green), and overestimations (in red) in the counting task performed in conditions of brief versus unlimited presentation of two, three, or four dots. Only patients RG and MT exhibited a significant rate of overestimation in the counting task in the unlimited time condition (red stars), with revisiting behavior as shown on the ocular traces of the typical illustrated counting trials. All patients exhibited a significant underestimation rate (green stars), except that this rate was significant only for four dots in patient MO ( $t = 3.1$ ,  $P = 0.02$ ; and not for 3 dots,  $t = 1.27$ ,  $P = 0.14$ ) and for three and four dots in patient RG ( $P$ s  $< 0.0006$ ). Stars indicate percentages significantly higher than controls ( $P < 0.05$ ; Crawford modified  $t$ -test). On the right are shown typical ocular traces for each patient in the unlimited counting task and in the visual search task for comparison.

modified  $t$ -test,  $t = 3.1$ ,  $P = 0.025$ ). Interestingly, this percentage of underestimation in the brief presentation condition did not match the severity of PCA reflected by the patients' MMSE and CDR scores (Table 1), whereas the percentage of overestimation in the unlimited presentation condition did. Indeed, only the two patients exhibiting the lowest MMSE scores (patients MT and RG) produced significantly more overestimations of the number of dots (in red) than controls, while, for example, MC showed the highest percentage of underestimation but the best MMSE score. As can be seen in the ocular traces recorded in the counting condition with unlimited presentation time (Fig. 1), scanning in these two most severe patients was characterized by ocular revisiting of the dots that they had already viewed

and counted; they likely considered them to be new dots (hence overestimated the number of dots).

**Visual search times and omissions.** As shown in Figure 2, only patient MO did not omit more targets than controls (all  $t$  values  $< 2.6$ ,  $P > 0.11$ ). Patient MC exhibited a significant percentage of omissions when the target was presented on the three right columns of the visual display (Crawford modified  $t$ -tests,  $t$  values  $> 10.2$ ,  $P < 0.009$ ), while patients RG and MT presented a significant decrease of target detection rate everywhere (Crawford modified  $t$ -tests,<sup>31</sup>  $t$  values  $> 81.1$ ,  $P < 0.0002$ ). The deficit was so severe for patient MT that she did not provide enough trials for statistical individual ANOVA of target detection time. In these rare trials with target



**Figure 2.** Percentage of valid trials (in which the target was detected) collected for each patient and the controls, for a target presented at different spatial locations on the visual search display (center, far or near periphery in the right and left visual fields). For example, if the proportion of valid trials is 60%, it means that there were 40% of omissions (trials in which the subject indicated that no target was present in the display) when the target was presented at this position. Stars with a different color attributed to each patient indicate when hits percentages are significantly lower than controls ( $P < 0.05$ ; Crawford modified  $t$ -test).

detection, detection time was between 4 and 16 s, equivalent to patient RG's detection times (Fig. 3), and it was clear from the ocular traces of these two patients (provided in Fig. 1) that when the targets were found, it was incidentally during inefficient ocular search. Consistent with the lateralized rightward bias of exploration shown by the typical ocular trace of patient MT (Fig. 1), we could not record for her any trial with target detection when targets were presented in the far-left column. Patient RG exhibited the same spatial disorganization in ocular behavior, but with opposite (leftward) lateralized bias of exploration (Fig. 1). Consistently, patient RG, like patient MC, responded faster when targets were presented in the near-left horizontal segment (Fig. 3). However, factorial ANOVAs revealed a significant advantage for the left visual field only for patient MC ( $F(1,115) = 6.9$ ;  $P < 0.05$ ) with no eccentricity effect (near versus far peripheral locations). The lack of statistical difference between detection time in left and right visual fields in patient RG is probably due to the high variability of the temporal measures (Fig. 3) consequent to the low percentage of hits (around 50%, Fig. 2). For patient MO, the individual factorial ANOVA showed no significant effect of either visual field ( $F(1,140) = 1.7$ ;  $P = 0.18$ ) or eccentricity ( $F(1,140) = 0.2$ ;  $P = 0.61$ ) and no interaction. However, comparison with the control group using Crawford modified  $t$ -tests<sup>29</sup> showed that her detection times were significantly longer than controls only for targets presented in the right visual field (in the two right columns,  $t$  values  $> 2.3$ ,

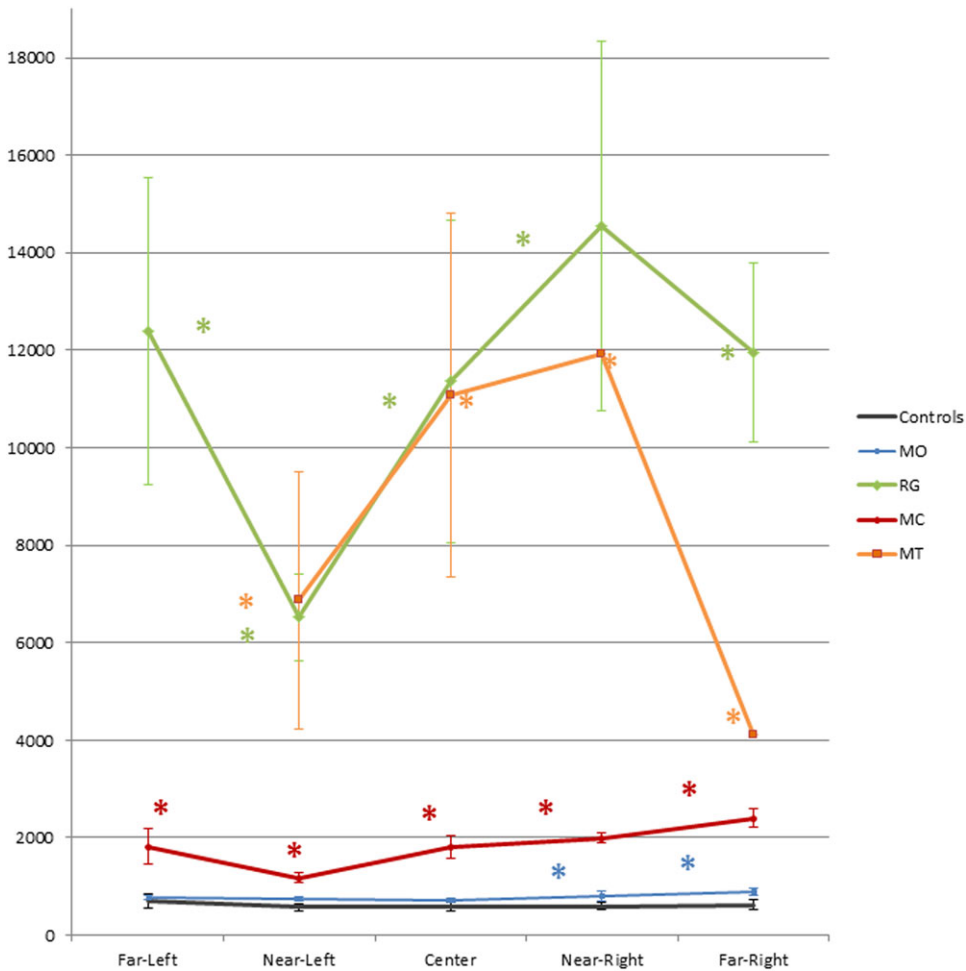
$P < 0.05$ , Fig. 3). In patients MT, RG, and MC, the detection times were markedly pathological, that is, significantly longer (all  $t$  values  $> 7.7$ ;  $P$ s  $< 0.01$ ), for targets presented everywhere in the visual display (Fig. 3).

**Ocular exploration biases.** Figure 1 shows that patient MT searched for dots more toward the right space in the counting task with unlimited presentation time and consistently exhibited a lateralized rightward exploring bias in visual search, while patient RG exhibited a similar ocular behavior in visual search and counting tasks but with opposite (leftward) lateralized bias.

## Discussion

Simultanagnosia is revealed clinically when the patient tends to report local elements before a global understanding of a complex visual scene (e.g., they report several fruits of Arcimboldo's painting but rarely and only secondly the face). This symptom generally occurs after bilateral parietal lesions with heterogeneous severity and recovery. It is also the most common symptom observed in neurodegenerative PCA with heterogeneous severity.

Neglect severity and recovery are also heterogeneous. Spatial remapping impairment consecutive to right inferior parietal damage has been postulated to contribute to the severity of neglect.<sup>17</sup> Spatial remapping has been classically considered to be the mechanism underlying perceptual stability of the visual world during and across eye movements.<sup>30</sup> However, Bays and Husain<sup>31</sup>



**Figure 3.** Mean time (in milliseconds) to detect the target among distractors when it was presented at its four possible horizontal positions in the visual display, for each patient (with individual standard deviation) and for the control group (with interindividual standard deviation). Patient MT data are not complete because she never detected the target when it was presented in the far left column, see Fig. 2. Stars with a different color attributed to each patient are provided on the graph when he/she was significantly slower than controls to detect the target at a given location using Crawford modified *t*-tests (all *t* values >2.3, *P*s < 0.05).

have proposed that impaired spatial remapping would rather produce visuomotor (including oculomotor) and SWM deficits. An “impaired SWM across saccades”<sup>11</sup> has been shown to cause ocular “revisiting” behavior in neglect patients: when the classical visual cancellation test used to diagnose neglect of left space is performed in the absence of visible cancellation marks or of distinctive object identities that provide spatial landmarks, the patients cannot compensate for their inability to keep track of the locations previously explored and therefore not only are biased toward the right space, but also re-explore the same objects and consider

them as new ones.<sup>11,12</sup> This spatial disorganization of ocular exploration could be due to a faulty use of the saccade efference copy to update saliency maps, and thus, as already suggested by Duhamel *et al.*,<sup>15</sup> independent of the attentional deficit.

Isolated SWM deficit across saccades can be observed in the entire space following transcranial magnetic stimulation over the right inferior parietal cortex<sup>26,27</sup> and in patients with constructional apraxia after full neglect recovery.<sup>22,23</sup> Conversely, patients with superior parietal damage sparing the right inferior parietal cortex have been shown recently to have contralesional attentional

orienting deficit without clinical neglect,<sup>32–34</sup> and transcranial magnetic stimulation of the right or left superior parietal lobule has been shown to induce left or right extinction, respectively.<sup>35</sup> A double dissociation can thus be drawn between patients with pure spatial disorganization symptoms following structural damage limited to the right inferior parietal cortex and patients with pure deficit of covert attention following structural damage limited to the dorsal attentional network.<sup>36</sup> Since this dorsal attentional network is involved in the covert orienting of attention toward peripheral locations in the contralateral visual field,<sup>36</sup> bilateral damage in PCA patients causes simultanagnosia because patients are left with only attention to central locations. A lateralized attentional bias may also add to the restricted spatial deployment of visual attention of these PCA patients from asymmetrical damage of this dorsal network or from an interhemispheric imbalance in this dorsal network caused by a lesion elsewhere, especially in the right inferior parietal cortex.<sup>39</sup> Indeed, Corbetta *et al.*<sup>37</sup> have shown that, when the right inferior parietal cortex is structurally damaged, there is a functional hypo-activation in the superior parietal lobule of the same hemisphere. However, this functional dependence seems to be only temporary in stroke patients since the balanced level of superior parietal lobule (SPL) activation between hemispheres is recovered progressively as a correlation with recovery of attentional balance between visual fields.<sup>37</sup> Thus, it might be meaningful to find a single dissociation between attention and SWM deficits and not a double dissociation, in patients with neurodegenerative diseases as in stroke patients in acute stage. It would mean that attentional-orienting and spatiotemporal-integration processes rely on structurally dissociated posterior cortical systems, but the SPL is functionally dependent on the sparing of the IPL, and not vice versa.

In order to investigate these complex relationships between attentional and spatiotemporal integration systems and whether it is the combination of attentional deficit and revisiting behavior that leads to a severe handicap in PCA patients, we recorded performance and ocular behavior in four patients during visual search in order to compare with the literature of neglect-revisiting behavior and its functional consequences. We also designed two counting tasks aimed at dissociating

covert attentional field reduction using brief dots presentation versus impaired spatiotemporal integration using unlimited dots presentation and a sequential response mode favoring serial ocular exploration.

In contrast to the dot-counting task performed on paper presentation (in the VOSP test), our two computerized counting tasks (brief versus unlimited duration of dots presentation) allowed us to isolate simultanagnosia from revisiting behavior. Indeed, the deficit in deploying spatial attention broadly and shortly, causing a high rate of underestimation in the task consisting of evaluating the number of dots in the brief presentation condition (simultanagnosia), even when severe as in patient MC, was not systematically associated with revisiting behavior in the condition of unlimited presentation (causing a re-count of the same dots several times and hence overestimation of the number of dots). Indeed, patients MC, MT, and RG showed an equivalent rate of underestimations in the brief presentation of dots (Fig. 1) that reflects an equivalent severity of simultanagnosia, but only patients MT and RG exhibited overestimations in the unlimited condition. In healthy subjects, evaluating the number of dots in an array is considered to involve two different processes: subitizing or counting. Subitizing is the ability to detect up to three or four dots simultaneously when presented quickly with high accuracy; beyond that, a serial and time-consuming process of counting is observed.<sup>38</sup> With the brief presentation preventing eye scanning movement, we therefore imposed a subitizing process based on a large and automatic deployment of attention, and provided the best sensitivity to reveal subclinical simultanagnosia. With the unlimited presentation and the serial mode of response in presence of the stimuli, we think that the subjects were engaged in serial counting processes. Clinical study in simultanagnosic patients has suggested that subitizing is preserved as opposed to counting processes.<sup>39</sup> In contrast, in our condition of brief presentation (200 ms preventing saccadic exploration) of a small number of dots, we established that the subitizing process was impaired in our four PCA patients: they all made more underestimations than controls, revealing their reduced attentional field (simultanagnosia). In the condition of unlimited presentation time, their behavior differed (Fig. 1). In patients MC and MO, these underestimations

(revealing simultanagnosia) were canceled, as in the paper version of the VOSP test, thanks to an efficient exploration strategy that allowed them to displace their reduced attentional field to overtly scan all the dots (as can be seen on the ocular traces). In patients RG and MT, overestimations were produced and reflect a disorganized scanning of the dots during the serial counting process engaged in this condition of unlimited presentation time. This reveals that the overestimations of the number of dots cannot be attributed to simultanagnosia itself but to the combination of the reduction of the attentional field (revealed for all patients in the condition of brief presentation) and the SWM deficit across saccades. This combination also caused a high rate of omissions in the visual search task and a gaze stacked within a restricted area of the visual search display. Interestingly, the presence of overestimations in the unlimited condition (attributed to a SWM deficit) matched the MMSE scores, whereas the percentage of underestimation in the brief presentation condition (attributed to simultanagnosia) did not match these scores. This suggests, as it has been suggested following unilateral right damage for neglect patients,<sup>17</sup> that SWM deficits have more negative functional consequences than restriction of spatial attention itself. Indeed, patients with only simultanagnosia are able to compensate their reduced attentional deployment by strategic and efficient ocular sampling of visual information. Preserved spatiotemporal integration of the location of the different visual snapshots allows them to efficiently cover the entire visual display, keep track of where in external space the visual information was taken, and build a late but consistent spatial representation of the visual scene. Their attentional deficit is therefore only expressed as search time increases (with respect to controls), which reflect the increase of the number of saccades necessary to scan the entire visual display with a smaller attentional field. The same pattern can be mimicked in healthy subject by imposing on them a gaze-contingent moving visible window when they perform the visual search task, which leads to an increase in the number of saccades but does not produce revisiting behavior.<sup>40</sup>

While all properties necessary for attentional selection (selective enhancement or inhibition of stimulus representation) and working memory across saccades (inhibition of return processes) have been identified within priority maps of the lateral

intraparietal areas in monkeys,<sup>41,42</sup> they might reflect processes that occur elsewhere.<sup>43</sup> In humans, attentional priority maps may correspond to bilateral representation of space in the symmetrical dorsal attentional network;<sup>36</sup> but spatiotemporal integration needed for an efficient and organized visual search over the entire space (SWM across saccades and/or remapping processes) might rely on a specialized right-hemispheric inferior parietal network.<sup>13,14,17,18,22–27</sup>

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## Conflicts of interest

The authors declare no conflicts of interest

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