

# “Sequence Agnosia” in Bálint’s Syndrome: Defects in Visuotemporal Processing after Bilateral Parietal Damage

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## Abstract

■ Bálint’s syndrome is characterized by visuospatial dysfunction, with failure to attend to multiple objects in space and poor spatial localization manifested as impaired reaching and saccadic targeting. Less investigated in this disorder is perceptual processing along the dimension of time. We studied the performance of a patient with Bálint’s syndrome on two oddity paradigms in which she had to indicate which of three objects was different in color, shape, or structure. Her initial difficulty with processing multiple objects present simulta-

neously in different locations recovered, but she had persistent difficulty processing objects seen sequentially at the same location. Further studies showed that this deficit was not due to impairments in sustained attention or in distributing attention over time, but to impaired processing of temporal sequences. The deficit was also present with auditory stimuli, indicating a multimodal failure of temporal sequencing. These findings show that bilateral parietal lesions affect not only the spatial but also the temporal organization of perception. ■

## INTRODUCTION

Current concepts of visual processing in cerebral cortex postulate two main visual pathways: a dorsal occipitoparietal stream for processing spatial information (the “where” pathway) and a ventral occipitotemporal stream for identifying objects (the “what” pathway) (Ungerleider & Mishkin, 1982). The classic picture of bilateral dorsal stream damage is Bálint’s syndrome, a triad of associated deficits that includes *simultanagnosia*, the failure to attend to more than one object in space at a time; *optic ataxia*, inaccurate reaching to visual targets; and *oculomotor apraxia*, impaired generation and targeting of saccades (Rizzo & Vecera, 2002). An underlying theme of these deficits is a failure in visuospatial processing in either the spatial distribution of attention or the extraction of accurate spatial coordinates to guide hand or eye movements.

Notably absent from descriptions of Bálint’s syndrome are impairments of visual processing in the fourth dimension: time. This is a curious omission because space and time are both equally important variables in the visual control of action, another purported role of the dorsal stream (Milner & Goodale, 1995). Given the dynamic nature of the world, spatial attention and spatial coordinates are only useful when one also has concurrent information about the temporal properties of stimuli. Furthermore, there have been recent data suggesting that the right inferior parietal lobule is part of a network involved in temporal perception. Duration

discrimination is associated with activation in the right inferior parietal cortex on functional magnetic resonance imaging (Rao, Mayer, & Harrington, 2001), and patients with right parietal lesions have problems with duration perception (Harrington, Haaland, & Knight, 1998) and prolonged attentional blink (Husain, Shapiro, Martin, & Kennard, 1997). These considerations make it likely that defects in temporal processing are also present in Bálint’s syndrome. In this report, we provide evidence of a failure in maintaining temporal sequences of stimuli in S.L., a patient with Bálint’s syndrome from bilateral occipitoparietal strokes (Figure 1).

We tested S.L.’s ability to identify and discriminate a variety of simple visual stimuli using several different experimental paradigms. We first asked her to identify single stimuli to confirm that her processing of color and form was intact. Next, we administered two oddity tasks that required her to state which of three stimuli was the odd one out. This involved either simultaneous presentation, so that S.L. had to attend to stimuli at three different spatial locations but seen at the same time, or sequential presentation, so that S.L. had to attend to stimuli seen in the same spatial location but at three different times. These were all easy tests that an age-matched control subject performed with 100% accuracy.

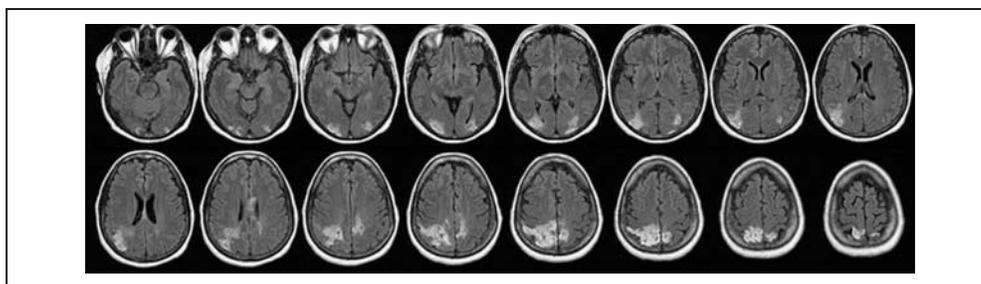
## METHODS

S.L. is a 49-year-old woman who suffered bilateral occipitoparietal infarctions from primary central nervous

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**Figure 1.** Axial magnetic resonance imaging, with fluid-attenuated inversion recovery (FLAIR) sequences of S.L. showing bilateral occipitoparietal strokes as white high-intensity regions.



system vasculitis 2 months prior to the start of testing (Figure 1). Her initial examination showed a left inferior quadrantanopia, inaccurate saccades with imperistence of fixation, and poor pursuit. She had neglect, as assessed with the Sunnybrook Neglect Assessment Battery (Leibovitch et al., 1998). Clinical observations also showed that she had optic ataxia when using either hand, in that she often missed when reaching for objects and failed to orient her grasp correctly to the axes of objects like pencils. She showed simultanagnosia, as tested on four complex displays of visual scenes. For example, with the Cookie Theft picture (see [http://pages.slc.edu/~ebj/IM\\_97/Lecture10/cookie\\_theft.gif](http://pages.slc.edu/~ebj/IM_97/Lecture10/cookie_theft.gif)), a drawing from the Boston diagnostic aphasia examination that depicts several people and events distributed evenly across the scene, which required distributed attention to multiple items for correct reporting (Goodglass & Kaplan, 1983), S.L. initially reported seeing only “a boy’s face . . . eyes,” failing to notice the mother on the right side of the display or the second child aiding the first one, or to describe what action was occurring. Neuropsychological evaluation showed normal attention, language and, verbal memory functions, although reading skill was in the borderline impaired range, with a tendency to guess at words based upon the first or last letters. She had left–right disorientation and finger agnosia, and her calculation skills were in the borderline range. She was able to recognize simple line drawings of objects and to identify colors and simple shapes.

Over the next few months she improved. At the time of testing, her visual acuity was 20/40, her inferior quadrantanopia had resolved, and she had no signs of hemineglect. She saw multiple items on the cookie theft picture but could not relate the elements to each other. Saccadic accuracy was better, and there was only mild misreaching to visual targets with the left hand. Recognition of objects in line drawings was normal. Further testing at this time also showed that she had “local capture” with hierarchical Navon letters (big letters made up of an arrangement of small letters), in that she saw only the local letters and not the global letters, using stimuli and parameters similar to those used in prior reports of this phenomenon in Balint’s syndrome (Jackson, Swainson, Mort, Husain, & Jackson, 2004; Karnath, Ferber, Rorden, & Driver, 2000).

S.L. viewed stimuli on an Apple Multiscan 1705 monitor in standard, dim room lighting, at a viewing distance of 57 cm. Experiments were run on a Powermac G4 using Superlab 1.71 (Cedrus, Phoenix, AZ), and stimuli were generated with either DeltaGraph Pro 5.6 (RockWare, Inc., Salt Lake City, UT) or Adobe Photoshop CS (Adobe Systems Inc., San Jose, CA). To avoid any issues related to optic ataxia, S.L. indicated her answers verbally and these were entered with keypresses by the examiner.

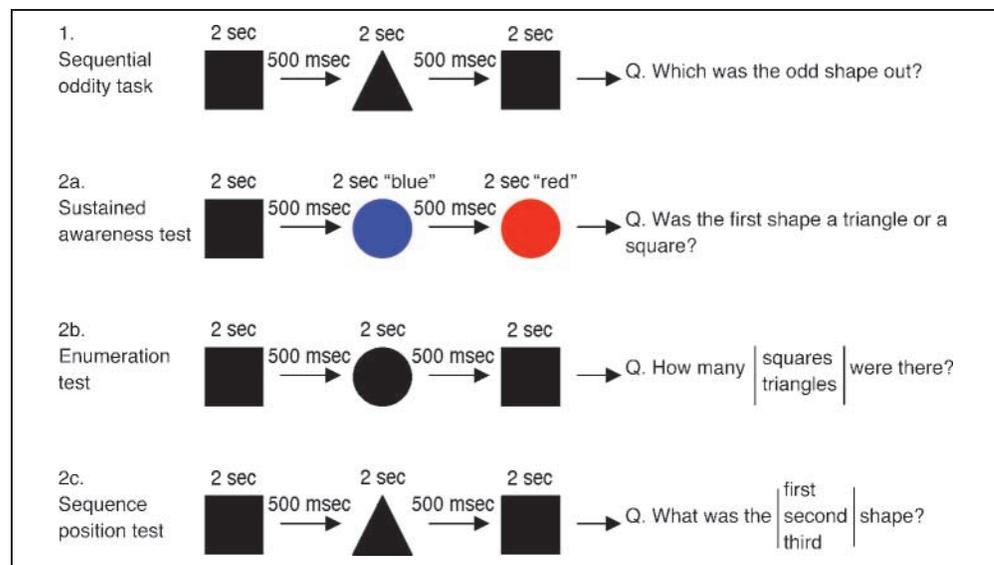
We tested S.L. on three visual stimulus categories taken from tests we use in our laboratory to assess form and color perception, processes that her initial neuropsychological evaluation suggested were relatively preserved. These were colors, shapes, and dot arrangements (Table 1). All were shown on a white background. The stimuli for the color tests were  $2.5^\circ$  squares of either a red or a blue hue. Stimuli for the shape tests were squares and equilateral triangles of  $2.5^\circ$  height. In one set, the stimuli were thick black outlines; in the second set they were solid black. We also tested S.L. with dot patterns similar to those used in prior studies of form processing by our laboratory (Barton, Cherkasova, Press, Intriligator, & O’Connor, 2004). These consisted of four small black disks ( $0.45^\circ$  diameter) arranged in patterns spanning a height of  $2.5^\circ$ . There were five versions of this test. In one, the four dots were arranged in an irregular trapezoid and the target pattern had one dot shifted laterally by 24 pixels. In the second, the four dots were connected by a cross, with the target pattern again having a dot shifted by the same 24 pixels. In the third, the four dots were connected to form an outline. In the fourth version, the target pattern differed in that one of the four dots of the trapezoid was missing. In the last version, the four dots were arranged in a symmetric diamond shape, with the target again having one dot shifted laterally by 24 pixels. All tests were given in separate blocks.

For several of the stimuli, we first established that S.L. could perceive the differences in objects by having her identify them. Each color and shape stimulus was presented alone in the center of the screen for an unlimited time, and S.L. was asked to name the relevant attribute of color or shape. For the regular diamond dot patterns, S.L. was asked to state whether the pattern was vertically

**Table 1.** Percent Accuracy on the Different Tasks

<i>Stimulus 1</i>	<i>Stimulus 2</i>	<i>Identification</i>	<i>Simultaneous Oddity at 2 Months</i>	<i>Simultaneous Oddity at 4 Months</i>	<i>Simultaneous Oddity at 5 Months</i>	<i>Sequential Oddity at 5 Months</i>
		100		100		68
		100	56			72 (78)
		100	59			67 (72)
			22		83	67
				50	100	44
				50	100	61
		94		89	100	67
		100	56		100	61
Sounds: camera	Sounds: whip	100				67

**Figure 2.** Diagram of the different sequential-stimuli tests. The top row shows one example of how a trial from the sequential oddity task proceeded over time, from left to right. The second row shows an example of a trial from the sustained awareness test, where a test shape was followed by two colored discs that the subject had to name before being asked to recall what the test shape was. The third row shows an example of a trial from the enumeration test, where the subject had to state how many of a certain shape (square or triangle) were shown in that trial. The fourth row shows an example of a trial from the sequence position test, where the subject had to state which stimulus had occurred at a certain point in the sequence. Questions were always asked after the end of the stimuli sequence.



symmetric or asymmetric. For the irregular dot patterns, she was asked whether there were three or four dots in the pattern. For the remaining dot stimuli, no obvious identification task could be performed. Twelve trials were presented for each stimulus, with separate blocks for color, shape, and dot patterns. Her accuracy was excellent on these identification tests, being 100% for color, all shape tests, and judgments of symmetry for the diamond dot patterns. With the latter, her accuracy was 94% when she had to state the number of dots present.

We next used two oddity tasks. Each trial showed three stimuli, two identical and one different, and asked S.L. to indicate which stimulus was the odd one out. In the *simultaneous oddity task*, all three stimuli were visible at the same time on the screen, but in different locations, being arranged in triangular configuration with  $7.8^\circ$  separating each stimulus from another. The odd target had an equal likelihood of occurrence at each of the three positions. The stimuli had unlimited duration, terminating only when S.L. indicated whether the left, right, or top stimulus of the three was the odd one out. Eighteen trials were given for each block.

In the *sequential oddity task*, only one stimulus was present at a time in the same location at screen center (Figure 2). Each stimulus was shown for 2000 msec, each separated by a 500-msec mask; 2000 msec was used because her median reaction time in the identity tasks (which included the time it took for the experimenter to hear her response and hit the key) ranged between 1000 and 1970 msec. This duration also allowed enough time to minimize possible effects of attentional blink (Husain et al., 1997) and has been used in prior studies of Bálint's syndrome (Jackson et al., 2004). The odd target again had an equal likelihood of appearing in each of the three positions in the sequence. At the end of the sequence, S.L. was asked to indicate whether the first, second, or third stimulus was the odd one out. Again, 18 trials were given for each block. A male control subject aged 46 years also performed these tasks and easily obtained scores of 100% correct on both tasks.

Two weeks after her performance of the sequential oddity task, we administered a second series of three tests aimed at identifying the nature of the difficulty underlying her problem with this sequential oddity task (Figure 2). All of these tests used similar shape stimuli and the same timing parameters as the sequential oddity paradigm. All tests were done twice, once using outlined shapes and once using solid shapes. Each test consisted of 18 trials. A male control subject aged 46 years also performed these tasks and obtained scores of 100% correct on all three tests, confirming again that these are easy tasks for healthy subjects.

For the *sustained awareness test*, one of the two shapes (square or triangle) was shown as the first stimulus. This was then followed by two disks of  $4.3^\circ$  diameter and of a red or blue color as the second and third stimuli. S.L. had to name the colors of these disks aloud as a sim-

ple distracting task. At the end of the sequence, S.L. had to indicate which shape had been the first stimulus.

For the *enumeration test of distributed attention*, three shapes were shown one after the other. At each temporal position, the shape shown was randomly determined, so that each trial could contain anywhere from zero to three of a given shape. At the end of each trial S.L. was asked to state how many of one type of shape had been shown, either squares or triangles. Because the questions asked were randomly ordered, S.L. did not know at the start of the trial which stimulus to count. Also, on a third of the trials a circle was substituted for one of the shapes, so that S.L. could not simply keep a running count of one stimulus and derive the answer by subtracting this count from 3 if the question involved the other stimulus. Rather, to answer the question accurately, S.L. would have to recall the shape information about all three stimuli at the end of each trial.

For the *sequence position test*, the sequential oddity task for shapes was shown to her again. This time, though, each trial was followed by one question about which stimulus had occurred at the first, second, or third position in the sequence. The order of the questions was randomly determined so that S.L. did not know until the end of the trial which position was going to be probed.

Finally, the third test set explored whether S.L.'s sequencing difficulties extended to auditory stimuli. We used the sounds of a camera shutter and a cracked whip, taken from audio files included with the Mac OS 9.2 operating system. Each lasted approximately 1 sec. S.L. was first tested on her ability to identify the two auditory stimuli by playing each stimulus and asking her to name the sound. There were 12 trials in random order. Next, the sounds were given in a sequential oddity task, with three sounds presented one after the other, two identical and one the alternative sound. Each auditory stimulus lasted approximately 1 sec and was followed by a 2-sec interstimulus silent pause, making the total trial duration 7 sec, about the same as for the visual sequential oddity tests. S.L. was asked to indicate which of the three stimuli was the odd one out.

## RESULTS

Table 1 shows S.L.'s performance on the various identification and oddity tasks on the three different days she was tested, at 2, 4, and 5 months after onset. When first tested on the simultaneous oddity paradigm at 2 months after onset, she performed poorly with a number of shape and dot pattern stimuli, scoring below the threshold value of 67% (i.e., halfway between chance performance at 33% correct and ceiling performance at 100% correct) for all tests although the identification testing showed that she could perceive these accurately when asked to respond to one stimulus at a time. By 5 months, despite continuing evidence of simultanagnosia on tests

with complex pictures and local/global hierarchical stimuli, she had recovered the ability to do the spatial oddity task, scoring 100% with all stimuli except the random four-dot pattern, where she scored 83%. However, at this point, when tested with the sequential oddity task, she consistently performed near threshold regardless of the type of stimulus. This remained true on retesting 1 week later (numbers in parentheses). Note that these are very easy tasks that the control subject did with 100% accuracy: Setting an expected accuracy rate of 99%, binomial proportions show that the likelihood of making just 2 errors out of 18 (89% correct) is less than 0.01. For those five tests that S.L. did in both simultaneous and sequential presentation on the same day, she was significantly better on the simultaneous task than on the sequential one: paired  $t$  test,  $t(4) = 5.69, p < .005$ .

These data clearly show that with stimuli that S.L. could identify flawlessly on either the identification task or the simultaneous oddity task (with the single exception of the irregular four-dot configuration stimulus), she was consistently impaired when she had to discriminate them when they were sequentially presented. Hence, her problem is not with the stimuli but with the paradigm. Although she initially had difficulty with the simultaneous oddity task, which requires processing of several targets seen at different locations but at the same time, she recovered but still was left with a defect on the sequential task, which requires processing of several targets seen at the same location but at different times.

What could be the reason for S.L.'s difficulty with the sequential oddity task? We considered several possibilities. One is an inability to sustain awareness of objects over time. Previous studies of simultanagnosia have documented such problems (Rizzo & Robin, 1990; Rizzo, Hurtig, & Damasio, 1987). It may be that S.L.'s difficulties with the sequential oddity task stems from a failure to maintain awareness of stimuli over the 7 sec of each trial. To test this possibility, we administered a test of her ability to recall the first stimulus of each trial (test 2a in Figure 2), as the first stimulus would be the most distant in time from her response and therefore the most vulnerable to a failure of sustained attention. S.L. performed at 100% on these sustained awareness tests for both outlined shapes and solid shapes.

A second possibility is impaired distribution of attention to multiple objects across time. Simultanagnosia is classically defined as the inability to attend to more than one object in a scene. This implies a failure to distribute attention across multiple spatial locations and multiple objects that are seen simultaneously. However, it may be that the constriction of attention in simultanagnosia is also accompanied by problems in distributing attention across sequentially occurring objects. To test this possibility, we showed S.L. trials containing a sequence of three objects followed by a request that she tell us how many of a certain type of object were shown (test 2b in Figure 2). To enumerate this accurately, she would have

to retrieve the identity of all three stimuli, but not necessarily the order in which they were seen. Accurate performance on this test would also exclude a third explanation—that she failed to process the second or third stimuli because of a prolonged attentional blink that has been described in some patients with neglect from right parietal lesions (Husain et al., 1997). On these enumeration tests, S.L. was 96% accurate with the solid shapes and 100% accurate with the outlined shapes.

If S.L. performed the enumeration task well, this would suggest that her problem lies not in attending and processing all the stimuli in the sequence, but in recalling the sequence itself. To confirm this, we used a task in which, after the sequence had been shown, S.L. was asked to name the stimulus shown in the first, second, or third position (test 2c in Figure 2). In contrast to her performance on sustained awareness and enumeration, her accuracy on this sequence position test was 72% for outlined shapes and 61% for solid shapes.

A final test was added to see if S.L.'s problem with sequence processing affected other modalities as well. Instead of visual stimuli, we used two different sounds, that of a camera shutter and that of a cracked whip. Although S.L. was flawless in identifying these sounds when heard individually, she was again impaired when discrimination was tested using the sequential oddity task (Table 1).

## DISCUSSION

To summarize, S.L. had significant difficulty with an oddity task that required her to indicate which of three sequentially viewed objects were different. This was despite the fact that she could identify test objects by name or discriminate them when they were viewed simultaneously, confirming that her problem was not with recognizing the objects themselves, but with the paradigm used to present them, a conclusion also supported by the fact that the problem was seen with a wide array of objects using the same sequential paradigm. The follow-up experiments showed that this was not due to failures to sustain attention over the 7-sec duration of each trial, or to impaired distribution of attention to each of the three objects, or to attentional blink degrading the processing of one stimulus following another. Rather, her problem lay in maintaining the correct temporal order of the sequence of stimuli, a problem we call “sequence agnosia.” Furthermore, this deficit is not specific to the visual modality but also affects auditory processing, consistent with demonstrations that other deficits in Balint's syndrome such as spatial localization may also affect other modalities besides vision (Phan, Schendel, Recanzone, & Robertson, 2000; Holmes, 1918).

S.L.'s impaired sequence processing is not likely related to the limitations of attentional capacity in simultanagnosia. It is conceivable that a failure to process more

than one object may have both a spatial and a temporal dimension. Indeed, such a failure may underlie the prolonged attentional blink described in patients with neglect after right parietal lesions (Husain et al., 1997) and which may play a role in the visual extinction after such lesions (di Pellegrino, Basso, & Frassinetti, 1998). However, the follow-up experiments we performed showed that S.L. has sufficient attentional capacity to enumerate the number and type of several stimuli seen over the 7-sec period of the sequential task, and, therefore, this cannot account for her difficulties with the sequential oddity task. Nevertheless, it is possible that failures in attentional distribution across time may have been found in S.L. if such tests had been applied closer to the time of onset, when her clinical deficits were more severe.

Rather, S.L.'s persistent difficulties with sequence information may have important parallels with the impairments in spatial localization and targeting that have been described in Balint's syndrome (Rizzo, Rotella, & Darling, 1992; Jakobson, Archibald, Carey, & Goodale, 1991; Perenin & Vighetto, 1988). Patients with spatial disorientation or optic ataxia have difficulty in accurately assigning objects their correct spatial coordinates (Phan et al., 2000). Difficulty with spatial "tagging" may have caused S.L.'s early inability to perform the simultaneous oddity task, which required her to give "left," "right," or "top" as the answer: Given that these are tests that are quite easy, it remains possible that S.L. may still have had some subtle spatial tagging problems at 5 months. Her more persistent and obvious difficulty at that point, though, is with tagging objects with their correct temporal coordinates, as defined by their relative position within a sequence, in order to give the answer "first," "second," or "third." Whether problems with spatial or temporal tagging (determining that an object belongs to a certain location or time) are related to other issues of object binding (determining that properties such as color and motion at the same location or at the same time belong to a single object) is uncertain. However, there is one report of a patient who had difficulty with both spatial feature binding and object localization in space (Friedman-Hill, Robertson, & Treisman, 1995). Although we did not investigate temporal binding in our patient, there is doubt as to whether this phenomenon exists or is as strong as spatial feature binding in normal subjects (Keele, Cohen, Ivry, Liotti, & Yee, 1988). On the other hand, another study of a patient with Balint's syndrome showed impaired binding in the spatial domain but better binding in the temporal domain, suggesting that temporal binding may not be affected by parietal lesions (Robertson, Treisman, Friedman-Hill, & Grabowecky, 1997).

Our findings add to a growing body of evidence that the parietal cortex plays a significant role in not only spatial but also temporal processing (Walsh, 2003). In monkeys, neurons in the lateral intraparietal cortex have

been shown to signal the perception of elapsed time (Leon & Shadlen, 2003). Patients with right parietal damage have difficulty judging the temporal order of two successive contralateral stimuli separated by several hundred milliseconds (Snyder & Chatterjee, 2004). Also of potential relevance to our results is evidence from functional imaging experiments that sequence learning may involve the parietal cortex (Hazeltine, Grafton, & Ivry, 1997; Grafton, Hazeltine, & Ivry, 1995), findings that have led to a proposal that some forms of sequence representation involve the parietal cortex, particularly those representations that do not require encoding across separate stimulus dimensions or sensory modalities (Keele, Mayr, Ivry, & Hazeltine, 2003). Our data are consistent with this proposal in that they indicate a problem with the organization of perceptual information in time in Balint's syndrome, a new deficit that suggests that not only is the dorsal occipitoparietal network a "where" pathway (Ungerleider & Mishkin, 1982), but is also part of a "when" pathway.

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