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An eye on reading: The role of eye-movements in normal readers and in patients with acquired dyslexia

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INDEX

1. General introduction - Reading in normality and pathology

Reading is a multi-componential and a highly complex task involving a precise integration of vision, attention, saccadic eye movements, and high-level language processing. Several cognitive stages are required, from the letter features detection and integration to the comprehension of meaning and pronunciation of the words. The acquisition of reading skills is a slow process (Dehaene & Cohen, 2007) and it is a fundamental ability for all members of our society. Coherently, the topic has been largely investigated within the field of cognitive psychology. In particular high level lexical and low level visual factors have been greatly studied in literature.

From a cognitive perspective, different models have sought to investigate the mechanisms at the basis of word recognition. Single (Seidenberg & McClelland, 1989; Plaut, McClelland, Seidenberg, & Patterson, 1996) and dual route (Coltheart, 1978; Coltheart, Rastle, Perry, Langdon, & Ziegler, 2001) mechanisms models have been proposed as the basis of the visual word recognition task. The single-route perspective claims the existence of a single mechanism - where all sources of information are available in parallel - which learns the statistical consistencies between graphemes and phonemes (Seidenberg & McClelland, 1989; Plaut, et al., 1996) and allows reading of both words and pseudowords. On the other hand, the dual route model of reading aloud (Coltheart, 1978; Coltheart et al., 2001) argues that two distinct processes are needed: A sublexical process that enables a linear mapping between orthographic and phonological patterns (used in reading pseudowords and non-familiar words) and a lexical process that retrieves word-specific information from the lexicon, where the lexical representations of the known words are stored. Similarly to what found in more opaque orthographies like English, frequency effects (high-frequency words read faster than low-frequency words) and lexicality effects (words read faster than pseudowords) have been reported in reading Italian aloud (Burani, Arduino, & Barca, 2007; Pagliuca, Arduino, Barca, & Burani, 2008). These effects have been interpreted, within the DRC model, as evidence of lexical reading even a in a language with transparent orthography as Italian (Tabossi & Laghi, 1992).

Recently, a connectionist dual process model of reading aloud has been proposed (CDP++, Perry, Ziegler & Zorzi, 2010) which represents an attempts of integrating single and dual route models. The cited model explains many psycholinguistic effects, like frequency, lexicality, consistency, orthographic and phonological neighbourhood, but also syllable number and word length. However, even in their most recent form, the cognitive models of reading have not deeply studied the involvement of the visual factors. Conversely, this topic has been largely investigated by psychophysics, where basic visual factors such as contrast, letter size, inter-letter spacing and length have been explored and the visual system intrinsic limitations have been highlighted. Reading is, indeed, a visual task and visual acuity is determinant in accomplishing the task. Visual acuity has been defined by Anstis (1974) as "The reciprocal of the visual angle, in minutes, subtended by a just resolvable stimulus" (pg. 589). Visual acuity reaches its maximum in the fovea and shows a progressively decline out to the periphery of the retina, where letter size needs to be larger in order to be recognized. Not only visual acuity limits letter recognition and reading at larger eccentricities, but also crowding, the phenomenon by which recognition of detail is radically impeded by patterns or contours that are nearby (Strasburger, Harvey, & Rentschler, 1991; Strasburger & Rentschler, 1995; Pelli, Palomares, & Majaj, 2004). Crowding is a large effect that impairs word recognition in the periphery when the center-to-center letter spacing is smaller than half of the viewing eccentricity (i.e. 4 deg for letters located at 8 deg from the fovea, Bouma, 1970). Since texts are typically printed at constant spacing, most of the words for most of the time are unrecognizable because of crowding. A number of studies found that crowding in normal periphery is limited by the critical spacing between letters, but not by the letter size (Hariharan, Levi, & Klein, 2005; Levi, Hariharan, & Klei, 2002a and b; Pelli et al., 2004, 2007; Strasburger et al., 1991; Tripathy & Cavanagh, 2002). Globally it has been claimed that vision is usually limited by object spacing (crowding) rather than size (acuity). On the same vein, Legge, Mansfield, & Chung (2001) demonstrated that reading rate is limited by the visual span, the number of letters that can be correctly processed in a glance. The visual span's size decreases from at least 10 letters in central vision to 1.7 letters at 15° eccentricity determining a slower reading rate in the periphery (Legge et al., 2001). Since visual span is limited by crowding the reader needs to move the eyes in order to foveate letters and correct identify them.

The relevance of the visual factors associated with reading also determines that problems associated with the human visual system can dramatically affect the speed and the accuracy with which words can be recognized. For example amblyopia is a developmental visual disorder which typically affects just one eye and is usually associated with childhood strabismus or anisometropia. Amblyopia resulting from childhood strabismus is due to extensive crowding and reduced visual acuity, contrast sensitivity, and position acuity (Ciuffreda, Levi, & Selenow, 1991; McKee, Levi, & Movshon, 2003) which may cause difficulties in reading. Levi, Song & Pelli (2007) showed that, in central reading, the amblyopic eye has an abnormally large critical spacing but amblyopes read all larger spacing at normal rates, indicating that the entire amblyopic reading deficit is accounted for by crowding. A different disorder but still causing reading difficulties is due to age-related macular degeneration (AMD). Patients with AMD have a central vision loss and experience severe difficulty with everyday tasks, like recognition of faces and facial expressions, watching television, cooking, driving, and particularly in reading (Vingerling, Dielemans, Hofman, Grobbee, Hijmering, Kramer, & de Jong, 1995; Blackmore-Wright, Georgeson, & Anderson, 2013). Due to the central vision loss, AMD patients rely on peripheral vision, which is, however, crowded and thus lead patients to inefficient reading. Recently, Blackmore-Wright et al. (2013) demonstrated that crowding is the major cause of the poor reading abilities in AMD patients and that its effects can be reduced with enhanced text spacing. Authors recommend that double line spacing and double-character word spacing should be employed in order to maximize patients' reading efficiency. On the same vein, Crutch & Warrington (2007, 2009) described the reading profile of two patients affected by posterior cortical atrophy (PCA). PCA is a progressive neurodegenerative syndrome mainly characterized by progressive visuospatial and visuoperceptual dysfunction in a profile of preserved memory, insight, and judgment (Benson, Davis, & Snyder, 1988). Additional symptoms of PCA patients are: alexia, agraphia, acalculia, apraxia and some or all of the features of Balint's syndrome like simultanagnosia, oculomotor apraxia, optic ataxia, environmental agnosia (Tang-Wai, Josephs, Boeve, Petersen, Parisi, & Dickson, 2003;

Mendez, Ghajarania, & Perryman, 2002; Renner, Burns, Hou, McKeel, Storandt, & Morris, 2004; Charles & Hillis, 2005; McMonagle, Deering, Berliner, & Kertesz, 2006; Lehmann et al., 2011). These patients made a large amount of reading errors and their error pattern lead authors to refer to the reading disorder as "crowding dyslexia" since a link between pathologically excessive visual crowding (i.e., abnormally increased critical spacing) and the acquired peripheral dyslexia shown by these patients has been established (Crutch & Warrington, 2007 and 2009).

Both high level cognitive and low level visual factors have been explored using the eye-tracking technique. Such method has been widely employed to investigate cognitive processes during reading (for a review see Rayner, 2009). Eye movements are a fundamental part of the reading process, since saccades (i.e., the eye movements themselves) lead to fixations (the period of time when the eyes remain fairly still and new information is acquired) in order to foveate word's letters serially (that is, orienting the eye so that the letter falls on the part of the retina - the fovea- that yields the greatest resolution). In fact, although acuity is very good in the fovea, it is progressively worse in the parafovea and in the periphery, where also visual crowding avoids correct features and letter identification, as described above. Hence, while reading, viewers need to move their eyes so as to place the relevant part of the stimulus in the fovea. Normally, readers move their eyes along the lines of text and along the letters of a word. This task is accomplished in a highly efficient way by making a saccade approximately every 250 ms (for a review, see Rayner, 2009). It is thus widely accepted that fine, accurate, precisely controlled and coordinated eye movements allow letter scanning and their adequate processing, leading to correctly read words (Heinzle, Hepp, & Martin, 2010). Eye movements are motor responses that involve a large brain circuit in order to be planned and executed (Anderson, 2012; Ptak & Muri, 2013). As so they requires a timing, which may be variable according to the task and the visual stimulus used (Rayner, 2009). This may represent a bottleneck in limiting normal reading speed.

In the present thesis my focus will be on the relationship between eye movements and reading integrating the cognitive and the psychophysical approaches. In the first part I will consider reading in normal adult readers trying to understand how reading rate can be estimated and what is the role of eye movements in such an estimate. Using the Rapid Serial Visual Presentation (RSVP) technique it is possible to investigate reading speed netted from the necessity of executing saccadic eye movements. We will demonstrate that letter masking and the necessity of executing eye movements slows down reading speed dramatically, sentence context and memory contribute with a factor ranging between 1.4 and 1.8, while we found no evidences of a parafoveal preprocessing advantage.

In the second part of the thesis, the focus will be on an acquired reading deficit, i.e., Neglect Dyslexia. Patients with Neglect Dyslexia omit or misread left sided letters (in reading single words) or entire words (in sentences or paragraphs reading). The role of eye movements in determining the reading disorder has been explored. Reading errors will be shown to be the epiphenomenon of the concomitant presence of unilateral spatial neglect and an eye movement deficit, which prevents adequate saccadic movements towards the letters and, thus, accurate reading. In the last study the accuracy in the eye movement pattern of neglect patients during a non-reading task (i.e., a scene exploration and description task) has been proved to be predictive of the presence of reading errors in both single words and paragraphs reading.

PART I

2. Factors limiting reading speed in normal readers

Reading is a complex task that involves several cognitive and sensory-motor components from letter feature detection to the comprehension of meaning and the pronunciation of the words. It takes many years to master this skill and during this long-lasting training each of the components improves substantially showing specific learning effects. Literate adults read with near perfect accuracy at an impressive speed, optimizing each process and performing them in parallel. Carver (1982) proposed that, through a long lasting practice, reading approaches an optimal rate of about 300 words per minute (wpm) to simultaneously enable orthographic decoding, pronunciation and comprehension of meaning. Carver created the term 'rauding' (Carver, 1984, 1990) to indicate the processing through which reading and listening (or auding) lead to the ability of understanding what has been read. According to Carver readers may slow down or speed up their rate at the expenses of some of the cognitive components involved when achieving different goals. If the reader's aim is learning what is been read, the rate does not exceed 200 wpm, and this will be even lower if memorizing is required (around 140 wpm). Vice versa higher rates may be achieved if the task requires to find and report, in a text, only transposed words (i.e., skimming), with readers achieving a speed of 450 wpm. Furthermore, when finding a target word in a text (visual scanning), the rate increases up to 600 wpm (Carver, 1992).

Since reading involves many components it may be claimed that reading rate is a multiple-factor measure. The processing time needed to read a word or a sentence (without any special memorizing or learning requirement) may be roughly divided into three general components, i.e. eye movement execution, decoding and speech production. In Carver's rauding estimate of 300 wpm, all these components exert an effect and the specific time required by orthographic decoding is not isolated from all other components. In keeping with Carver's suggestion of reading speed as a stable trait of task execution, recently De Luca et al. (2013) revived the Buswell's (1921) idea of eye-voice span and made an effort in separately describing the components involved in reading aloud. The results indicate that the distance in time between decoding (as assessed by fixation position on a line of text) and pronunciation varies with reading skill, and represents an idiosyncratic trait of the reader.

In general, psycholinguists and cognitive psychologists devoted little interest to the speech production component of the task. A large amount of this literature is based on vocal reaction times (RT) measured to assess orthographic processing minimizing the role of pronunciation time. Indeed, RTs indicate the onset of the observer's response after stimulus appearance, isolating the decoding from the pronunciation time. Vocal RTs allowed fundamental advances in understanding the role of psycholinguistic variables (such as frequency, lexicality, age of acquisition, etc.). Based on these data, researchers constructed models of word recognition (e.g., connectionist dual process, CDP++; Perry, Ziegler, & Zorzi, 2010). More generally, we know a lot about decoding time measured by RTs, and these measures present puzzling contrasts with time measured in standard reading conditions.

Adult readers' vocal RTs to single short words is about 400 ms, which gives an estimated reading speed of 150 wpm notably lower than the 300 wpm obtained with functional text reading (Carver, 1992). How can this difference be explained? There are various elements to consider. On the one hand, multiple stimulus arrays (such as a texts) may enable the integration of the sub-components of reading, with associated time benefits. Indeed, Zoccolotti et al. (2013) showed a clear advantage in reading time per item with multiple item arrays with respect to discrete items. On the other hand, although RTs exclude the utterance of the response, they include all the sensory-motor components before the start of utterance (i.e. visual analysis, motor preparation), estimated to last slightly below 400 ms; that in single items presentations are not performed in parallel on several words and add to the total time a component invariant across subjects (Martelli et al, 2013). Finally, several experimental studies on eye movements in reading showed that we often skip short words, function words and predictable words; this reduces the number of fixations while reading a standard text, and consequently reduces the time spent for fixations (these latter are very time-consuming, on average about 350 ms per fixation) (Balota et al. 1985; Binder et al. 1999; Ehrlich & Rayner 1981; Rayner et al. 2001; Rayner & Well 1996; Schustack et al. 1987; O'Regan 1979; 1980; Gautier et al. 2000). By contrast, RT experiments do not allow skipping words, and provide information on the decoding (plus sensory-motor components) of each individual stimulus.

The rapid serial visual presentation technique

To bypass the single item constraint and provide a more direct estimate of orthographic decoding several authors measured reading rate with the Rapid Visual Serial Presentation (RSVP) procedure. This is a well-known psychophysical paradigm which, minimizing the role of eye movements and of speech preparation and production, gives estimates of reading up to 700-1000 wpm (Rubin & Turano, 1992; Legge et al., 2001). In this procedure, one word at the time is briefly presented, followed by another one and so on (4 to 8 words are typically presented in a single stream). Each word is presented at the center of the screen, in the same spatial position, limiting the necessity for eye movements. Moreover, the phonological and articulatory components do not directly exert a role on the estimation of reading rate, since the stimulus duration is independent from the response onset and no time limit is given to complete the response. RSVP is a technique "*capable of revealing very rapid, presumably automatic and perhaps elementary cognitive and linguistic operations, such as those that structure a string of words into a sentence*" (Potter, 1984, pag. 97). In fact, compared to other reading techniques, RSVP gives the opportunity to "speed up" reading rate. Indeed, Potter et al. (1982) showed that reading and recall is still excellent at 12 words per second (i.e., 720 wpm). RSVP has been widely used for studying many low level aspects of visual processing (e.g., see Chung, 1998, Pelli et al., 2007). However, it is surprising that different studies, although using the same paradigm, stumbled in very different reading rates. In some cases the advantage given by the RSVP technique in speeding up reading rate is relatively small, showing a mean reading rate of 300 wpm (Chung et al., 1998; Fine et al., 1997; Fine et al, 1999; Latham & Withaker, 1996; Pelli et al, 2007) while, in other studies, reading rates exceeding 1500 wpm have been reported (Rubin & Turano, 1992; Latham & Whitaker, 1996). What is the origin of such discrepancies?

Our working hypothesis is that, separating through experimental manipulations the various components that are part of the reading process in RSVP procedure, we may assign a weight, in terms of processing time, to each of them and we can clarify the sources of the contrasts in the literature described above. First, we aim to tear apart different stages involved in the reading process together with their time costs. Second, once identified the contribute of each stage, we may investigate the origin of differences in estimated reading rates by focusing on the methodological differences among similar paradigms, and provide a vademecum to measure reading speed. Thus, various experiments were designed to manipulate the relevant variables in the RSVP procedure.

Effect of sequence and masking between items in the sequence in the RSVP

When using the RSVP technique reading rate is estimated based on the duration threshold necessary to reach typically 80% of accuracy. Notably, such threshold is calculated considering the total number of words reported, without distinguishing between the ordinal position of each word in the sequence stream. However, not all words in the stream have the same properties and the first and last words may have an advantage. In particular, Pelli & Tilman (2007) noted that "*in order to minimize end-effects in the 6-word sequence of a trial, we added a random letter string before the first word in a trial and another after the last word […] Without temporal flankers, the first and last words in a trial showed a strong advantage over the middle four. With the temporal flankers, there is no longer any advantage for the last word in a trial. The primacy effect, higher report of the first word with respect to the following words, was reduced, but not eliminated, by the addition of temporal flankers*". The authors refer to the visual masking phenomenon i.e., the fact that a stimulus is reported with less accuracy if presented close in time to other stimuli, with the first one acting as a mask on the following (Felten & Wasserman, 1980; Breitmeyer, 1984; Enns & Di Lollo, 2000). However, this question needs further analysis, especially because some, although not all, studies included a mask before presenting the first word and after the last one in the stream. We hypothesize that this methodological difference can be responsible for part of the discrepancies in reading rate reported in the literature. Moreover, the advantage for the first and last words has been only cited by Pelli & Tilman (2007) but the phenomenon has never been studied in detail; thus, in experiment 1 to 3, we evaluated the possibility that not all the words in the stream are correctly read with equal probability.

Eye movements and parafoveal preprocessing in standard reading vs. RSVP

The RSVP paradigm was originally developed and used to minimize the weight of the eye movements which are necessary when reading a text distributed across the whole screen or page (Gilbert 1959a, b; Potter, 1982). Rubin & Turano (1992) compared reading rates using two modes of presentation: RSVP and static text. Authors systematically found higher reading rates for the RSVP condition (about 1000 wpm) as compared to the static text condition (about 300 wpm), showing that the necessity of programming and executing eye movements imposes an upper limit to the reading rate. However, having a text displayed on the screen (or on a printed page) enables for parafoveal preprocessing (while fixating a cluster of letters). Parafoveal preprocessing contributes to the next fixation location accuracy (for a review see Rayner, 1998), and may also favour the decoding of the next word. Thus, the speed reduction due to eye movements may be underestimated due to a partial compensation by parafoveal preprocessing.

Evidence on the role of parafoveal preprocessing comes from various studies. Using the moving-window paradigm in which letters outside of a "window" spanning a given number of character spaces are Xed out, McConkie and Rayner (1975) verified that the region from which useful visual information can be processed (i.e., the perceptual span) is much larger than a single word and spans about 15 character spaces on the right. This suggests that, in text reading, more information than what comprised in a single word can be encoded. Rayner et al. (1982) found that individual letters to the right of fixation are more critical than word integrity (i.e., if word's letters are completely visible within a moving window or not) suggesting that partial word information is processed parafoveally. Studies of the parafoveal preview effect indicated that, during normal reading, peripheral preprocessing of a word can reduce the duration of the subsequent fixation on that word (Schilling et al., 1998). Further, partial-word information, obtained parafoveally, is used in computing where to look next (O'Regan, 1979, Pollatsek & Rayner, 1982). Finally, since some predictable words or function words are sometimes skipped, it seems that these words can be fully and more rapidly identified without fixations (Ehrlich & Rayner, 1981; O'Regan, 1979). Overall, parafoveal preprocessing during reading is documented, and its effect may represent a confound when evaluating the speed cost of eye movements. In the present study we measured the costs on reading rate associated with the execution of eye movements together with the benefits of parafoveal preprocessing. This was done using a modified version of the RSVP technique, where (in contrast to standard technique) eye movements were necessary to read the words displayed. This issue was investigated in experiments 4 to 6.

Semantic context in RSVP

Notably, most psychophysical studies of reading rate are concerned with the visual properties of the stimuli and generally ignore the lexical and semantic status of the words. However, top-down, contextual and semantic factors may affect reading speed because the presence of sentence context may greatly improve speed (Fine, Peli & Reeves, 1997). Consequently, differences in the estimated reading rates in different studies may also be due to this often uncontrolled source. So far, different studies using the RSVP paradigm have not been consistent with regard to the type of materials used for reading: sentences, scrambled sentences and random words have often been used interchangeably neglecting the potential effect of these different reading materials.

In 2007, Pelli and colleagues studied the differences in reading rate when an ordered or scrambled sentence is presented; they found that scrambled sentences reduce the variability in the rate measure. However, to our knowledge, the reading rate gain for sentences (ordered or scrambled) against random words has not yet been studied. In Experiments 7, we investigated the effect of semantic context in reading rate and, we contrasted it with the role played by low-level factors, such as visual masking.

Role of working memory in RSVP

In experiment 8, we studied the role of working memory in association with that of semantic context. In the literature on reading rate using the RSVP there is no agreement on the number of stimuli that should be displayed on each trial and on the effect that such variable may exert on the reading rate estimate. The number of items used in the stream varies considerably: in particular, in some studies, this number is within the short term memory span as described by Baddeley (1986). These studies (e.g., Fine et al., 1999; Pelli & Tilmann, 2007; Latham & Withaker, 1996) produce an estimated rate ranging from 300 to

1300 wpm (median: 419). Other studies used stimuli exceeding the memory span (e.g., Kwon & Legge 2012; Know, Legge & Dubbles, 2007; Yu et al., 2007, 2010; Pelli et al., 2007; Lee et al., 2010; Chung, 1998; Yager, 1998) obtaining rates ranging from 250 to 800 wpm (median: 590). A direct comparison between conditions characterized by different numbers of items per trial (carried out in Exp. 8) may help explaining some of the discrepancies found in the literature about reading speed as a function of span requirements.

2.1. Experiment 1. Role of a mask in modulating reading rate

Studies using the RSVP procedure to investigate reading speed can be roughly divided between those that used a mask (e.g., Kwon & Legge, 2012; Know, Legge, & Dubbles, 2007; Pelli & Tilmann, 2007; Yu et al., 2010; Yu et al., 2007; Fine et al., 1999; Fine, Peli, & Reeves, 1997) and those that did not (e.g., Lee et al., 2010; Chung, 2002; Chung 1998; Yager 1998; Latham & Withaker, 1996; Rubin & Turano 1992). Notably, this factor is rarely considered in the interpretation of the obtained findings. We propose that the presence/absence may have substantially contributed for the different results obtained.

In experiment 1, the role of the mask in reading aloud is quantified by comparing a condition where observers are asked to read aloud a stream of four words, preceded and followed by a mask (a string of identical symbols) with a condition where the masks are not used.

2.1.1 Stimuli

Two lists of 160 6-letter words were selected from the LEXVAR database (http://www.istc.cnr.it/grouppage/lexvar, Barca, Burani, & Arduino, 2002). The lists were matched for word frequency (mean frequency = 50.6 and 50.2 for list 1 and list 2 respectively; $p > .1$) and bigram frequency (11.2 and 11.7, respectively; $p > .1$). Words were rendered in Courier New font, a proportionally spaced font. Each letter subtended 0.4 deg of visual angle.

2.1.2 Participants

Nine subjects participated in the study. Subject had a mean age of 25.5 years (s.d. = 2.8; range = 21 - 30) and all had normal or corrected to normal vision.

2.1.3 Procedure

Participant seated 57 cm away from a 15.5 in Sony Vaio laptop (refresh rate = 60 Hz). A fixation point (a black square subtending 0.2 deg of visual angle) was presented at the center of the screen for 2000 msec. In the first condition, immediately after the offset of fixation point, words were presented using the RSVP paradigm, i.e. four words were presented sequentially, one word at a time, at the same location on the display and participants were asked to read them aloud as quickly as possible. No time limit was imposed. There was no blank frame (zero inter-stimulus interval) between words. The same paradigm was adopted in the second condition with the addition, immediately before the first word and immediately after the fourth word, of a mask (######). The mask had the same stimulus size and duration. In both conditions, participants were asked to read the words presented.

We measured the duration threshold for each participant by varying exposure duration in a 40-trial run using the improved QUEST staircase procedure with a threshold criterion of 80% correct responses (Watson & Pelli, 1983). The adaptive QUEST procedure increased or decreased the presentation rate (starting from 500 ms) according to the participant's accuracy. Word omissions, mispronunciations and substitutions were considered errors.

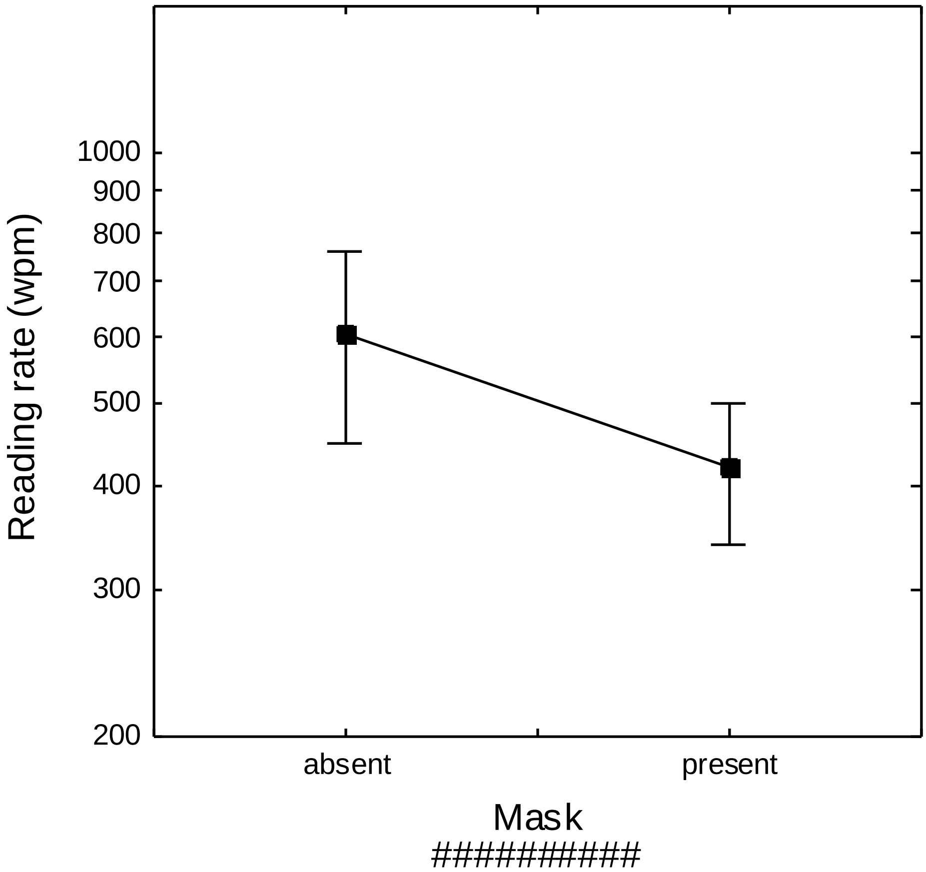
2.1.4 Data analysis

Reading rate (*i.e.* words per minute, wpm) was measured as 60/duration threshold*1000. In this experiment as well as all subsequent ones, log-transformed values of reading rate were entered in the statistical analyses. In all experiments, the effects of experimental manipulations were compared by means of ANOVAs (factors are presented in the single analyses). LSD post-hoc tests were used whenever appropriate.

2.1.5 Results and comments

Reading rates for words presented in the mask and no mask conditions are presented in figure 2.1. An ANOVA run to compare the two conditions showed that the effect of mask was significant [$F_{(1, 8)}$ = 12.34, p = .008]: the presence of the mask reduced reading speed from 604 to 420 wpm, i.e., by a factor of 1.5.

Figure 2.1. *Reading rate (expressed in words per minute) in the absence (left) and in presence (right) of mask. The features of the mask are shown above.*



Results of the first experiment highlight the importance of the presence of a mask presented before the first word and after the last of the stream. The presence of a mask determines a steep decline of reading rate with an estimated cost of around 200 wpm. With the mask the first and last words of the stream become more comparable perceptually to the other words of the stream; in fact the second and third words of the stream are preceded and followed by words; presumably, these act as masks, making the target word less visible.

The decline of the reading rate when two masks (one at the beginning and one the end of the sequence) are used indicates that the detectability of the first and last word of the stream play an important role in the overall evaluation of reading rate. It is likely that word sequence affects reading rate reported. We address this issue in the second experiment.

2.2 Experiment 2. Effect of stream sequence on the reading rate with the RSVP

In experiment 2, we investigate the weight of each word in determining the duration threshold within the four-word stream. To this aim, we ask participants to read streams of 4 words (as in standard RSVP) and measure the duration threshold separately for each ordinal position in the sequence (i.e., either the first, second, third or fourth position). Note that this procedure differs from the standard measurement, where the threshold is calculated by averaging together the report for all words, independent of their position in the sequence.

2.2.1 Stimuli

We generated 4 lists of 120 stimuli each selected from the LEXVAR database (http://www.istc.cnr.it/grouppage/lexvar, Barca et al., 2002). The four lists were matched for frequency (mean frequency = 54.5, 54.7, 54.5 and 54.3, all p_s > .1, respectively) and bigram frequency (11.22, 11.20, 11.23, and 11.25, all p_s > .1, respectively). Stimuli were 4- and 6-letter in length (N = 48 and 72, for each list, respectively). Letters' size and font were the same than in experiment 1. No mask was present.

2.2.2 Participants

Six subjects (others than those engaged for previous and successive experiments) participated in the study. Subjects had a mean age of 25.7 years (s.d.= 3.7; range = 19 – 28) and all had normal or corrected to normal vision.

2.2.3 Procedure

Equipment and general procedure were the same as those of Experiment 1 except for the following: a) No mask was used and b) The duration threshold estimate was separately evaluated, based on the accuracy on either the first, second, third or fourth word (in four different runs). Word omissions, mispronunciations and substitutions were considered as errors.

2.2.4 Results and comments

A repeated measure ANOVA was run with word ordinal position as repeated factor. The main effect of word ordinal position was significant [$F_{(3,\ 15)} = 54.44$, $p < .0001$]. To compare the reading rates between the four word levels a LSD post-hoc test was used. As shown in Figure 2.2, the first and the last words had the highest reading rates (1365 and 1787 wpm, respectively). The first word had a higher reading rate than the second (696 wpm, p = .0001) the third (496 wpm p < .0001) word. Similarly, the fourth word in the stream had a higher reading rate than the other three words in the stream (all p_s <.05). The difference between the second and the third word was also statistically significant (p = .009), with a higher reading rate for the second word.

Figure 2.2. *Reading rate measured separately for each of the four words of the stream.*

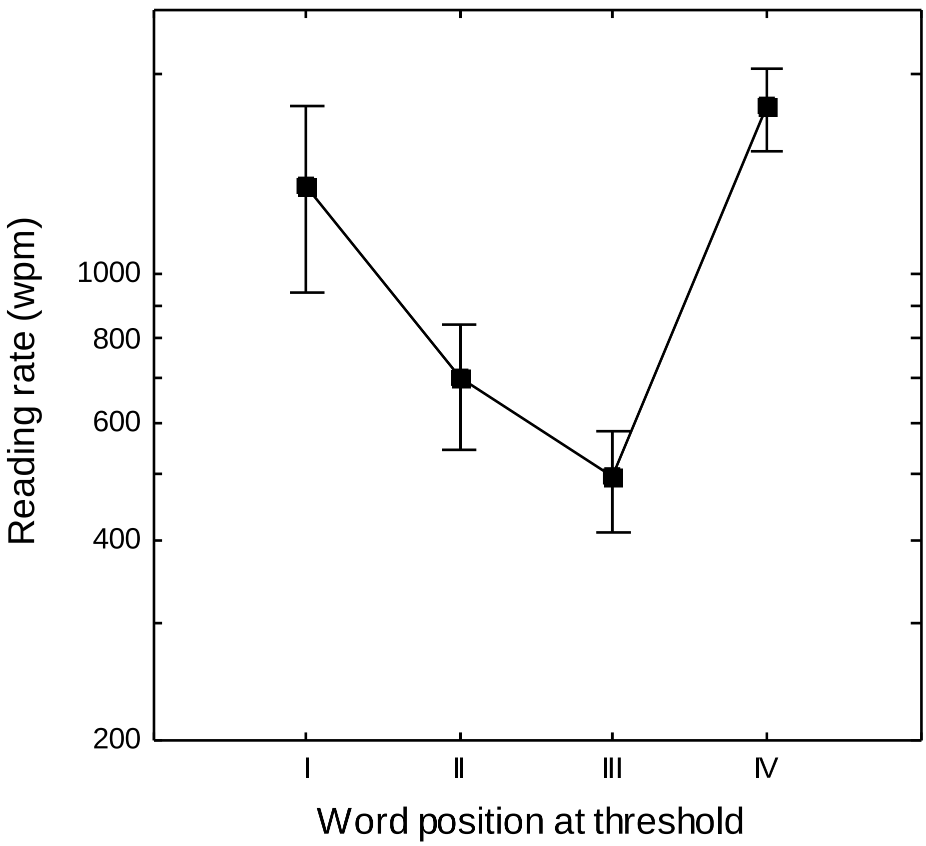


Figure 2 shows that the four words in the RSVP stream are not equally visible. In particular, the finding that the first and the last words have the highest rate indicates that these words are more easily reported. Vice versa, the second and the third word have the lowest rate at threshold. Notably, in standard RSVP, reading rate is estimated taking into account the accuracy on all the words in the stream.

In keeping with the results of Experiment 1, we propose that the words with a central position in the sequence suffer from visual masking. A test of this hypothesis was the aim of Experiment 3.

2.3 Experiment 3. Reading rate as a function of word ordinal position and mask

To further investigate the role of the non-verbal mask in modulating reading rate, we repeated here the four experimental conditions of Experiment 2, i.e., we measure the duration threshold separately for each ordinal position in the sequence. All stimuli and conditions are the same with the exception that we introduce a non-verbal mask (######) immediately before the first word and immediately after the last word of the stream. A new group of subjects participate to the experiment.

2.3.1 Stimuli

The same lists of words of Experiment 2 were used. Letters' size and font were the same than in Experiment 1.

2.3.2 Participants

Ten subjects (others from previous experiments) took part in the study. Their mean age was 26.7 (s.d. = 1.64; range = 25-29). All had normal or corrected to normal vision.

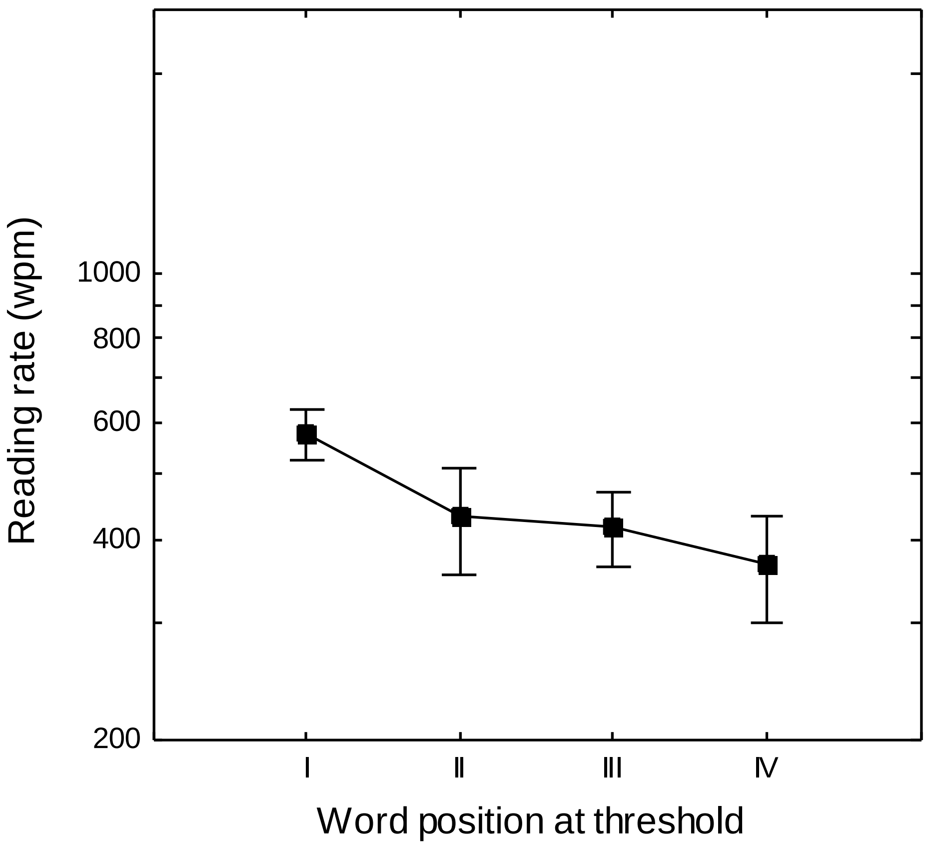
2.3.3 Procedure

The same as in Experiment 2 with the exception that a non-verbal mask (######) immediately preceded and followed the first and last words of the stream (as in Experiment 1). The mask had the same stimulus size and duration of the words.

2.3.4 Results and comments

Results are shown in Figure 2.3. A repeated measure ANOVA showed the main effect of word ordinal position was significant [$F_{(3, 27)} = 9.92$, $p = .0001$]. Post-hoc comparisons showed that the first word had a reading rate (578 wpm) significantly higher than the second, third and fourth words in the stream (431, 418 and 365 wpm, respectively; all ps < .01). Reading rates between the second, third and fourth ordinal positions were not significantly different (all $p_s > .1$).

Figure 2.3. *Reading rates separately for each of the four word ordinal position in the stream. The first word was immediately preceded and the last word was immediately followed by a non-verbal mask.*



2.3.5 Comparison between data from Experiments 2 and 3

In order to directly compare the effect of the non-verbal mask on the four words of the stream (Experiment 2 vs. Experiment 3) a 2 x 4 ANOVA with mask (presence, absence) as between factor and word ordinal position (first, second, third and fourth) as repeated factor was performed. Results indicated that the main effects of the mask [$F_{(1, 14)}$ = 18.02, p = .0008] and of the word ordinal position [$F_{(3, 42)}$ = 39.74, p < .0001] factors were significant. Moreover, the mask by word ordinal position interaction was significant [$F_{(3, 42)}$ = 37.01, p < .0001]: the non-verbal mask reduced the reading rate for the first and last words in the stream (both p_s <.01). By contrast, the presence of the mask did not modify the reading rate for the middle words (both p_s > .1).

2.3.6 Comments

The results from Experiment 3 confirm the idea that the second and third-position words are masked by consecutive words; the first and last word are masked by the non-verbal mask. The standard measure of RSVP represents an average of the different thresholds measured for the four word positions that are influenced either by the presence of a non-orthographic mask (in some experiments) or by words (in all experiments). We have measured here the effect of masking between consecutive items presented in the same spatial position; its cost is large, ca. 600 wpm. The similar effect of orthographic and non-orthographic material on word reading thresholds indicates that masking may occur at an early stage of processing (either features or letters), before words are lexically encoded.

2.4 Experiment 4. The effect of eye movements on reading speed

The reading speed with RSVP is greatly enhanced by the reduced need for eye movements (Rubin & Turano, 1992). In this experiment, we aim to quantify the role of eye movements by comparing a condition where the four words are presented in the same spatial position (i.e., eye movements were minimized) with a condition in which words are presented simultaneously along the horizontal meridian and subjects have to move their eyes to read them.

2.4.1 Stimuli

We generated two lists of 120 stimuli each selected from the LEXVAR database (http://www.istc.cnr.it/grouppage/lexvar, Barca et al., 2002). The two lists were matched for frequency (mean frequency = 54.5 and 54.7respectively, p > .1) and bigram frequency (11.22

and 11.20 respectively, $p > .1$). Stimuli were 4- and 6-letter long (N = 48 and 72, respectively, for each list). Letters' size and font were the same as in Experiment 1.

2.4.2 Participants

Eight subjects (others than in previous experiments) participated in the study. Subject had a mean age of 23.9 years (s.d.= 2.03; range = 21 – 27) and all had normal or corrected to normal vision.

2.4.3 Procedure

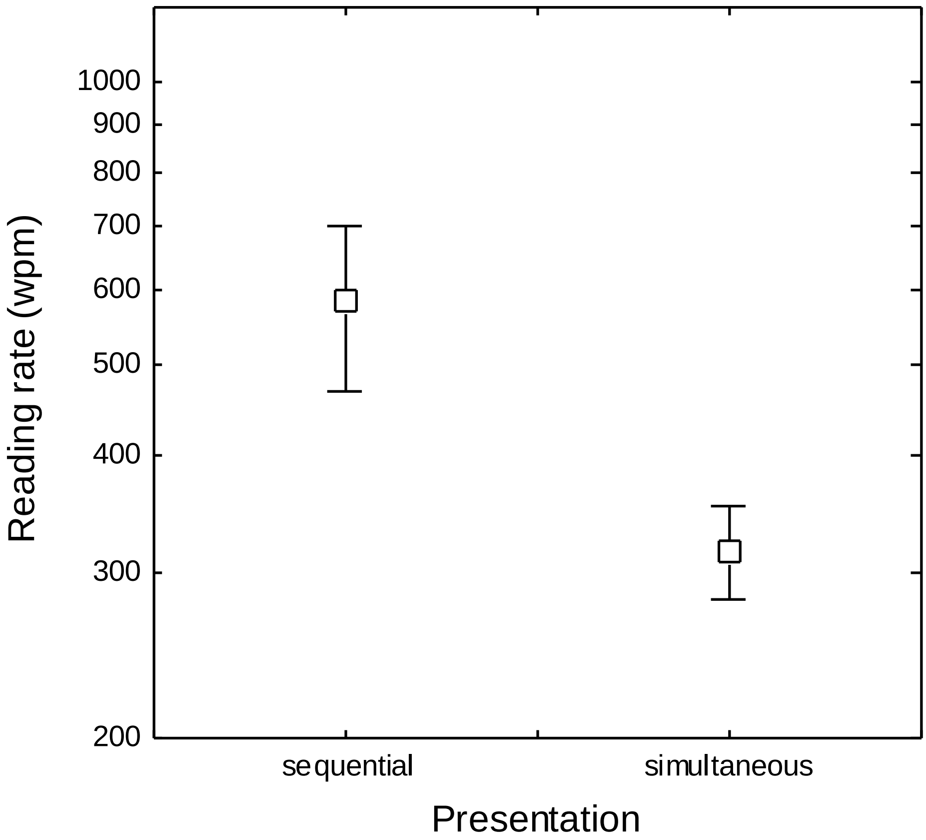
Procedure was the same as in Experiment 1 (standard RSVP). No mask was used. As in Experiment 1, we measured the duration threshold for each participant by varying exposure duration in a 40-trial run using the improved QUEST staircase procedure with a threshold criterion of 80% correct responses (Watson & Pelli, 1983). For each condition participants were asked to read aloud the four words. In the first condition, words were consecutively presented in the same spatial position at the center of the visual field, while, in the second condition, words were simultaneously presented along the horizontal axis being arranged along the entire extension of the screen. In the latter, eye movements are required in order to make a fixation on the words presented on the screen.

We measured the reading rate (wpm) for the two (simultaneous, sequential) conditions. Word omissions, mispronunciations and substitutions were considered errors.

2.4.4 Results and comments

As shown in Figure 2.4, reading rate was much lower (316 wpm) with the horizontal lay-out of the stimuli (requiring eye movement scanning) than with the same spatial presentation of stimuli (585 wpm) where eye movements are minimized [$F_{(1, 7)} = 8.88$, $p = .02$].

Figure 2.4. *Reading rate (wpm) for words presented sequentially in the same spatial position and simultaneously along the horizontal axis.*



By using streams of words presented in the same spatial location, thereby limiting the need for eye movement scanning, the RSVP procedure effectively maximizes reading rate. In fact, when eye movements are made necessary to read words of comparable difficulty, reading rate drops considerably. The cost of eye movement execution is large, ca. 300 wpm.

However, the effect of eye movements in determining the reading speed might even be underestimated in the present experiment. In fact, in the simultaneous condition (i.e., with four words displayed horizontally) parafoveal previewing may favor reading speed (for a review see Schotter, Angele, & Rayner, 2012), partially compensating for the decline due to the eye movement requirement. This possibility was addressed in Experiment 5.

2.5 Experiment 5. Effect of parafoveal previewing on reading speed

Here, we address the question of the role of the parafovea in reading aloud by presenting a stream of words along the horizontal meridian in two different conditions. In the first one, the four words are presented sequentially, one at the time, along the horizontal meridian; to read the words observers must execute eye movements but the benefits of parafoveal preprocessing are minimized due to the delayed onset between words. In the second condition, words are presented along the horizontal axis (as in Experiment 4) and observers may take advantage of parafoveal previewing since all words are simultaneously available on the screen.

2.5.1 Stimuli

The two lists of 160 6-letter words of Experiment 1 were used. All the characteristics of the stimuli were the same as in Experiment 1.

2.5.2 Participants

Sixteen subjects (others than in previous experiments) participated to the study. Subjects had a mean age of 23.4 years (s.d. = 2.37; range = 18-26) and all had normal or corrected to normal vision.

2.5.3 Procedure

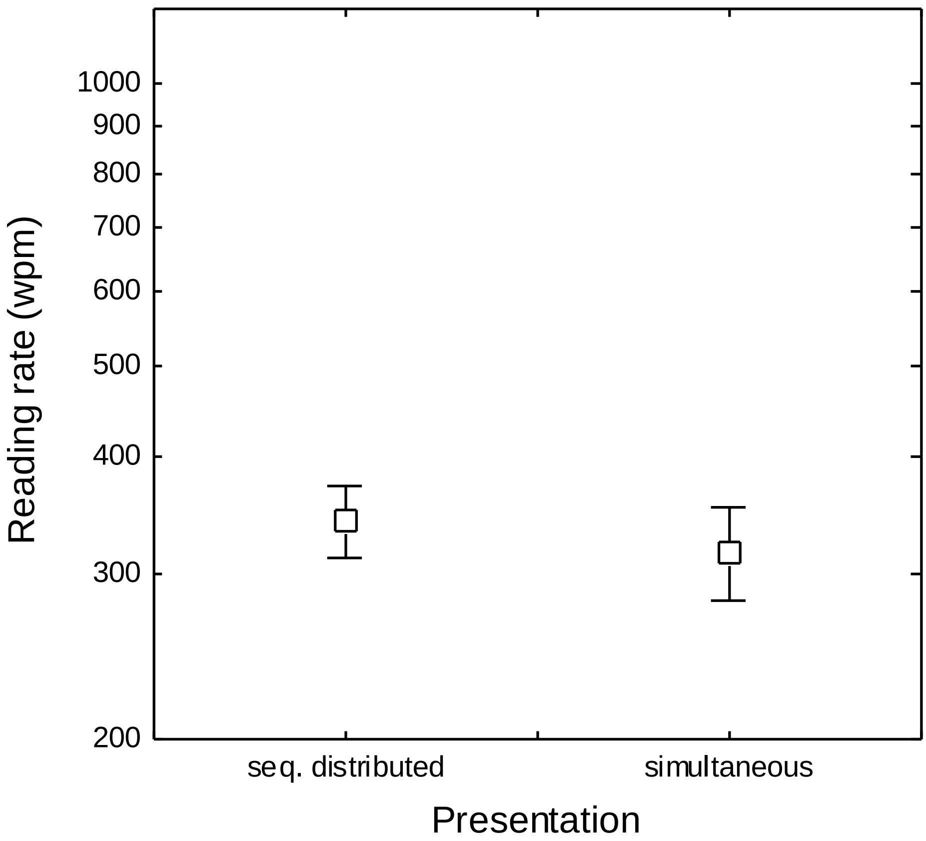
Equipment and general procedure were the same as in Experiment 1. After the fixation point offset, the words were presented using, in two separate conditions, two different versions of the RSVP paradigm. In the first condition (called *sequential distributed in space*) four words were presented sequentially, one at a time, along the horizontal axis of the screen and participants were asked to read them aloud as quickly as possible. The first word was displayed on the far left. After 500 ms (only for the first trial; in the subsequent trials the stimulus duration varied depending on the participant's accuracy) the next word appeared and so on. No ISI was used, but the successive word appeared immediately after the disappearance of the previous one. In order to avoid position uncertainty of the next target, before the onset of the first word a black line of the same length of the words was displayed on the screen at the location where the word would appear next (below the word position). The four words disappeared simultaneously at the end of the trial. In the second condition (called *simultaneous*) the four words were simultaneously displayed on the screen.

Also in this case the subject was asked to read the words as quickly as possible. A non-verbal mask (######) was used in both conditions; this was presented immediately before the word appearance and immediately after their disappearance in the same spatial positions of the words and for the same time duration. As in the previous experiments, we measured a duration threshold for each participant by varying exposure duration in a 40-trial run using the improved QUEST staircase procedure with a threshold criterion of 80% correct responses (Watson & Pelli, 1983). The adaptive QUEST procedure increased or decreased the presentation rate (starting from 500 ms) according to the participant's accuracy. We measured the reading rate (wpm) for the two conditions: when words were presented sequentially and when they were presented simultaneously. Word omissions, mispronunciations and substitutions were considered errors.

2.5.4 Results and comments

As shown in Figure 2.5, the presence of the four words on the screen (i.e., simultaneous condition) did not determine an increase in reading rate as would be expected with a parafoveal preview benefit. Reading rate in the sequential distributed in space condition was 342 wpm, while that in the simultaneous condition was 244 wpm. An ANOVA on the two conditions indicated that words were read faster when they were presented sequentially than when they were presented simultaneously [$F_{(1, 15)} = 25.78$, $p = .0001$].

Figure 2.5. *Reading rate for the simultaneous and sequential distributed conditions with words presented horizontally.*



We expected a facilitation effect (with an increase in reading rate) in the simultaneous condition because of a parafoveal benefit. Contrary to our prediction, reading rate was slower in the simultaneous than in the sequential condition, indicating no evidence of a parafoveal benefit.

According to studies on the parafoveal preview effect, individual letters to the right of fixation are more critical than the entire word; this indicates that readers acquire partial word information, especially focusing on the initial letters, and use this information to compute where to look next (Rayner et al., 1982) thus reducing the total viewing time on that word (Lima and Inhoff, 1985). We note that, in the simultaneous condition (requiring eye-movements), we provided the spatial information on the location of the next stimulus; further, all target words had the same (predictable) length. Thus, the two conditions did not differ because only one of them conveyed the information on the spatial landing of the impending saccade. Rather, they actually differed mainly because only in one case (simultaneous condition) parafoveal pre-viewing was allowed. The slower rate in the simultaneous condition is consistent with the view that parafoveal previewing is useful to compute the landing of the next target, but not (or much less) in the pre-analysis of the next word.

An alternative interpretation of the present results is that flashing words in sequence along the horizontal axis introduces an external trigger for saccades, and this is a condition different from standard reading, where eye movement are self-paced. Thus, one may claim that the control condition is not as good as it should to the extent in which externally-paced saccades might have a lower cost than self-paced saccades. According to this view, at least a portion of the time-cost of eye movements would be due to internal "starting" of the movement (self-pacing). The present experiment does not allow excluding this alternative; in any case, when eye movements are required, the reading rate is about 300 wpm. This latter result is consistent with the measure of the effect of eye movements found in Experiment 4. Thus, it appears that the value observed in Experiment 4 does not represent an underestimation due to the experimental conditions. Eye movements have a cost and this cost fixates the upper limit of reading rate to about 300 wpm.

2.6 Experiment 6. Further investigation of the role of eye movements on reading speed

In Experiment 4, we investigated the weight of eye movements on reading speed. We found a significant advantage in reading rate when participants read words without the need of eye movements (i.e., words presented in same spatial position vs. words displayed horizontally on the screen, Experiment 4). In the present experiment, we further address the role of eye movements by comparing the duration thresholds for the four words of the stream horizontally displayed in two different conditions: in the first one, in each trial the fixation point is presented before the occurrence of the stimuli at the center of the screen; in the second one, the fixation point is presented at the far left of the screen, where the first letter of the first word will appear. As in Experiments 2 and 3, we separately measure the duration thresholds for each ordinal position in the stream, which in this case also indicates the proximity to the initial fixation point.

2.6.1 Stimuli

The same four lists of 120 stimuli used in Experiment 2 were used in the present experiment. All the characteristics of the stimuli were the same as in the previous experiments.

2.6.2 Participants

Twelve subjects (others than in previous experiments) participated in the experiments. Six subjects performed the first condition (central fixation point; mean age = 26.7 years, s.d. = 4.5, range = 20-34) and 6 subjects performed the second condition (left sided fixation point; mean age = 27.5 years, s.d. = 4.1, range = 21-33). All subjects had normal or corrected to normal vision.

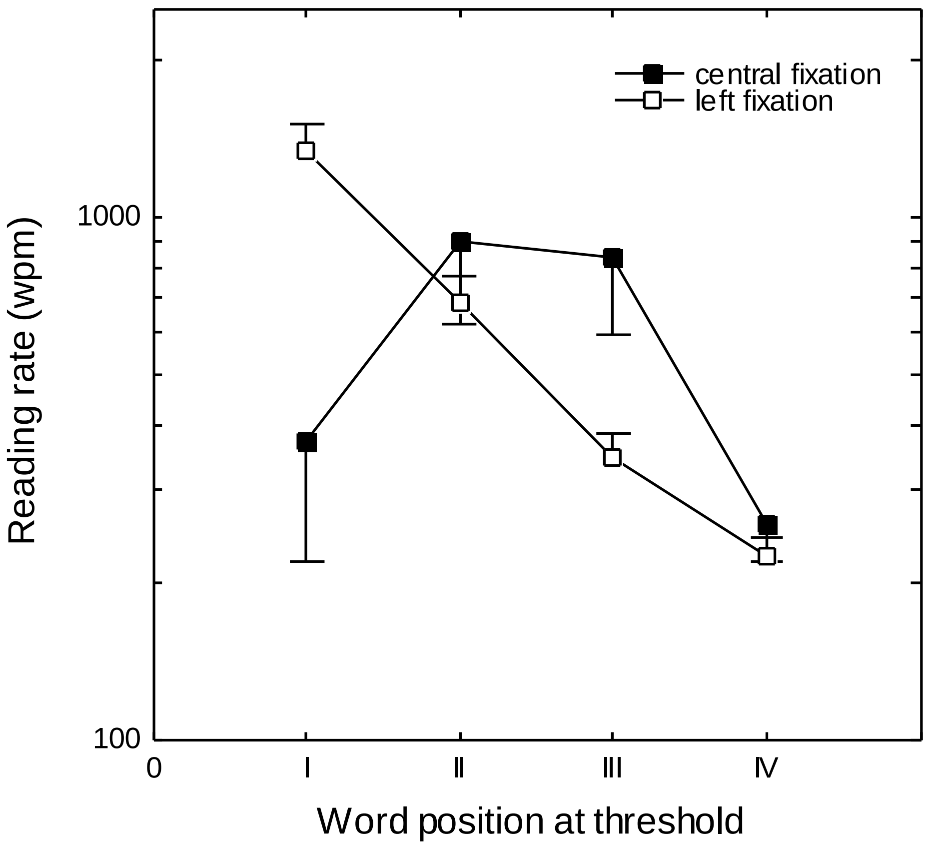
2.6.3 Procedure

Equipment and general procedure were the same used in the simultaneous condition of Experiment 4. In the first condition, a fixation point (a black square subtending 0.2 deg of visual angle) was presented at the center of the screen for 2000 msec. In the second condition, the same fixation point was displayed on the left-side (at the same position where afterwards appeared the first letter of the most left-sided word). In both conditions, immediately after the fixation point offset, words were presented using a modified RSVP paradigm, i.e. four words were displayed simultaneously along the horizontal axis on the screen. Participants were asked to read and report them aloud at the end of the trial. No mask was used. We measured a duration threshold for each participant by varying exposure duration in a 30-trial run using the improved QUEST staircase procedure with a threshold criterion of 80% correct responses (Watson & Pelli, 1983). The adaptive QUEST procedure increased or decreased the presentation rate (starting from 500 ms) according to the participant's accuracy. For each condition participants were asked to read aloud the 4-word stream. However, in different conditions, the duration threshold estimate was based on the accuracy on the first, second, third or fourth word. We measured the duration threshold at 80% of accuracy for each word of the stream separately for the central fixation and left-sided fixation conditions. Word omissions, mispronunciations and substitutions were considered errors.

2.6.4 Results and comments

Results of experiment 6 are reported in Figure 2.6.

Figure 2.6. *Duration threshold for the four words presented horizontally and simultaneously when the fixation point was central (black squares) or left-sided (white squares).*



Two separate ANOVAs were run for the two conditions in order to investigate the effect of the eye movements as a function of initial fixation point.

When the fixation point was centrally presented the main effect of word position was statistically significant [$F_{(3,\ 15)}$ = 5.99, p = .007]. The LSD *post-hoc* test revealed that the second word had a higher reading rate (901 wpm) than the first (374 wpm, p = .01) and fourth word (257 wpm, p = .002), but not of the third one (840 wpm, p = .3). Reading rate for the third position tended to be higher than the that in the first (p = .07) and it was higher than the fourth position (< .01). The difference between the first and the fourth word positions was not statistically significant (.4).

The ANOVA conducted on the left-sided fixation condition revealed a significant main effect of the word position [$F_{(3, 15)} = 123.39$, $p < .0001$]: reading rate for each word position was significantly different from the others (all ps < .001). The first word position had the highest reading rate (1332 wpm), followed by the second (689 wpm), third (348 wpm) and fourth (225 wpm).

To further analyze the effect of the eye movements necessary to read the word in relation to the initial fixation position, we run a 2x4 ANOVA with initial fixation position (central, left sided) as between factor and word position (first, second, third and fourth) as repeated factor. The main effect of word position was significant [$F_{(3, 30)} = 14.4$, $p = .00001$]. The interaction word position by initial fixation position was also significant [$F_{(3, 30)} = 9.6$, $p = .0001$]. Post-hoc comparisons revealed a significant difference for the first ordinal positions ($p = .0004$) with a higher reading rate when the fixation point was on the left than when it was on the center. For the second word position, the difference was marginally significant ($p = .06$) with an advantage for the central fixation point condition. The third word ordinal position exhibited a large advantage for the central fixation condition ($p = .01$). Finally, no difference in reading rate between the two conditions was present for the fourth word position ($p = .7$).

The strong effect of the eye initial position is in keeping with the idea that eye movements have a relevant cost on reading rate. Further, it might be noted that, with central fixation, no effect of saccade direction (leftward vs rightward) was found. This lack of asymmetry might, perhaps, result from a balance of contrasting tendencies. On the one hand, the habitual forward direction of saccades in reading might favor right-sided words; on the other hand, the standard beginning of reading from the leftmost place might favor jumping (with eye movements and attention) to the left-sided words.

2.7 Experiment 7. Context effects in RSVP reading

Context is an important factor in modulating reading rate in foveal reading (Chung et al., 1998; Fine & Peli, 1996; Fine, Peli, & Reeves, 1997; Fine et al., 1999; Latham & Whitaker, 1996a; Morris, 1994; Pelli et al., 2007). Consistently, it has been shown that the context gain in reading sentences as compared to scrambled words of the same sentences is usually greater than 1. However, Experiments 1 to 3 showed that another factor is very important in modulating the reading speed i.e., the masking between successive words presented on the same spatial position. This represents a confounding factor in assessing the exact role played by sentence context from the available data in the literature.

Here, we hypothesize that the extremely fast reading speed reported for context related materials is not due only to the effect of context. When sentences are presented with the RSVP procedure, successive words in the stream often have different lengths. Length differences would reduce masking between letters of consecutive words as compared to the case in which lists of same length words are presented. To disentangle the role of context from that of masking between letters, three stimulus types are used. The first type is ordered words of a sentence; the second type is scrambled words from a sentence; and the third type is random words with similar lengths (i.e., 4 or 6 letters).

2.7.1 Stimuli

For the first two conditions we used the Italian translation of “Alice in the wonderland” by Levis Carrol. In the ordered condition, the first 160 words of the first chapter of the book were presented in the exact order as they appeared in the text (mean length of the words was 4.85 letters, S.D. = 2.9). In the scrambled condition, the first 160 from the second chapter of the book were randomly presented in the streams of words (mean length of the words = 4.94 letters, S.D. = 3.1). In both conditions, punctuation was abolished and no capital letters were used. In the third condition a list of 160 words was generated from the LEXVAR database (http://www.istc.cnr.it/grouppage/lexvar, Barca et al., 2002). Stimuli were 4- and 6-letter words with (N = 48 and 72, respectively, for each list). Letters’ size and font for the three conditions were the same than in experiment 1. Testing with the three stimulus types were run using or not using a non-verbal mask (displayed at the beginning and the end of each word stream); this had the same length of the longest word of the list and the same size and time duration of the words. The different mask conditions were run in two different groups of subjects.

2.7.2 Participants

Six subjects (others than in previous experiments) participated in the first condition (ordered words, scrambled words and random words-no mask). Their mean age was 27.3 (range = 25-30, s.d. = 2.06). Six different subjects participated in the second condition (ordered words, scrambled words and random words-non-verbal mask). Their mean age was 27.2 (range = 25-30, s.d. = 1.92).

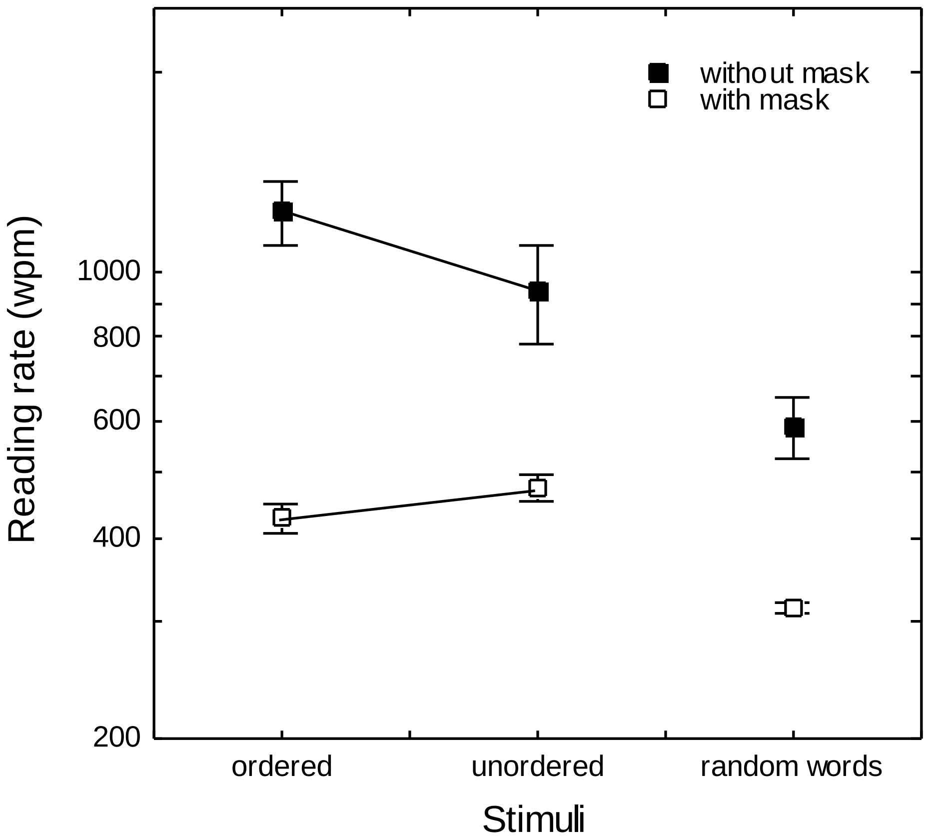
2.7.3 Procedure

Equipment and general procedure were the same as those of Experiment 1. A fixation point (a black square subtending 0.2 deg of visual angle) was presented at the center of the screen for 2000 msec. In the first condition immediately after the fixation point disappearance, words were presented using the RSVP paradigm, i.e. the four words were presented sequentially, one word at a time, at the same spatial location and participants were asked to read them aloud. There was no blank frame between words (inter-stimulus interval was zero). In the second condition immediately before the first word and immediately after the fourth word of the stream, a non-verbal mask (######) was presented; the mask had the same stimulus size and duration of the longest word in the sequence. We measured a duration threshold for each participant by varying exposure duration in a 40-trial run using the improved QUEST staircase procedure with a threshold criterion of 80% correct responses (Watson & Pelli, 1983). The adaptive QUEST procedure increased or decreased the presentation rate (starting from 500 ms) according to the participant's accuracy. Word omissions, mispronunciations and substitutions were considered errors.

2.7.4 Results and comments

Results are shown in Figure 2.7; black squares indicate conditions without mask and white squares indicate conditions in which data were collected with non-verbal mask.

Figure 2.7. *Reading rate for ordered and scrambled words derived from sentences, and, on the right side, reading rate for random words of 4-6 letter length. Data were collected in two groups of subjects in the absence (black squares) or in the presence (white squares) of a non-verbal mask before the first word of the stream and after the last one.*



The ANOVA for the no mask condition indicated a significant main effect of stimulus type [$F_{(2, 10)}$ = 13.21, p = .002]. P*ost-hoc* comparisons showed that, although ordered words were read faster (1239 wpm) than scrambled words (940 wpm), this difference did not reach significance (p = .09). Significant differences emerged when comparing ordered words with random words (588 wpm, p = 0.0005) and scrambled words with random words (p = 0.009).

The faster reading rate obtained with both ordered and scrambled words from a text as compared to the lists of random words of similar length is in keeping with the idea that a masking effect between letters of consecutive words within the stream is an important factor in modulating reading speed. In fact, with both ordered and scrambled types of stimuli, words of quite variable length followed one another. Presumably, this length difference produced a limited masking effect between letters. By contrast, masking between letters of consecutive words was maximized in the random word condition where 4- or 6-letter long words were presented. Notably, the effect of letter masking was much more evident than the semantic context effect, which was small and failed to reach a significant level.

However, two criticisms may be raised with regard to the interpretation of these findings: 1) "random words" were not drawn from the same context than the ordered and scrambled conditions; thus, random words might be different in several linguistic features (e.g., frequency) with respect to ordered/ scrambled words; 2) “random words” were 4- and 6-letter long and it would certainly be more appropriate to use words having all exactly the same length. These questions are addressed in Experiment 8.

As in the no mask condition with, a significant main effect of stimulus type emerged [$F_{(2, 10)} = 40.07$, $p < .0001$] in the condition with a non-verbal mask. Post-hoc comparisons indicated a marginally significant difference between ordered and scrambled words (428 and 475 wpm, respectively; $p = .055$) with scrambled words read faster than context ordered words. Both ordered and scrambled words were read faster than random words (314 wpm; both $p_s < 0.0001$).

As in the previous condition, random words had the lowest reading rate; this may be attributed to the extreme similarity in length for the words in this condition, but not for the other two (ordered and scrambled) conditions where successive words in the stream had very different lengths.

Finally, an inspection of Figure 7 shows a large difference between the conditions with and without a mask. As in Experiment 1, the presence of a mask lead to a rapid reduction in the reading speed in all conditions (ordered, scrambled and random words). To compare the conditions with and without the mask we run a 2x3 ANOVA with mask (yes, no) as between factor and stimulus type (ordered, scrambled, random words) as repeated factor. The analyses indicated the significant main effects of the stimulus type [$F_{(2, 20)} = 26.98$, $p < .00001$] and mask [$F_{(1, 10)} = 93.37$, $p < .00001$] factors. The stimulus type by mask interaction was significant [$F_{(2, 20)} = 4.71$, $p = .021$]: while in the no mask condition a significant difference emerges among all ordered, scrambled and random words, in the mask condition only the differences between ordered and random words, and between scrambled and random words are significant (p=.01 and .001, respectively). The difference between ordered and scrambled words is not statistically significant (p=.35).

The negative effect of an additional visual masking was associated to considerably lower reading rate confirming previous results (however, note that data were collected in different groups of subjects).

2.8 Experiment 8. Context gain and random words: role of letter masking and working memory

In experiment 8, we address the question of context gain and letter masking by comparing different stimulus types: ordered, scrambled and random 5-letter long words. Stimuli are taken from the same context, i.e. sampled from the same text passages. In the literature there is variability as to the number of words within each trial. Some studies used a number of targets falling within the working memory span (e.g., Latham & Withaker, 1996; Fine et al, 1999) while others used a number of stimuli greater than the span (e.g., Yager 1998, Chung et al., 1998, Pelli et al., 2007). Given the different results obtained in terms of reading rate between these two sets of studies, here we systematically test the weight of short term memory in modulating reading rate. To this aim, Experiment 8 was divided into two sub-experiments. In the first, a stream of 6 words is presented in each trial; in the second, each stream consists of 12 words. In both cases three conditions are run: ordered, scrambled and random words.

2.8.1 Stimuli

As in Experiment 7 we used the Italian translation of “Alice in the wonderland” by Levis Carrol.

First set. In the first set, six words were presented in each trial. For the ordered condition, the first 240 words of the first chapter of the book were presented in the exact order as they appeared in the text (mean word length = 4.9 letters, S.D. = 2.9). For the scrambled condition, words (the first 240) were taken from the second chapter of the book and were randomly presented in the stream of words (mean word length = 4.8 letters, S.D. =

2.8). In both conditions, punctuation was abolished and no capital letters were used. In the third condition, we selected 240 5-letter words from the whole book. Words in this condition had a similar percentage of nouns (34.8%), adjectives/adverbs (24.5%) and verbs (40.7%) than stimuli used for the ordered (35.4, 20.8 and 43.7%, respectively) and scrambled (37.3, 26 and 36.7%, respectively) conditions.

Second set. In the second set, 12 words were presented in each trial. For the ordered condition, the first 480 words of the first chapter of the book were presented in the exact order as they appeared in the text (mean word length = 4.7 letters, S.D. = 2.7). For the scrambled condition, words (the first 480) were taken from the second chapter of the book and were randomly presented in the stream of words (mean word length = 4.8 letters, S.D. = 2.7). In both conditions, punctuation was abolished and no capital letters were used. In the third condition, we selected 480 5-letter words from the whole book. Random words had a similar proportion of nouns (37.4%), adjectives/adverbs (23.7%) and verbs (38.7%) than stimuli used for the ordered (35.5, 20.9 and 43.6%, respectively) and scrambled (29.9, 28.5 and 41.6% respectively) condition.

2.8.2 Participants

Six subjects (others than in previous experiments) took part in the first (six words per trial) sub-experiment (mean age = 27 years, range = 23-32; s.d. = 3.9). Six different subjects participated to the second sub-experiment (mean age = 26.8 years, range = 25-32; s.d. = 4.07). All subjects had normal or corrected to normal vision.

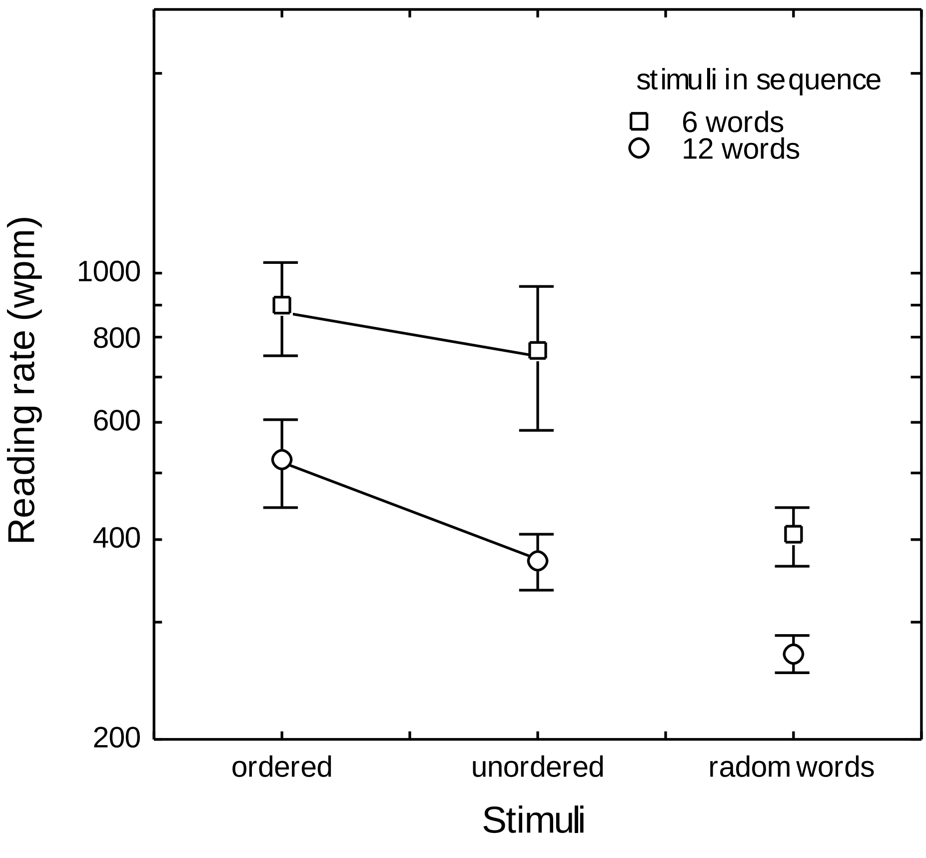
2.8.3 Procedure

Equipment and general procedure was the same of that used in Experiment 1. A fixation point (a black square subtending 0.2 deg of visual angle) was presented at the center of the screen for 2000 msec. Immediately after the fixation point disappearance, words were presented using the RSVP paradigm, i.e. words (either six or twelve depending on the experimental condition) were presented sequentially, one word at a time, at the same spatial location and participants were asked to read them aloud. There was no blank frame (inter-stimulus interval) between words. No mask was used. We measured the duration threshold for each participant by varying the exposure duration in a 40-trial run using the improved QUEST staircase procedure with a threshold criterion of 80% correct responses (Watson & Pelli, 1983). The adaptive QUEST procedure increased or decreased the presentation rate (starting from 500 ms) according to the participant's accuracy. Word omissions, mispronunciations and substitutions were considered errors.

2.8.4 Results and comments

Results are shown in Figure 2.8.

Figure 2.8. *Reading rate (in wpm) for ordered, scrambled and random (5-letter) words. Two conditions were used: 6-word sequences (black squares) and 12-word sequences (white squares).*



For the first sub-experiment (6-word trials), an ANOVA showed that the main effect of type of stimulus was significant [$F_{(2, 10)} = 43.06$, $p < .0001$]: words in the ordered context and the scrambled words (896 and 769 wpm, respectively) were read faster than random words

(405 wmp, both ps <.0001). The difference between ordered and scrambled words was not significant ($p = .12$).

The same analysis was conducted for the second sub-experiment (12-word trials). The main effect of type of stimulus was statistically significant [$F_{(2,\ 10)} = 49.16$, $p < .0001$]: a significant context gain was present with ordered words read at a faster rate (524 wpm) than scrambled words (369 wpm, $p <.0001$). Both ordered and scrambled words were read faster than random words (269 ms; both $p_s <.0001$).

A significant context gain was obtained only when a large set of words was employed. Therefore, it seems likely that the advantage of an ordered context is mediated by the global understanding and remembering of the sentence. At any rate, note that the context contribution to reading rate was quantitatively small (by a 1.4 factor). By contrast, here as well as in Experiment 7, random words, having all the same length (5 letters in the present experiment) produced the slowest reading rate as compared to both ordered and scrambled conditions.

While the difference with the ordered condition could in principle be attributed to the absence of a helping context for random words, the significant difference with scrambled words requires a different explanation. Overall, data support a low processing level of explanation, i.e., letter masking. When a stream of words is presented sequentially in the same spatial position and words have the same length masking between letters belonging to consecutive words reduces the visibility of the letters (and, thus, of the words). Vice versa when words in the stream have different lengths this masking effect is reduced favoring letter visibility in non-overlapping positions and appreciably increasing reading rate.

Finally, in the present experiment, we examined the role of working memory when reporting words using the RSVP technique. To this aim we compared the reading rate for ordered, scrambled and random words in the two sub-experiments with either 6 or 12 target stimuli in each trial. A 2x3 ANOVA was run with trial numerosity (6, 12 target stimuli) as between factor and stimulus type (ordered, scrambled and random words) as repeated factor. Results indicated significant main effects of the trial numerosity [$F_{(1,\ 10)} = 11.16$, $p = .007$] and stimulus type [$F_{(2,\ 20)} = 86.27$, $p < .0001$] factors. The trial numerosity by stimulus type interaction was significant [$F_{(2,\ 20)} = 4.18$, $p = .03$]: reading rate for all types of stimuli was higher with fewer number of items per trial but the advantage was greater for the scrambled and ordered words (p_s=.001 and .01, respectively) than for random words (p=.04).

Overall, results indicated that the overload of working memory lead to a decline in reading rate by a factor of 2 whenever words were ordered, scrambled or random, with a smaller effect for random words. This finding explains some of the inconsistencies found in literature and will be further examined in the general discussion.

2.9 General discussion

In the literature very different values have been reported as estimates of the reading speed ranging from 100 to 1500 WPM. In the present study, we systematically investigated, in eight experiments, a number of variables that modulate the reading rate estimate. In the following, we provide a recipe for targeting different components that contribute to reading rate.

Our results indicate that, when decoding a single word or a word in a sequence, but unmasked by the other elements, of the sequence, we can read as fast as 1220 wpm (Experiment 2). When words are presented in sequence, the letter masking imposes a speed limit of 600 wpm (Experiments 1 and 3). This finding emphasizes that not all the words in each trial have the same weight on individual performance: if no mask is added to the stream the first and last words are more visible and greatly influence the reading rate estimate. When the initial and last words in the trial are not masked, the context helps reading rate by a small amount (factor of 1.4) but only when the words in the trial exceed the memory span (12 words). However, memory imposes a speed limit ranging between 250 wpm and 500 wpm (Experiments 7 and 8) depending on the load determined by the materials used (sentences, scrambled text, random words). Finally, in Experiments 4 to 6 we demonstrated the important role played by eye-movements and confirmed the significant upper limit they impose on reading speed, settling the reading rate value at around 300 wpm.

In this study we aimed at evaluating the maximum reading speed that can be reached by normal adult readers. So far the reported rates point to different responses but the problem of such a discrepancy has not received much attention. Our data indicate that there is not just one response to this question as multiple low and high level factors play a significant role in the estimate of reading rate. The role of each of these factors was isolated and analyzed in depth. Altogether, present data help understanding and reconciling the discrepancies found in literature among reading rates.

The role of the visual mask (or temporal flanker, as also labeled) has been taken into account: In some experiments, a mask was added at the beginning and at the end of the word stream, limiting the advantage for the first and last words. However, such shrewdness was not used systematically. Pelli & Tilman (2007) underscore the importance of this point by stating that the absence of a visual mask in the stream alters the supposed perceptual similarity between words. Here, we found that the presence/absence of the mask drastically affects the estimation of reading rate and can explain the discrepancies found in literature about such a measure. When a mask is used, the median of the reading rate described in literature is around 470 wpm (Kwon & Legge 2012; Know, Legge & Dubbles, 2007; Yu et al., 2007, 2010; Fine 1997, 1999; Pelli & Tilmann 2007; Pelli et al, 2007). Conversely, when no visual mask is used reading rate increases considerably, with a median of around 565 wpm (Chung 1998; Rubin & Turano, 1992; Yager 1998; Chung, 2002; Latham & Withaker, 1996). Here, we show that the first and last words have a large advantage over the other words in the trial. Thus, not all the words within the stream have the same visibility. Since reading rate is typically measured at around 80% correct, we can conclude that the thresholds are heavily weighted by the visibility of the first and last words.

More generally, visual masking refers to the reduction in visibility of a stimulus due to the preceding (forward) or subsequent (backward) presentation of another stimulus in the same spatial position (Felten & Wasserman, 1980; Breitmeyer, 1984; Enns & Di Lollo, 2000). In the case of a stream of words, as for the RSVP paradigm without mask, the first and last words are less affected by the masking phenomenon because they are submitted only to either backward (first word) or forward (last word) masking. Conversely, the central words undergo both backward and forward masking effects. The addition of a non-verbal mask blunts these effects and smoothens the perceptual differences among words in the stream, making them more similar to each other. This is relevant since the estimate of reading rate takes into account the subject's performance on all the words independently of their ordinal position in the stream.

What is the nature of the masking effect? In this study we find that a non-orthographic mask has a very similar effect on the preceding item than a word, suggesting that masking occurs at a feature or letter level rather than at the word level. By contrast, a preceding non-orthographic mask has a weaker effect on the first word in the trial, showing a primacy effect. Different accounts have been proposed in literature to explain the difference among stimuli within the RSVP stream and attentional phenomena have been studied in depth. Specifically, Ariga and Yokosawa (2008) demonstrated the existence of an attentional limitation for the detection of a target in the RSVP stream when it appeared early in the stimulus stream. Authors proposed that the deficit with early presented targets arises because an attentional preparation is required for setting up the visual system to detect brief targets within a rapid sequence of events. This mechanism has been labeled attentional awakening and it has been distinguished from the attentional blink by Ambinder & Lleras (2009). The attentional blink refers to the difficulty in identifying a second target in a stream if presented close in time (around 200 ms) to the first target. The attentional awakening does not seem to play any role in the specific case of reading all the words presented, since the first word of the stream is always read better than the others (Experiments 2 and 3) differently from what found by Ariga and Yokosawa (2008). This discrepancy may be due to the different tasks used, although in the context of a similar procedure. In our experiments, participants were asked to read all the words presented in the stream, so that no active inhibition was required. Vice versa in the experiments testing the attentional effects, signal selection was required: a letter, differently colored from the distracters, had to be identified. Thus, subjects are, implicitly, instructed to ignore all the non-target letters. This may elicit the action of blocking the stimulus following the target.

The direction of the effects found in the present study seem to be more in line with what expected based on the attentional blink. Different theories have been provided to explain attentional blink. According to the filter theory (Di Lollo, Kawahara, Ghorashi, & Enns, 2005), the attentional blink is due to the blocking of input during the stream that is triggered by the appearance of a distracter immediately following the target. As for the attentional awakening theory, this explanation seems to be particularly suitable for conditions where an inhibition process is required, like when a target has to be identified among many previous and successive distracters which do not need to be identified. In our case, the task demand is different since participants are required to read all the words (or as many words as possible) within the stream. A different theory of the attentional blink is provided by bottleneck models (Chun & Potter, 1995) which postulate that the difficulty to process the stimulus following the target is due to the cognitive amount of processing still devoted to the previously seen target. Consequently, the second target's perceptual representation cannot be encoded into memory (Dux, Asplund, & Marois, 2008, 2009; Dux, Ivanoff, Asplund, & Marois, 2006). If the attention blink can explain the drop of performance with the second and third word it cannot easily explain the improvement with the fourth word (Experiment 2). Also, it cannot explain results from experiment 3 where, vice versa, the fourth word does not show the speed up seen in Experiment 2. We believe that the same feature or letter masking mechanism provide a simpler account for both forward and backward effects.

Our measurements confirm the important role of eye movements in limiting the speed of reading. Interestingly, the rate obtained with lines of random words closely resembles the one obtained by Carver's 300 wpm rauding speed (Carver, 1992). Naturally, the speed of functional reading is heavily limited by pronunciation time, that is not involved in RSVP reading. However, we may suppose the eye movement cost for text reading to be weaker than what measured in our case. When reading a text the majority of words are fixated but some are skipped so that foveal processing of every word is not necessary. Function words are fixated less frequently (about 35% of the times) than content words (about 85%) both because they are more predictable and because they are short (Carpenter & Just, 1983; Balota et al., 1985). As length increases, the probability of fixating a word increases (Rayner & McConkie, 1976). While texts contain both short function and long content words, the words we presented in the horizontal layout (Exp. 4) did not benefit from skipping fixations. Comparisons of our ordered text (read without skipping fixations but minimizing saccades) with Carvers's estimate indicate that, if eye movements cost 300 wpm, skipping fixations contribute little to the final speed.

When the word to the right of fixation is not yet identified, some initial parafoveal processing occurs. It is known that reading is difficult or impossible on the basis of only parafoveal information. Bouma (1973) showed that, in parafoveal vision, only the initial and final letters are available and partially spared from visual crowding (see also Pelli et al., 2007). Thus, this partial information is likely to be useless when reading long unrelated words. Indeed, Balota et al. (1985) found that readers obtained more information to the right of fixation when the upcoming word was highly predictable from the preceding text. Additionally, previewing the first three letters belonging to the word on the right of fixation, reduces the total viewing time on that word (Lima and Inhoff, 1985). However, the preview effect in terms of time advantage may be minimal when the word must be fixated and not skipped as in our paradigm. Indeed, Rayner and Pollatsek (1987) suggested that "*perhaps this preview benefit should be added to the fixation time on the word and should be subtracted from the time spent on the prior word*" knocking-out the overall benefit. As a consequence, it is not entirely surprising in failing to observe a parafoveal benefit for reading long unrelated words in the absence of spatial position uncertainty.

Leveling the playing field by controlling for the lexical status of the stimuli the present study reconciles the differences in reading speed measures obtained from different laboratories providing an estimate of the weight of the various cognitive components.

PART II

3. Peripheral reading disorders and neglect dyslexia

Reading abilities may be impaired due to a deficit concerning the visual word form processing. Such disabilities are referred to as peripheral dyslexia and are distinct from central dyslexias which are characterized by difficulties specific to the phonological or lexical reading pathways. Peripheral dyslexias are disorders affecting the initial stages of reading and include: attentional dyslexia, pure alexia and neglect dyslexia.

Attentional dyslexia is a rare reading disorder by which patients are able to read the whole word (e.g., HOUSE) but are not able to name the single elements that constitute the word (e.g., H, O, U, S, E). Patients perform better when word stimuli are presented in isolation rather than flanked by other words and letters. Consequently text reading is also very impaired. The lesion is usually in the left parietal lobe (Shallice & Warrington, 1977; Warrington, Cipolotti, McNeil, 1993).

Pure alexia is characterized by the ability of recognizing and naming of individual letters but patients show problems in correctly reading single words (Behrmann, Nelson & Sekuler, 1998; Behrmann, Shomstein, Black & Barton, 2001). Patients may apply a letter by letter reading strategy, which cause a length effect, with an increase in latency and errors with longer stimuli. The anatomical substrate mostly involves the left fusiform gyrus (Binder & Mohr, 1992; Price & Devlin, 2003; Dehaene & Cohen, 2011). The disorder is labelled "pure" since writing and spelling abilities are within normal ranges.

Finally, neglect dyslexia (ND) is a component of the unilateral spatial neglect (USN) and is characterized by reading errors involving the left sided letters in case of single word reading or left sided words in case of paragraphs reading. Most common errors include letter or word omissions or substitutions (for a review, see Vallar, Burani & Arduino, 2010). The features of ND were clearly defined by Kinsbourne and Warrington (1962), who, in six right-brain-damaged patients, confirmed the association of a reading disorder, with left USN. These patients are typically unaware of the ND (Kinsbourne and Warrington 1962). The topic has received a large attention by researchers in the last 50 years. Specifically the role of lexical factors has been investigated (Mozer & Behrman, 1990; Riddoch, Humphreys, Cleton, & Fery, 1990; Ladavas, Umiltà & Mapelli, 1997; Arduino, Burani & Vallar, 2002; Rusconi, Cappa, Scala & Meneghello, 2004). Conversely few studies focused on the early visual components of the reading disorder, investigating the visual stimulus exploration made by patients. To the best of our knowledge only two studies (Di Pellegrino, Ladavas & Galletti, 2002; Behrmann, Black, McKeeff & Barton, 2002) investigated this topic. The cited papers will be further discussed below.

My focus in the following two studies will be on neglect dyslexia. Specifically, the role of eye movements has been deeply investigated in order to shed a light on the early visual exploration components and uncover a possible role of such an exploration in ND patients' reading pattern.

4. Single word reading in patients with neglect dyslexia: the role of eye movements.

Unilateral spatial neglect (USN) is a neuropsychological disorder characterized by a deficit in detecting and identifying objects or executing movements in the portion of space contralateral to the lesion (Halligan, Fink, Marshall, & Vallar, 2003). The disorder is most frequently associated with right-hemisphere brain lesions. The most common anatomical correlates of left-sided neglect are the right inferior parietal lobule (supramarginal gyrus) and the temporo-parietal junction. Lesions involving the premotor cortex or confined to subcortical structures may also cause neglect (Vallar, 2001). Neglect dyslexia (ND) is a reading disorder often associated with other manifestations of the USN syndrome. When patients with ND read single words, pseudowords or sentences and lines of text they may misread some elements that occupy the controlesional side. Errors in single-word reading are considered markers of ND and are characterized by different types of errors (Ellis, Flude & Young, 1987). The most common errors are omissions [e.g., the target word *orologio* (clock) read as *logio*] and substitutions [e.g., the target word *tavolo* (table) read as a nonword like *sevolo* or another word like *cavolo* (cabbage)].

The relationship between the reading disorder and the more general USN syndrome is controversial (see the review by Vallar, Burani, & Arduino, 2010). In fact, in USN reading abilities show associations and dissociations with other visuo-spatial tasks. In a large recent survey of neglect impairments, Lee et al., (2009) showed that the reading deficit co-occurred with other spatial deficits in 40% of patients. However, few cases of double dissociations between left ND and right USN have been described (Katz & Sevush, 1989; Cubelli, Nichelli, Bonito, De Tanti, & Inzaghi, 1991; Costello and Warrington, 1987), suggesting that the disorders may be due to different mechanisms. But, as noted by Vallar et al. (2010), these double dissociations and cases of ND without USN are generally associated with a lesion involving at least the left hemisphere or both hemispheres (Patterson & Wilson 1990; Warrington 1991; Cohen & Dehaene 1991; Binder, Lazar, Tatemichi, Mohr, Desmond, D.W., & Ciecierski, 1992; Haywood and Coltheart 2001; Arduino, Daini, & Silveri, 2005), which casts doubts about whether these cases should really be considered as neglect dyslexia (see the review of Vallar et al., 2010 for a discussion).

In a study of patients with ND and USN, Martelli, Arduino & Daini (2011) suggested that in neglect dyslexia omission errors are associated with the USN deficit and that substitutions might arise from a more perceptual impairment. The authors showed that the number of letters omitted in reading single words and pseudowords correlated positively with the number of errors in line and letter cancellation tasks. Omission errors seem to be a characteristic marker of the unilateral spatial neglect disorder in reading. Weinzierl, Kerkhoff, van Eimeren, Keller & Stenneken (2012) compared the types of errors (omissions and substitutions) made by neglect patients with those of healthy controls whose performance was equated for accuracy by reducing exposure duration. They found that omissions were dominant in patients and that substitutions characterized controls' performance at threshold (with brief exposure durations).

Nevertheless, it is still unclear why only a fraction of patients with USN make reading errors. The reading pattern in ND might be due to impairment of one or more cognitive components involved in USN (e.g. Ptak, Di Pietro, & Schnider, 2012). Or, similarly to the interpretation of line bisection tasks, reading errors might arise as an epiphenomenon of the interaction between USN and an independent deficit. In line bisection tasks, it has been shown that hemianopic patients without USN compensate for their visual deficit by fixating toward the blind field (Ishiai, Furukawa, & Tsukagoshi, 1989; Barton, Behrmann, & Black, 1998) and that USN patients are unable to compensate for hemianopia because of their attentional deficit (Chedru, Leblanc, & Lhermitte, 1973; Girotti, Casazza, Musicco, & Avanzini, 1983; Ishiai et al., 1989; Karnath & Fetter, 1995; Barton et al., 1998). Thus, in line bisection tasks they show a larger bias than USN patients without visual field defects and their errors are opposite to those of hemianopic patients (D'Erme, De Bonis & Gainotti, 1987; Doricchi & Angelelli, 1999; Daini, Angelelli, Antonucci, Cappa, & Vallar, 2002). This example shows that, due to the composite nature of the USN syndrome, a concomitant deficit may result in qualitative and quantitative behavioral differences between patients. Our working hypothesis is that the eye movement pattern of non-hemianopic USN patients with and without ND may help clarify the nature of the reading deficit.

The role of eye movements is particularly important in studying reading. Eye movements are influenced by many perceptual and semantic aspects of orthographic material and can indicate the cognitive processes involved in reading. Oculomotor behavior is influenced by early perceptual factors such as stimulus length, letter size, spatial layout of the text and lexical factors (Inhoff, Radach, Eiter, & Juhasz, 2003; Juhasz, 2008; O'Regan, 1979, 1980; Rayner, 1979; White, Rayner, & Liversedge, 2005, for a review see Rayner, 2009).

Eye movements have been extensively investigated in neglect patients (Chedru et al., 1973; Girotti et al., 1983; Johnston & Diller 1986; Hornak 1992; Behrmann, Watt, Black, & Barton, 1997; Ptak, Golay, Mury & Schnider, 2009). Studies with USN patients have focused on tasks such as global scene description, visual search and object detection, and have shown impaired behavior on the neglected side. When a visual search task was adopted, studies showed that USN patients began exploring stimuli from the right hemifield. Furthermore, their exploration was mostly limited to the right side (Chedru et al., 1973; Hornak, 1992; Ptak et al., 2009) and when they explored the left hemifield their reaction times increased (Girotti et al., 1983). Coherently, Johnston & Diller (1986) found a strong negative correlation between an index of USN severity (derived from letter cancellation and visual matching task scores) and amount of exploration in the left hemifield. Behrmann et al. (1997) reported that in a letter detection task patients with USN made fewer fixations and engaged in shorter inspection time on the controlesional left side. These results demonstrated that in exploratory tasks omitted items were not fixated.

To our knowledge, very few studies have investigated eye movements during reading in patients with neglect dyslexia. In a single word and pseudoword reading aloud task, Di Pellegrino, Ladavas & Galletti (2002) analyzed an ND patient's (FC) first landing positions after the stimulus appeared and number of fixations. They found that the patient's probability of reporting the left-sided letters could not be predicted by the amount of time spent fixating the left side of the string. This indicates that left-sided eye movements are independent from awareness of the contralesional orthographic material. Coherently, using a covert attention task Ladavas, Zeloni, Zaccara & Gangemi (1997) found that neglect patients with fronto-parietal lesions could not inhibit left-sided saccades that were performed toward the unattended and otherwise ignored stimuli. Contrary to these findings, Behrmann, Black, McKeef, & Barton (2002) found a direct correspondence between the oculomotor performance of patients with neglect dyslexia and their reading behavior. In this paradigm, patients were asked to read sets of 15 words arranged in 5 columns that covered the whole screen. The authors found that, similar to unimpaired control subjects, USN patients without ND showed no difference in number of fixations and fixation duration in the left compared to the right visual field. Vice versa, patients with ND showed an abnormal eye movement pattern with very few brief fixations towards the left columns. Furthermore, they made more and longer fixations to the ipsilesional side compared with both the USN patients and the control group. The authors concluded that ND may be due to failure to register and perceive controlesional information.

Eye movement analysis in neglect patients highlighted important aspects of this syndrome that contribute towards explaining some of its specificities (e.g., object-based neglect, Walker & Findlay, 1996). A more systematic analysis of eye movements in patients with ND compared with the eye movement exploratory pattern in patients with USN without ND and controls might highlight important aspects of the reading impairment.

The first aim of this study was to investigate whether ND is associated with an abnormal eye movement exploratory pattern different from the oculomotor behavior shown by USN patients without ND, as suggested by Behrmann et al.'s results (2002) (Experiment 1). To evaluate the role of the oculomotor component independent of reading and to examine the relationship between USN and ND without using orthographic material, we investigated the eye movement pattern during a saccadic non-reading task (Experiment 2). Indeed, the ability to program and execute a saccade of the correct amplitude in simple non-verbal tasks is a prerequisite for appropriate saccade execution during reading (e.g. De Luca, Di Pace, Judica, Spinelli & Zoccolotti, 1999; Pavlidis, 1981). Finally, in Experiment 3 we aimed to clarify whether the co-occurrence of USN and the impossibility of producing exploratory eye movements during reading might be sufficient to induce the types of errors seen in neglect dyslexia.

For this purpose, we tried to simulate “ND-like” reading behavior in USN patients without ND and controls by preventing eye movements while they read at threshold.

4.1 General method

4.1.1 Participants

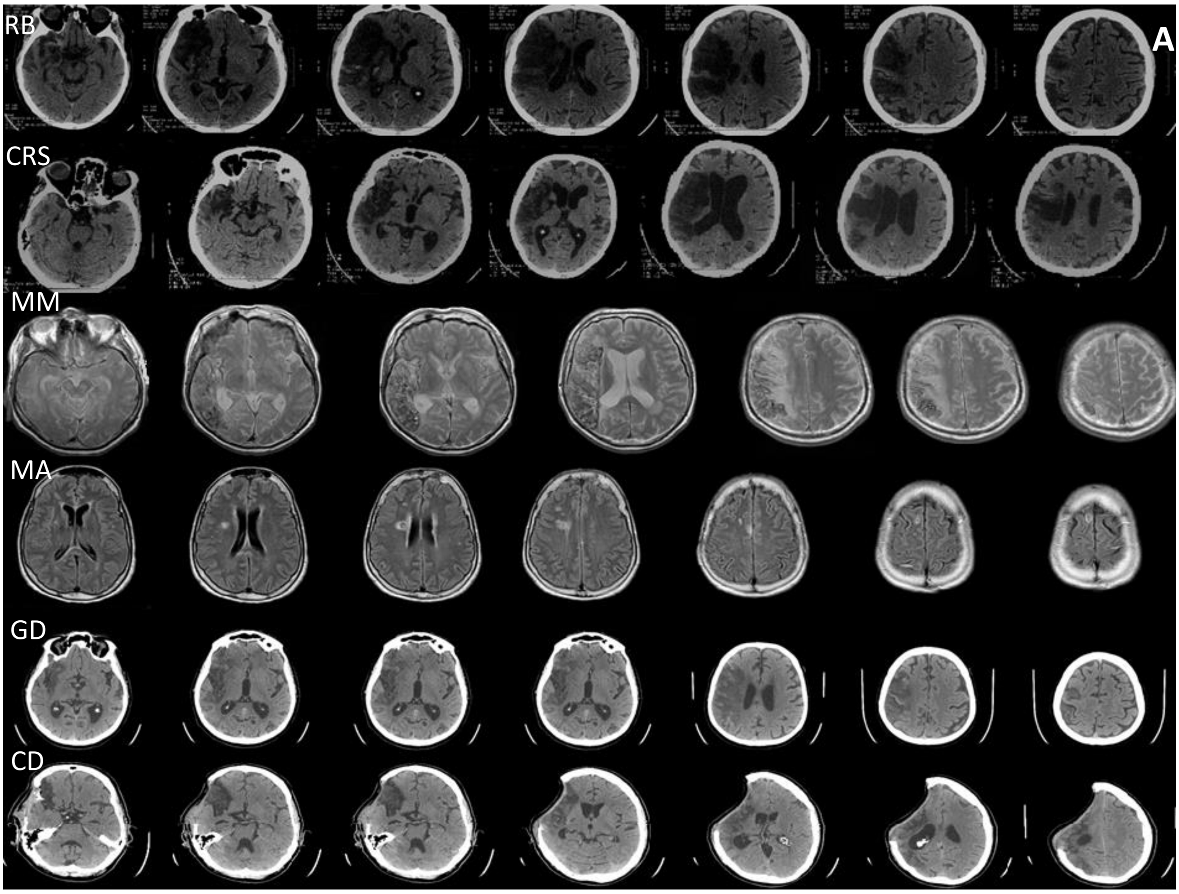
Participants were recruited from the inpatient population of the I.R.C.C.S. Fondazione Santa Lucia (Scientific Institute for Research, Hospitalization and Health Care, Santa Lucia Foundation). We identified 34 patients with USN on the basis of the screening battery results. Twenty-one patients in the original sample did not participate in the experimental sessions and were excluded for the following reasons: 9 had mental deterioration; 4 had visual field defects assessed by kinetic Goldmann perimetry; 5 were unable to still in front of the eye tracker and use the head rest; 2 had unintelligible speech; one had previous lesions. We selected 10 controls with right brain damage and no USN from the same inpatient population; none were excluded from the experimental sample. Thus, a total of 23 right-hemisphere-damaged patients participated in the study. All patients had suffered a cerebrovascular ischemic stroke. Thirteen patients (4 females and 9 males) suffered from USN (USN+); mean age was 70.92 years (SD ±7.7; range 58–82) and mean education was 10.5 years (SD ±5.3; range 2–18). In the neglect patients, mean disease duration was 1.85 months (SD ±0.77; range 1–3). Ten right-hemisphere-damaged patients without neglect (USN-) were matched for age (mean age = 68.9 years; SD = ±10.98; range = 52–86), education level (mean education = 10.8 years; SD = ±4.54; range = 5–18) and disease duration (mean duration = 1.55 months; SD = ±0.49; range = 1–2) and served as the control group. Demographic and neurological information is shown in Table 4.1. Lesion site was assessed using CT or MRI scans and images are shown in Fig. 4.1 for each USN+ patient. Unfortunately, no scan images were available for patient NR. All patients were right-handed. They had normal or corrected-to-normal vision, preserved visual fields, as assessed by Goldmann perimetry, and no history of previous neurological diseases. Informed consent was obtained from all subjects prior to their participation.

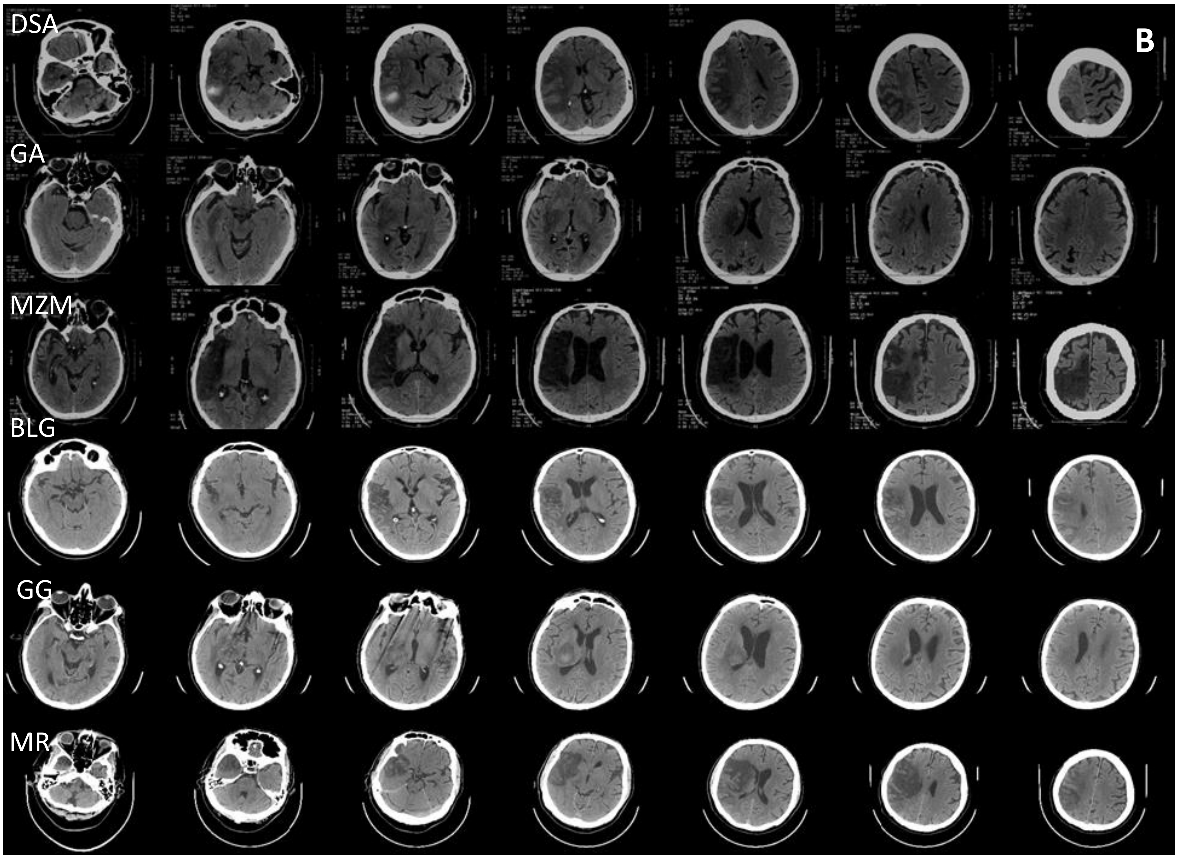
Table 4.1. *Demographic features of the fifteen right-brain-damaged patients.*

	Sex/Age/Education	*Duration of disease (months)*	*Lesion site*	*Presence of USN**
Patients (USN+)				
RB	M/73/8	3	FTP c-s	Yes
CRS	F/78/2	1	FTP c-s	Yes
MM	M/76/7	3	FP c-s	Yes
MA	F/62/8	1.5	F	Yes
GD	M/74/18	2	TP	Yes
CD	M/59/13	2	FTP	Yes
DSA	F/82/18	3	MCA	Yes
GA	M/71/13	1	FTP	Yes
MZM	M/58/8	2	MCA	Yes
BLG	M/68/13	1	FTP	Yes
GG	M/68/6	2	Th, In, RC	Yes
NR	F/80/5	1	F	Yes
MR	M/73/18	1.5	FTP c-s	Yes
Controls (USN-)				
SMP	F/77/8	2	s (right capsule)	No
RP	M/62/7	1	s (outer capsule and Th)	No
BM	M/78/8	2	F s	No
PG	M/59/18	1.5	MCA	No
TA	M/86/5	2	F s	No
LG	M/67/18	2	MCA	No
ML	M/58/8	1	BG	No
CG	M/52/13	1	P c-s	No
IMA	F/72/10	2	s (Pons Varoli)	No
GF	M/78/13	1	F	No

Lesion site: F: Frontal Lobe; P: Parietal Lobe; T: Temporal Lobe; c: cortical lesion; s: subcortical white matter; MCA: Middle Cerebral Artery. BG: basal ganglia; Th: Thalamus; In: Insula; RC: Radiate Corone; M/F: male/female. * See the section 2.2 for the results of the baseline assessment for visual spatial neglect

Figure 4.1. *Scan images for patients with Unilateral Spatial Neglect (A: patients with USN+ ND+; B patients with USN+ ND-).*





4.1.2 Baseline neuropsychological assessment

Presence and severity of unilateral spatial neglect were assessed using a diagnostic battery, which included the following tests:

a) *Letter cancellation* (Diller & Weinberg, 1977). The patient is asked to cross out all 104 letter H's printed on an A3 sheet of paper, that is, 53 on the left side and 51 on the right side. Targets are presented in alignment with other letter distractors. For healthy subjects, the maximum difference between omission errors on the two sides of the sheet is two (Vallar, Rusconi, Fontana, & Musicco, 1994).
b) *Line cancellation* (Albert, 1973). The task requires crossing out all 21 black lines (2.5 cm in length and 1 mm in width) printed on an A3 sheet of paper, that is, 11 on the left side and 10 on right side. Normal subjects make no errors on this task.

c) *Wundt-Jastrow Area Illusion test* (Massironi, Antonucci, Pizzamiglio, Vitale & Zoccolotti, 1988). The score on this test is the number of responses indicating that the patient do not show the illusory ("unexpected") effect arising from the left (range 0-20) side of the stimulus. Patients with right brain damage and left neglect make errors only on stimuli with a left-sided illusory effect.

d) *Sentence reading* (Zoccolotti, Antonucci, Judica, Montenero, Pizzamiglio & Razzano, 1989). Patients have to read aloud six sentences (medium length 8.5 words, 31.8 letters; range 5-11 words, 20-41 letters) printed in uppercase on a horizontally placed A4 sheet of paper. The score is the number of reading errors (range 0-6). Neurologically unimpaired subjects and right-hemisphere-damaged patients without neglect make no errors in this task.

Patients were considered to have USN if they obtained pathological scores on at least two of the four tests included in the diagnostic battery. Results of the assessment of visual spatial neglect are summarized in Table 4.2. As shown in the table, patient SMP was a dubious case because he produced 6 omissions on the left and 4 on the right side of the page in the letter cancellation task, which is considered a pathological performance. To further investigate his abilities, we gave her a gap-detection test (Ota et al., 2001). Results confirmed the absence of USN (number of left omissions/errors = 0/30; number of right omissions/errors = 0/30).

Table 4.2. *Baseline assessment for visual spatial neglect*

	Letter Cancellation (omissions)		***Line Cancellation*** (omissions)		***Wundt-Jastrow*** (unexpected responses)		***Sentence reading*** (errors)
	Left	*Right*	*Left*	*Right*	*Left*	*Right*	
Patients (USN+)							
RB	30/53*	10/51	0/11	0/10	0/20	0/20	1/6*
CRS	49/53*	15/51	0/11	0/10	6/20*	0/20	1/6*
MM	43/53*	24/51	7/11*	3/10	15/20*	4/20	3/6*
MA	42/53*	21/53	3/11*	1/10	4/20*	2/20	6/6*
GD	53/53*	37/51	11/11*	1/10	20/20*	1/20	6/6*
CD	53/53*	2/51	11/11*	6/10	20/20*	0/20	6/6*
DSA	53/53*	48/51	11/11*	6/10	20/20*	0/20	0/6
GA	4/53	2/51	0/11	0/10	11/20*	0/20	1/6*
MZM	53/53*	39/51	3/11*	0/10	9/20*	0/20	1/6*
BLG	18/53*	1/51	0/11	0/10	18/20*	0/20	0/6
GG	53/53*	42/51	11/11*	1/10	9/20*	4/20	1/6*
NR	30/53*	2/51	2/11*	0/10	0/20	0/20	0/6
MR	28/53*	1/51	1/11	0/10	17/20*	0/20	0/6
Controls (USN-)							
SMP	6/53*	4/51	0/11	0/10	0/20	0/20	0/6
RP	0/53	0/51	0/11	0/10	0/20	0/20	0/6
BM	0/53	0/51	0/11	0/10	0/20	0/20	0/6
PG	4/53	2/51	1/11	0/10	0/20	0/20	0/6
TA	0/53	0/51	0/11	0/10	0/20	0/20	0/6
LG	0/53	1/51	0/11	0/10	0/20	0/20	0/6
ML	0/53	0/51	0/11	0/10	0/20	0/20	0/6
CG	0/53	0/51	0/11	0/10	0/20	0/20	0/6
IMA	0/53	0/51	0/11	0/10	0/20	0/20	0/6
GF	0/53	0/51	0/11	0/10	0/20	0/20	0/6

Scores: (i) cancellation tasks: omission errors; (ii) Wundt-Jastrow Area Illusion test: “unexpected responses”; and (iii) Reading Task: the number of sentences in which patients showed left-sided errors. *Performance indicating left neglect.
Pathological scores for letter cancellation (omissions = or > 5 and left/right omissions differences = or > 2), line cancellation (omissions = or > 2), Wundt-Jastrow (left/right unattended responses difference = or > 2) and sentence reading (errors = or > 1) are defined on the basis of the norms provided by the screening battery (Pizzamiglio et al., 1989).
Note: USN+ and USN- refer to patients with and without unilateral spatial neglect, respectively; ND+ and ND- refer to patients with and without neglect dyslexia, respectively.

4.1.3 Baseline assessment of the reading disorder

Studies on ND patients mostly refer to a disorder in single word reading (e.g., Behrmann et al., 1990, 2002; Ladavas, 1997; Di Pellegrino et al., 2002; Warrington, 1991; Lee et al., 2009). Thus, a single-word reading test was used to assess the presence of ND. Two out of the three stimuli sets of Vallar, Guariglia, Nico & Tabossi (1996) were used; they included two lists of 38 words and 38 pseudowords. The word lists include thirty 4-9-letter words (five for each item length), three 10-letter words, three 11-letter words and two 12-letter words. The mean frequency of the words, which were selected from a corpus of the Italian written language of 1.5 million tokens (Istituto di Linguistica Computazionale, CNR), was 13.71 (range 0-47). The pseudowords were obtained from the 38 real words by changing one letter in the left half of each word, without violating the phonotactic and orthographic constraints of the Italian language. Each stimulus was printed horizontally in black uppercase letters (24-pt Geneva bold laser print) at the center of a 29.7 cm x 21 cm white sheet of paper. The participants' task was to read aloud the letter string. The experimenter manually scored responses. No feedback was given. If a patient misread or omitted the left portion of the stimulus, the item was classified as an ND error using the neglect point measure of Ellis et al. (1987). This measure defines neglect errors "as error in which target and error words are identical to the right of an identifiable neglect point in each word, but share no letters in common to the left of the neglect point" (p. 445). Patients were included in the ND group (ND+) if 50% or more of their errors were classified as neglect errors in both word and pseudoword reading tasks. The results of the assessment of neglect dyslexia in USN+ and USN- control patients are summarized in Table 4.3.

Table 4.3. *Percentage and number (in brackets) of neglect errors out of the total errors made by the patients on the reading task (Vallar et al., 1996).*

	Words (N=38)	*Pseudowords (N=38)*	*Presence of ND*
Patients (USN+)			
RB	1.0 (1/1)	1.0 (5/5)	ND+
CRS	.80 (4/5)	.92 (24/26)	ND+
MM	.66 (2/3)	.54 (6/11)	ND+
MA	.83 (15/18)	.88 (22/25)	ND+
GD	.66 (2/3)	.78 (22/28)	ND+
CD	.33 (1/3)	.78 (11/14)	ND+
DSA	0 (0/1)	1.0 (2/2)	ND-
GA	0 (0/1)	.66 (2/3)	ND-
MZM	0 (0/3)	0 (0/3)	ND-
BLG	0 (0/0)	0 (0/1)	ND-
GG	0 (0/0)	0 (0/0)	ND-
NR	0 (0/2)	0 (0/1)	ND-
MR	0 (0/1)	.5 (4/8)	ND-
Controls (USN-)			
SMP	0 (0/0)	.1 (1/10)	ND-
RP	0 (0/0)	0 (0/2)	ND-
BM	0 (0/0)	0 (0/0)	ND-
PG	0 (0/0)	0 (0/1)	ND-
TA	0 (0/2)	.3 (1/3)	ND-
LG	0 (0/0)	0 (0/0)	ND-
ML	0 (0/0)	0 (0/0)	ND-
CG	0 (0/0)	0 (0/0)	ND-
IMA	0 (0/0)	0 (0/0)	ND-
GF	0 (0/0)	0 (0/0)	ND-

Six out of 13 USN+ patients (RB, CRS, MM, MA, GD and CD) showed severe neglect dyslexia (ND+). The other 7 USN+ patients (DSA, GA, MZM, BLG, GG, NR and MR) and controls (USN-) were not affected by neglect dyslexia (ND-). A comparison between Table 2 and Table 3 reveals that USN+ ND- patients don't have a less severe disorder as assessed by non-reading tasks.

4.1.4 Eye movement recordings: apparatus, general procedure, and data analysis

Monocular eye movements were recorded in binocular vision via an SR Research Ltd. Eye Link 1000 eye tracker (SR Research Ltd., Mississauga, Ontario, Canada) sampling at 500 Hz, with spatial resolution of less than 0.04°. Head movements were avoided by using a headrest. Participants sat 57 cm away from a 17-in CRT Dell PC. A standard nine-point calibration procedure was run separately for each of the experiments before collecting the data. The calibration targets were presented randomly in different positions on the screen. Sometimes neglect patients had difficulty locating the targets on the left side of the screen, but all were able to shift their gaze toward the target when the experimenter specified its position verbally. Each experimental task started immediately after calibration.

Eye movement data were processed using EyeLink Data Viewer software (SR Research Ltd., Mississauga, Ontario, Canada). Fixation position, number, duration, and accuracy were analyzed (see details in the Experiment section below).

4.2 Experiment 1: eye movement pattern in reading

Eye movements were recorded during a reading aloud task of single pseudowords that varied for length. It has been shown that sensitivity to the morpho-lexical status and the amplitude of the lexical advantage for words is extremely variable across patients. This suggests that pseudowords, rather than words, may be more suitable stimuli for assessing neglect dyslexia (e.g., Riddoch, Humphreys, Cleton, & Fery, 1990; Behrmann, Moscovitch, Black, & Mozer, 1990; Arduino, Burani, & Vallar, 2002a,b; Martelli et al., 2011; for a review see Vallar et al., 2010). Both reading responses and eye movement parameters were analyzed to verify whether the behavioral and the oculomotor patterns of results were coherent (i.e., correspondence between reading performance and pattern of fixations).

4.2.1 Materials and procedure

Pseudowords were constructed so as to preserve pronunciation and minimize word similarity. We generated a list of 40, 5-to 8-letter pseudowords (10 for each length). The stimuli were written in capital Courier New font, which is characterized by consistent letter spacing. Letter size was kept constant (40 pt) and subtended 1.0 deg. Patients were shown two squared dots vertically displaced 1.5 deg apart in the center of the screen; these fixation marks remained on the screen for the entire experimental session. Stimulus onset was triggered when the patient steadily fixated the central marks for at least 50 ms. Each stimulus was presented at the center of the screen between the fixation marks (i.e. the central letter of each stimulus was vertically aligned to the fixation marks) and remained on the screen until onset of the patient's response. There was no time constraint for responding. Reaction times (RTs) were recorded using a microphone connected to the computer and were measured in milliseconds (ms). Patients were asked to read aloud each stimulus as accurately as possible. Pseudowords appeared in randomized order across participants. Responses were digitally recorded and errors were scored offline.

4.2.2 Results – Reading performance

Reading errors (i.e. omitting or misreading the pseudowords) were classified as "neglect" errors, according to Ellis et al.'s (1987) neglect point measure. Table 4.4 reports the number and percentages of neglect errors made by the patients. Both USN- and USN+ patients without neglect dyslexia (ND-) made few errors. By contrast, ND+ patients made many errors, most of which were classified as neglect errors. Following a letter-based analysis, letter omissions and substitutions were also measured and are presented separately for the left, middle and right side of the stimulus in Figure 4.2. The figure shows that in ND+ patients most reading errors concerned the left portion of the stimuli, but in ND- patients and USN- controls the error pattern of was not left-lateralized. A 3x3 ANOVA with group (ND+, ND- and USN-) as between factor and side of errors as repeated factor (left, middle and right) was performed. Analyses revealed a significant main effect of group [$F_{(2, 20)} = 21.27$, $p < .0001$], which indicates that more errors were made by ND+ patients than ND- and USN- patients (both $p_s < .0001$). The group by side interaction was statistically significant [$F_{(4, 40)} = 23.81$, $p < .0001$]. The Bonferroni post-hoc revealed that USN+ ND+ patients made a larger proportion of errors on the left side of the stimulus as compared to both USN- and USN+ ND- patients (both $p_s < .0001$); the difference for errors on the middle and right-sided letters was not significant (all $p_s > .1$). The number of errors in the left portion of the stimulus was 2 to 8 orders of magnitude greater than that shown by ND- patients, and 84% of these errors were letter omissions. The letter-based analysis showed that two patients classified as ND- (GA and MZM) made errors only in the left portion of the string. However it must be noted that these errors are not classified as neglect errors (Table 4) and differ in quantity and quality from those shown by ND+ patients (omissions: GA 0%, MZM 46%).

The RTs analysis showed a main effect of group [$F_{(2, 917)} = 126.39$, $p < .0001$], indicating that controls were faster (mean = 1512 ms) than both ND- (mean = 2264 ms, $p = .002$) and ND+ (mean = 5069 ms, $p < .0001$); and ND- patients were faster than ND+ patients ($p < .00001$).

Figure 4.2. *Experiment 1: Mean number (and standard errors) of letters omitted or substituted in the left, middle and right portion of the stimuli by USN+ ND+, USN+ ND- and USN- patients.*

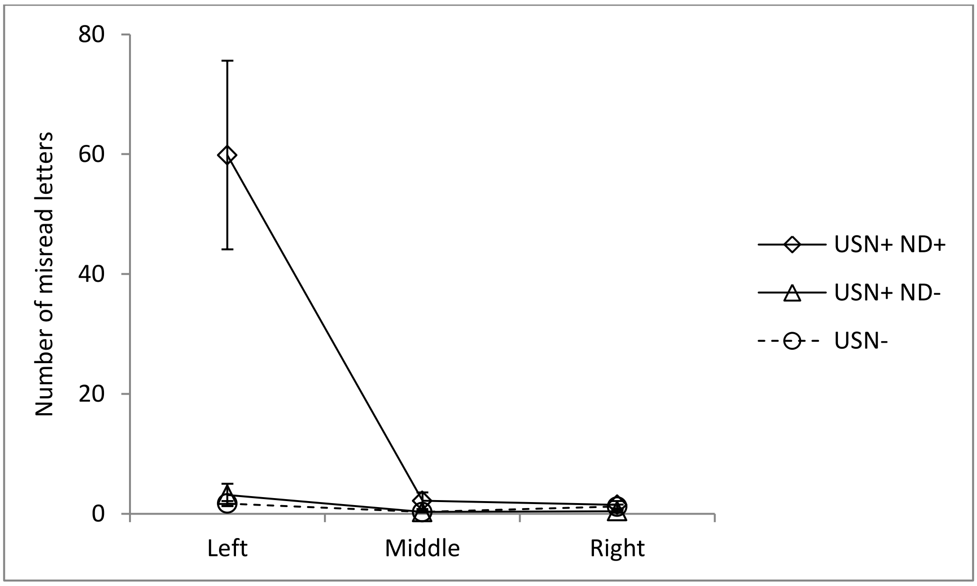


Table 4.4. *Experiment 1. Percentage and number (in parentheses) of neglect errors on the 40 pseudowords with respect to the total number of reading errors made by USN patients (USN+) and controls (USN-).*

	Neglect errors
Patients (USN+)	
RB ND+	.78 (14/18)
CRS ND+	.82 (32/39)
MM ND+	.66 (21/32)
MA ND+	.9 (36/40)
GD ND+	.79 (19/24)
CD ND+	.9 (20/22)
DSA ND-	1.0 (1/1)
GA ND-	.25 (1/4)
MZM ND-	.10 (1/10)
BLG ND-	1.0 (1/1)
GG ND-	.33 (1/3)
NR ND-	0 (0/3)
MR ND-	0 (0/0)
Controls (USN-)	
SMP ND-	.20 (1/5)
RP ND-	0 (0/2)
BM ND-	0 (0/0)
PG ND-	.4 (2/5)
TA ND-	.25 (1/4)
LG ND-	.3 (1/3)
ML ND-	0 (0/1)
CG ND-	0 (0/3)
IMA ND-	0 (0/0)
GF ND-	0 (0/2)

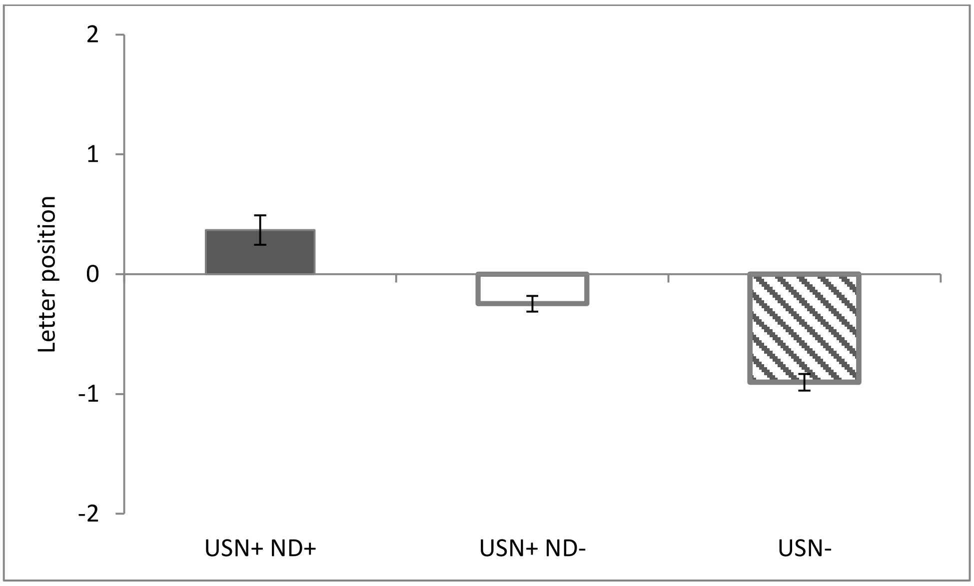
4.2.3. Results – eye movements

Four eye movement parameters were measured separately for each participant: first fixation position, mean fixation duration per item, mean number of fixations per item (separately for the entire string and for the left- and right-sided group of letters of the stimulus), and fixation accuracy per item.

First fixation position. For each item, letter positions were coded by attributing a zero value to the central letter, negative values to the letters on the left (i.e., the letter adjacent to the left of the central letter was coded as -1, etc.), and positive values to letters on the right; first fixation position value was determined using these values. An ANOVA with group

(USN-, USN+ ND-, USN+ ND+) as factor and first landing position as dependent measure was run and revealed a main effect of group [$F_{(2, 916)} = 65.87$, $p < .00001$]. Bonferroni post-hoc comparisons indicated that all group means were significantly different (all $p_s < .0001$). We contrasted the first fixation position towards the zero position (t-test comparison) separately for each group of patients. Figure 4.3 shows the mean position of the first fixation point after stimulus onset separately for each group. In the control group (USN-), the first fixation fell to the left (on average = -0.9; $t_{(797)} = -15.78$, $p < 0.0001$). Similarly, USN+ ND- patients showed a left-sided first fixation after stimulus onset (on average = -0.25; $t_{(558)} = -3.76$, $p < .001$). Vice versa, USN+ ND+ showed a right-sided first fixation position (on average = 0.37; $t_{(518)} = 3.24$, $p = .001$).

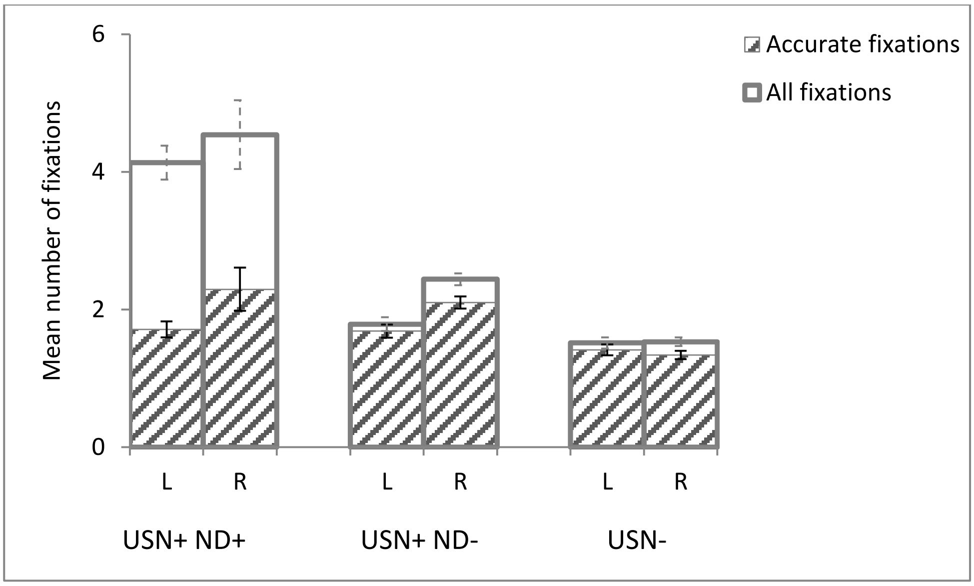
Figure 4.3. *Experiment 1: Mean position (and standard errors) of the first fixation for USN+ ND+, USN+ ND- and USN- patients, where 0 indicates the central letter of the string, positive values indicate the letter position on the right and negative values the letter position on the left.*



Number of fixations. Mean number of fixations was computed separately for each item and was based on all fixations performed after the stimulus onset and prior to the verbal response. In Figure 4.4, the mean number of fixations for each USN+ patient and for the USN- group is shown separately for the left and right side of the screen (white bars). An

ANOVA with group (USN-, USN+ ND-, USN+ ND+) as fixed factor and number of fixations as dependent measure was run and revealed a main effect of group [$F_{(2,\ 913)} = 118.61$, $p < .0001$]. Controls made a mean of 4.43 fixations (s.d. = 1.82), that is, fewer than both USN+ ND- patients (mean = 6.18, s.d. = 2.82, $p < .001$) and USN+ ND+ patients (mean = 11.25, s.d. = 9.97, $p < .0001$). The difference between the mean number of fixations made by the USN+ ND- and USN+ ND+ patients was also statistically significant ($p < .00001$).

Figure 4.4. *Experiment 1: Mean number (and standard errors) of accurate fixations per item (oblique dashed bars) over the total mean number of fixations (white bars) for USN+ ND+, USN+ ND- and USN- patients.*

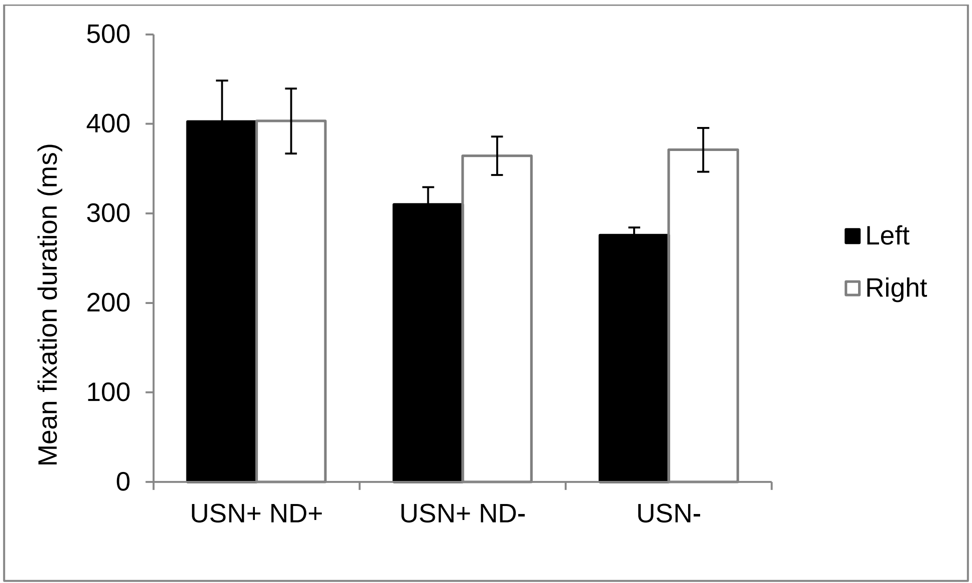


Note: L = Left letters, R = Right letters

Fixation accuracy. Fixations were considered "accurate" if they were no more than 1 degree of visual angle from the nearest letter. We calculated how many fixations actually fell on the letters composing the stimulus with respect to the fixations made all over the screen. In controls and ND- patients, most fixations were accurate (controls = 91.97%; ND- = 90.88%) and there was little distance between the non-accurate fixations and the nearest letter (mean distances: controls = 0.45 deg on the horizontal axis and 0.92 on the vertical axis; ND- patients = 0.45 deg on the horizontal axis and 1 deg on the vertical axis). In ND+ patients, only 55.2% of fixations were accurate. The non-accurate fixations of ND+ patients were far from the nearest letter (mean distance = 2.37 deg on the horizontal axis and 2.86 deg on the vertical axis). Analyses of variance with the percentage of accurate fixations as dependent variable and group (USN-, USN+ ND-, USN+ ND+) as fixed factor showed a significant main effect of group [$F_{(2, 20)}$ = 16.67, p = .00005], which indicates that only ND+ patients were impaired in correctly fixating the letters of the orthographic string and made a smaller proportion of accurate fixations compared with both USN- and USN+ ND- patients (both p_s < .0005). We compared the number of accurate fixations on the left and the right side of the stimulus (see Figure 4.4, dashed bars) when the side of the fixations (left *vs.* right) and the patients' group were factors. Effects of group [$F_{(2, 913)}$ = 16.94, p < .00001], side [$F_{(1, 913)}$ = 8.01, p =.005] and the interaction patients' group by side [$F_{(2, 913)}$ = 3.63, p =.027] were statistically significant. The Bonferroni post-hoc test on the patients' group by side interaction indicated that controls fixated less on the right side of the stimulus as compared with both USN+ ND+ and USN+ ND- (both p_s < .0001).

Fixation duration. Mean fixation duration of accurate fixations was computed separately for each item. An ANOVA was carried out to compare fixation duration in the three groups of patients. The group effect was statistically significant [$F_{(2, 917)}$ = 42.27, p <.0001], indicating that USN+ ND+ patients had a mean longer fixation duration (mean = 428.5 ms) than both USN- (mean = 328.9 ms, p < .0001) and USN+ ND- (mean = 345.4ms, p < .0001); the difference between these two groups was not statistically significant (p = .36). An ANOVA with group (USN-, USN+ ND-, USN+ ND+) and fixation side (fixations falling on the central letter were excluded) as factors and fixation durations as dependent measure was run and revealed a main effect of group [$F_{(2, 913)}$ = 4.38, p < .05] and a main effect of side [$F_{(1, 913)}$ = 9.95, p <.005]. The interaction group by side did not reach significance side [$F_{(2, 20)}$ = 3.04, p =.07]. The results are shown in Figure 4.5. Planned comparisons revealed that fixation durations on the left side of the stimulus are significantly longer for the USN+ ND+ group relative to the others (both p_s <.05), while on the right side no differences were found to be significant (all p_s n.s.).

Figure 4.5. *Experiment 1: Mean duration (and standard errors) of fixations falling on the left (grey bars) and right (white bars) side of the stimulus for the three groups of patients: USN+ ND+, USN+ ND- and USN-. Fixations falling on the central letter are not included.*



Analyses of fixations in the first 1000 ms after stimulus onset. Given that the stimuli observation times were significantly different in the three patient groups, we further analyzed the mean number of fixations executed in the first second after stimulus onset. USN- patients made a mean of 2.95 fixations, ND- patients a mean of 2.81 fixations and ND+ patients a mean of 2.49 fixations, with no statistical differences between the three groups. Although the USN- and ND- groups made a similar number of accurate fixations (mean number of accurate fixations = 2.76 and 2.83 respectively), only the ND+ group showed a statistically significant difference between the mean number of fixations and the mean number of accurate fixations made in the first second after the stimulus appearance [mean = 1.47; $F_{(2, 20)} = 7.73$, $p = .003$].

4.2.4 Comments

Results indicate that eye movement patterns are effective in determining the presence of neglect dyslexia. Specifically, we found that ND+ patients began exploring the stimulus from the right side (whereas both controls and USN+ ND- patients started from the left side), showed longer fixation duration, made more fixations and showed a larger proportion of inaccurate fixations, that is, they landed two or more degrees away from the letters. Vice versa, the overall distribution of fixations did not discriminate between patients with and without ND, given that both groups fixated more on the right side of the stimuli compared with patients who did not have USN. Relative to the other two groups, ND+ patients had longer RTs, which led to the large number of mostly inaccurate fixations (Figure 4.4). Leveling the playing field by confining the analysis to the first second of the trial showed that all patients made a similar number of fixations per time unit, but half of the fixations of the ND+ patients were inaccurate. These results suggest that the reading disorder of these patients may be due to their inability to perform the fine exploratory eye movements required for reading.

4.3 Experiment 2: Rightward-leftward saccade task

To assess whether the inappropriate eye movement pattern in ND+ patients was limited to the orthographic material or concerned general saccades execution on the horizontal axis, we administered a rightward-leftward and leftward-rightward saccadic task, specifically, a non-reading task in which gaze simulates the sequential eye movements involved in reading.

4.3.1 Material and procedure

A black dot subtending .2 deg of visual angle and displayed on a white background appeared along the horizontal meridian in five consecutive positions, 4.0 deg away from each other according to a synchronous paradigm (i.e., no gap). The dot appeared sequentially in the five positions and stayed on for two seconds in the two extreme positions and one second in the three central ones. The sequence started with the extreme left dot and each dot appeared in turn until the extreme right dot appeared, then the reverse sequence took place. The rightward and leftward sequences were repeated twice in each trial. Three trials were administered. Patients were required to follow the dot as quickly and as accurately as possible.

4.3.2 Results

Accuracy (percentage of fixations on the dot when it was on the screen) and saccade latencies (time elapsed from the appearance of the dot to the beginning of the saccade) were measured and are summarized in Table 4.5. We excluded analysis of both fixations made on the first dot in the sequence and anticipatory saccades (i.e. saccades starting before the appearance of the following dot). We also excluded analysis of fixations that were far from the target with respect to its vertical axis (i.e. over 2 standard deviations calculated on the vertical fixation positions of the control group). The remaining fixations were considered "accurate" if they fell no more than 1 degree of visual angle away from the current target.

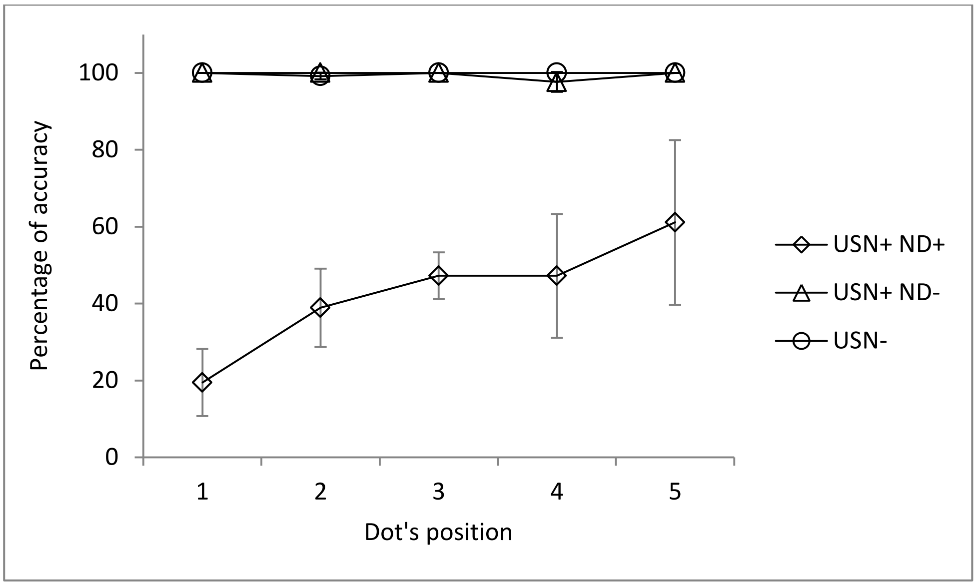
Table 4.5. *Experiment 2. Leftward-Rightward Saccade task: percentage of accuracy and latencies for the USN patients and control group in the two directions.*

	DOT DIRECTION					
	Left-Right		***Right-Left***		***All***	
	% accuracy	*latencies*	*% accuracy*	*latencies*	*% accuracy*	*latencies*
Patients (USN+)						
RB ND+	29.2	387.3	41.7	n.e.	35.4	387.3
CRS ND+	16.7	n.e.	4.2	n.e.	10.4	n.e.
MM ND+	83.3	161.3	4.2	n.e.	43.8	161.3
MA ND+	33.3	376.7	33.3	363.6	33.3	368.5
GD ND+	87.5	123.9	41.7	548.7	64.6	283.2
CD ND+	95.8	241.8	41.7	523.0	68.7	331.8
DSA ND-	100.0	208.5	100.0	252.8	100.0	232.8
GA ND-	100.0	120.4	100.0	209.4	100.0	177.4
MZM ND-	100.0	132.2	100.0	246.9	100.0	192.05
BLG ND-	100.0	112.9	100.0	166.3	100.0	145.8
GG ND-	100.0	193.2	91.6	290.3	100.0	244.0
NR ND-	100.0	189.1	100.0	212.7	100.0	200.7
MR ND-	100.0	144.3	100.0	177.6	100.0	160.1
Controls (USN-)						
SMP	100.0	143.7	91.7	122.6	95.8	138.4
RP	100.0	120.3	100.0	79.6	100.0	103.3
BM	100.0	118.7	100.0	118.7	100.0	118.7
PG	100.0	93.7	100.0	113.3	100.0	105.4
TA	100.0	170.2	100.0	172.0	100.0	171.0
LG	100.0	151.0	100.0	136.3	100.0	142.6
ML	100.0	148.5	100.0	126.4	100.0	133.0
CG	100.0	142.3	100.0	194.3	100.0	172.4
IMA	100.0	243.9	100.0	250.7	100.0	246.9
GF	100.0	135.4	100.0	157.1	100.0	142.6

Note: n.e. = not evaluable.

USN- patients performed a mean of 18.2 anticipations, USN+ ND- patients a mean of 6.6 anticipations and USN+ ND+ patients a mean of 2.2 anticipations. ANOVAs were carried out on percentages of accuracy and latencies, with target direction (left-right *vs.* right-left) as repeated factors and group as fixed factor. The analyses of accuracy revealed main effects of group [$F_{(2, 20)} = 60.03$, $p < .00001$], target direction [$F_{(1, 20)} = 7.77$, $p = .011$] and a statistically significant interaction group by target direction [$F_{(2, 20)} = 5.79$, $p = .01$]. The Bonferroni post-hoc analysis of the group by target direction interaction indicated that ND+ patients were significantly less accurate in both the left-right (58.3%) and right-left direction (28.5%) than both USN- (left-right = 100%, right-left = 99.2%) and USN+ ND- patients (left-right = 100%, right-left = 98.8%) (all $p_s < .001$); the difference between USN- and USN+ ND- patients was not significant in either direction. An analysis of latencies indicated significant main effects of group [$F_{(2, 17)} = 34.03$, $p < .00001$], target direction [$F_{(1, 17)} = 22.61$, $p <.001$], and a significant interaction group by target direction [$F_{(2, 17)} = 9.27$, $p = .002$]. A Bonferroni post-hoc analysis on the group by target direction interaction indicated that USN+ ND+ patients were significantly slower than both USN- and USN+ ND- patients only in the right-left direction (respectively = 478 ms, 147 ms and 219 ms, all $p_s < .001$) but not in the left-right direction (respectively = 247 ms, 147 ms and 156 ms). Controls were not significantly different from USN+ ND- patients in either direction (both $p_s > .1$). As shown in figure 4.6, ND+ patients were inaccurate in fixating the dot regardless of whether it was in the left or the right position on the screen. To further investigate accuracy as a function of the position of the target on the screen, an ANOVA was carried out on percentages of accuracy with target position (1st, 2nd, 3rd, 4th and 5th, from left to right respectively) as repeated factors and group as fixed factor. Analyses revealed main effects of group [$F_{(2, 20)} = 54.6$, $p < .00001$], target position [$F_{(4, 80)} = 4.29$, $p = .003$] and a statistically significant effect of group by target position [$F_{(8, 80)} = 3.99$, $p = .0005$]. The Bonferroni post-hoc analysis revealed that the USN+ ND+ group of patients was significantly impaired in fixating the target in all five positions compared with both USN- and USN+ ND- groups (all $p_s < .005$). No difference in accuracy for the five targets in the different positions was found between USN- and USN+ ND- (all $p_s > .1$).

Figure 4.6. *Experiment 2: Percentage of accurate fixations (and standard errors) for USN+ ND+, USN+ ND- and USN- patients in the five different dot positions where position 1 corresponds to the extreme left position and position 5 to the extreme right position reached by the moving dot.*



4.3.3 Comments

The results of Experiment 2 extend the findings of Experiment 1 to non-orthographic material. Unlike ND- patients and controls, ND+ patients were profoundly impaired in performing a simple saccadic task on the horizontal meridian. Although the nature of this exploratory eye movement pattern is still underspecified, it may be the cause of the reading errors. It should be noted that the observed abnormal oculomotor pattern does not show a lateralization bias. Thus, rather than proposing an oculomotor explanation for the reading deficit, our working hypothesis rests on the idea that the presence of reading errors is due to the inability of executing correct eye movements, while the left lateralization of such errors reflects the same spatial bias shown by neglect patients for non-orthographic material.

4.4 Experiment 3: Duration threshold measurement and reading at threshold

Taken together, the results of Experiments 1 and 2 suggest that the reading errors in neglect dyslexia could be due to the association between the unilateral spatial neglect disorder and a distorted eye movement pattern. Our working hypothesis was that ND reading errors reflect the gradient in the spatial deficit when the fine eye movements required for reading are not performed. Although the free-viewing condition allowed enough time for eye movements, ND+ patients' exploratory behavior was insufficient for accurate letter decoding and the left-lateralized neglect deficit also emerged in single-word reading. In USN+ ND- patients, word-centered errors were prevented because of their preserved automatic gaze and attentional shifts to the left of the string, which placed most words, presented centrally, in the preserved portion of space. We believe that impairing the eye movement behavior in these patients should eliminate differences in single-word reading compared to ND+ patients. To test this hypothesis, we restricted the eye movements of both USN- and USN+ ND- patients during reading. The prediction was that only USN+ patients (not USN- controls) would manifest the left-lateralized reading errors that characterize ND+ performance. By contrast, we predicted that the USN- control group would show no specific lateralization of errors even when their eye movements were artificially suppressed.

We restricted exploratory eye movements by reducing exposure duration far below 200 ms. To equate performance across patients, we selected exposure duration individually by previously measuring reading thresholds. For each patient, we selected the exposure duration that yielded 50% correct word reading. With unlimited time exposure, ND+ patients performed worse than our USN- and USN+ ND- patients at threshold and barely reached the criterion of 50% correctly read words (median 30%, range 0% to 55%, Table 4.4). This indicates that additional time did not help the ND+ patients. Thus, reading thresholds could not be estimated because performance was almost independent of stimulus duration. Regarding USN- and USN+ patients, the criterion level of task performance was chosen to approach the performance level of ND+ patients while keeping the estimate in the steeper range of the psychometric function by relating percent correct to exposure duration (typically, reading rate thresholds are estimated at higher levels of performance, that is, 80%, e.g. Legge, Mansfield, & Chung, 2001). Further lowering of the criterion would have restricted the threshold measurements to the shallow portion of the psychometric function and would have generated unreliable measures with high standard deviations.

4.4.1 Materials and procedure

We generated two lists of 40 pseudowords that were 5 to 8 letters long (10 items for each length). One list was used to measure the duration threshold, the other to score reading errors at threshold (see below). As in experiment 1, pseudowords were constructed to preserve pronunciation and minimize word similarity. The stimuli in the two lists were matched for bigram frequency, number of orthographic word neighbours (N-size) and summed frequency of neighbours (N-frequency) (Wagenmakers & Raaijmakers, 2006). The stimuli were written in capital Courier New font, which is characterized by consistent letter spacing. Letter size was kept constant (40 pt) and subtended 1.0 deg. Patients were shown two vertically displaced squared dots that were 1.5 deg apart in the center of the screen; these fixation marks remained on the screen for the entire experimental session. Stimulus onset was triggered when the patient fixated the central marks for at least 50 ms. Each stimulus was presented at the center of the screen between the fixation marks (so that the middle letter of each stimulus appeared vertically aligned with the fixation marks). Patients were asked to read aloud each stimulus as accurately as possible. Pseudowords appeared in randomized order across participants.

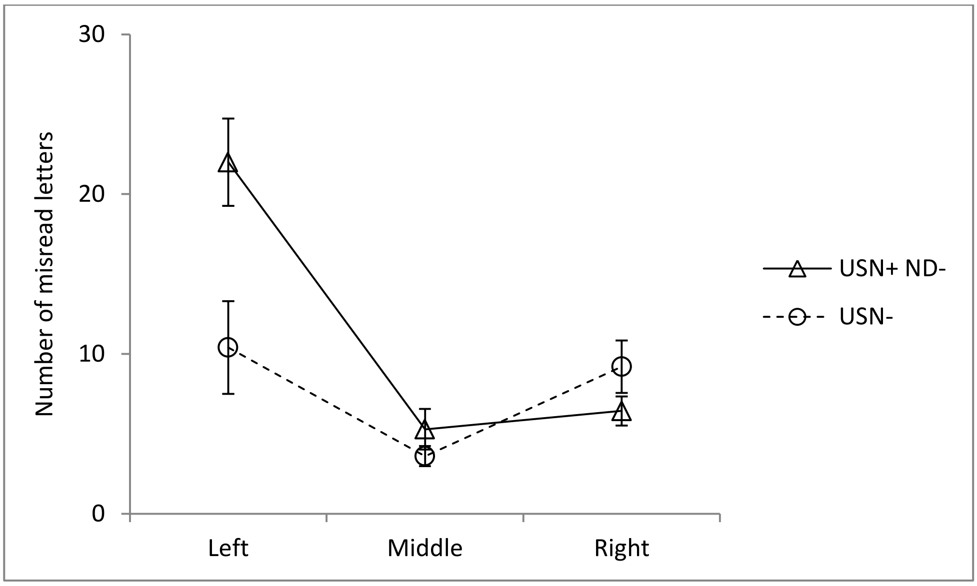
Duration thresholds. Thresholds were measured by varying exposure duration using a procedure similar to that of Rapid Serial Visual Presentation (RSVP), which minimizes eye movements (Rubin & Turano, 1992). One pseudoword was presented centrally in each trial and patients were asked to read it aloud without a time limit after the stimulus off-set. Patients' duration threshold (the rate at which the pseudowords were presented) was estimated in a 40-trial run using the improved QUEST staircase procedure with a threshold criterion of 50% correct responses (Watson & Pelli, 1983). The experimenter scored the patient's reading performance as correct or incorrect by pressing a key after each trial). The adaptive QUEST procedure increased or decreased the presentation rate according to the patient's accuracy. Omissions, mispronunciations and substitutions were considered errors. The mean estimated threshold durations for USN- and USN+ ND- groups were 73.8 ms (SD = 43.0 ms) and 107.6 ms (SD = 55.4 ms), respectively. These durations at threshold are generally consistent with the finding that in central viewing normal subjects can read words presented at a rate of 60-100 ms (Legge et al., 2001; Pelli, Tillman, Su, Berger & Majaj, 2007).

Reading at threshold. Once the patients' duration threshold was established, they had to read aloud the 40 new experimental pseudowords. The experimental procedure and the characteristics of the stimuli were identical to those used in Experiment 1, except for stimulus duration: In the present experiment, the stimulus duration was different for each patient (according to each duration threshold previously evaluated) and did not allow for eye movements.

4.4.2 Results

Overall, USN- patients made 43% errors and USN+ ND- patients, 55.4%. Errors were classified as occurring on left-side, middle or right-side letters of the stimuli and are shown in Figure 4.7. An ANOVA was run with side of errors (left, middle and right) as repeated measures and group as fixed factor and revealed a main effect of side [$F_{(2, 30)} = 30.09$, $p<.00001$] but not of group ($p = .09$), according to the measuring purpose of comparing patients at the same level of performance. Moreover, a statistically significant group by side of errors [$F_{(2, 30)} = 11.11$, $p = .0003$] analysis revealed that USN+ ND- patients made more errors than the control group on the left side of the stimulus (mean = 22 *vs.*10.4, $p = .001$) but not in the middle (5.3 *vs.* 3.6, n.s.) or the right (6.4 *vs.* 9.2, n.s.).

Figure 4.7. *Experiment 3: Mean number (and standard errors) of letters omitted or substituted in the left, middle and right portion of the stimulus when reading at threshold for USN+ ND- and USN- patients.*



4.4.3 Comments

We prevented exploratory eye movements by asking patients to read at the duration threshold, and found that USN+ ND- patients (unlike USN- patients) made left lateralized errors similar to ND+ patients. This supports the idea that left lateralized reading errors, characteristic of ND, are present in USN patients when their eye movements pattern is artificially made similar to that of ND+ patients. When the fine exploratory eye movements required for reading are prevented, partial and incomplete information about left-sided letters prevents correct reading in USN patients. By contrast, controls made evenly distributed errors on the left and right side of the string. This indicates that the absence of exploratory eye movements alone, not associated with USN, determines the presence of reading errors, but does not justify their left lateralization. This is to be expected if perception is the only limiting factor and errors are explained by reduced visual acuity for peripheral letters.

4.5 General discussion

In the above described study, we conducted three experiments on 23 right-brain-damaged patients with and without unilateral spatial neglect (USN+ and USN- or controls, respectively). Six of the neglect patients showed neglect dyslexia (ND+) and 7 did not (ND-). Unlike the other two groups, the ND+ patients produced left lateralized errors paralleled by an abnormal pattern of oculomotor behavior in reading aloud pseudowords. Their eye movement pattern consisted of a large number of fixations, very few of which landed accurately on the target stimulus. This disorder was present in the orthographic material (Experiment 1) as well as in a saccadic task with non-orthographic material (Experiment 2). We carried out a third experiment in which we reduced the possibility of USN+ ND- and USN- patients accurately performing the exploratory behavior. In this reading condition, only USN+ ND- patients exhibited an asymmetrical leftward increase in errors.

We found that patients diagnosed as suffering from neglect dyslexia on the basis of the left lateralized errors in single word/pseudoword reading, showed an abnormal eye movement pattern with both orthographic and non-orthographic material. The eye movement deficit cannot, however, directly explain the reading errors since it is not lateralized. Indeed, experiment 3 shows that preventing eye movements leads to non-lateralized errors in USN- patients because they are unable to effectively explore the text. We suggested that both USN deficit and the eye movement impairment determine the left lateralized reading deficit. Specifically, to observe ND reading errors in USN patients, a concomitant altered oculomotor behavior is necessary. In fact when eye movements are possible and effective, USN+ ND- patients make few or no errors in reading (Exp. 1). Centrally presented stimuli fall in a portion of space sufficiently preserved in these patients to allow for the automatic leftward shift of gaze and attention triggered by reading, enabling correct letter decoding (Exp. 1, eye movements and behavioral data). On the contrary, when their eye movements are prevented, and fixation is forced on the central letter of the string, USN+ ND- patients show the error pattern typical of ND (Exp. 3). Moreover, restricting the eye movements in patients without USN produces errors that are evenly distributed on the left and right side of the string (Exp. 3). Taken together, this evidence indicates that both the presence of USN and an altered oculomotor behavior are necessary conditions to observe the left lateralized reading errors typical of ND+ patients.

Generally, ND+ patients do not perform adequate eye movements in non-reading tasks. While reading these patients are unable to perform an automatic shift in gaze toward the left of the string and to produce the needed correct oculomotor behavior. Therefore, as a consequence of their right-sided first landing position and the many useless fixations, they omit the part of the string that falls in the neglected area of space. This behavior parallels left-lateralized errors produced by patients with neglect when gaze shifting (and consequently overt spatial attention) is hindered by presenting stimuli at short durations (<200 ms).

Overall, we found that when USN patients read strings without a time limit an abnormal number of inaccurate fixations is diagnostic of the presence of ND. Alternatively, we can conjecture that ND+ and USN+ ND- patients differ only in terms of the speed of processing of the left side of a stimulus related to the underlying spatial bias. In this case, constraining time (Exp. 3) would impair USN+ ND- patients because of an underlying processing delay of the left relative to the right side, which is hit at threshold. Contrary to this conjecture, USN+ ND- and USN- patients showed similar and shorter fixation durations on the left than the right side of the string. This result, together with the finding that the first landing position for these patients was on the left is interesting and coherent with the general finding that gaze duration of normal subjects is minimal for an initial fixation location in the first part of a word and increases to the right of most letters (O'Regan, Levy-Schoen, Pynte, & Brugaillère, 1984). On the contrary, ND+ patients produced longer fixation durations without a left-side advantage, which further supports the absence of a preserved oculomotor pattern in their reading behavior.

When Di Pellegrino et al. (2002) measured fixation time on the left and right side of words and pseudowords, they found that FC’s word superiority effect (i.e. better performance for words than pseudowords) was associated with an imbalance in exploratory behavior that varies according to type of stimulus. The Authors suggested that the larger rightward bias in the case of pseudowords might account for the more profound neglect dyslexia found with these stimuli. According to this explanation, partially processed letters on the contralesional side receive top-down support from lexical representations stored in memory and cause the word superiority effect. Here we measured exploratory behavior using pseudowords and found that similarly to patient FC, our ND+ group globally showed a rightward bias in the first landing position and mean number of fixations. Moreover, ND+ patients showed a large number of inaccurate fixations (data not provided for FC). This finding can be interpreted according to Di Pellegrino et al. (2002): Due to low accuracy the partial and incomplete information about letter identity does not allow for pseudoword reading. Unlike previous studies in which the eye movement pattern in neglect dyslexia patients was evaluated only in a reading task (e.g., Behrmann et al., 2002; Di Pellegrino et al, 2002), in this study we found that the abnormal oculomotor behavior extended to non-orthographic material. This supports the notion that the rightward spatial bias causes reading errors when the fine eye movements required for reading are impaired and a guessing strategy is ineffective with pseudowords.

We found that USN+ ND- patients made left lateralized errors when exposure duration was reduced. Arduino, Vallar and Burani (2006) reported a relative reduction of neglect errors in ND+ patients when they were tested with a 500 ms exposure duration. This seems to contradict our interpretation that ND+ patients' omissions are due to neglect. This is not the case. First of all, Arduino et al (2006) classified errors according to Ellis et al's (1987) criterion into neglect and visual errors and considered the percentage of neglect errors to the total. They presented 3 patients (PP, MN and CI) and two of them (PP and MN), showed that reducing time increased, not reduced, the absolute number of neglect errors. Since reducing time also causes a large increase in visual errors, the proportion of neglect errors to the total leads to a relative reduction. On the contrary, CI showed an increase both in the absolute as well as in the relative number of neglect errors. Why should reducing time cause an increase of visual errors relative to neglect errors in PP and MN? A possible explanation is that they are mainly substitution errors, that are located on the left side of the string. For example, the word "elefante" read "etepante" would be considered a visual error following Ellis's criterion, while according to a letter positional analysis (as proposed by Martelli et al. (2011) and used in the present study), it would be counted as two left-side substitutions ("l" as “t” and “f” as “p”). This interpretation is consistent with Arduino et al.’s (2002) observation that, unlike the performance of CI and our ND+ group of patients that mainly produced omissions, the performance of PP and MN was characterized by a very high percentage (i.e. 90%) of substitution errors.

Why do some USN patients show an eye movement impairment and others do not? It is possible that a component of the cortico-subcortical system which regulates visual eye-movement guidance towards a horizontal lateral point (prosaccade and antisaccade) is compromised in ND+ patients. According to Neggers et al. (2012), this system involves the medial FEF, the right putamen, and the fiber tracts connecting these two regions in visually guided saccades. Recently, the crucial role played by white matter pathways in complex functions connecting regions involved in more specific functions was highlighted (e.g. executive functions: Krause et al., 2012; USN: Urbanski et al., 2011). As Shuett, Heywood, Robert, Kentridge, & Zihl (2008) state: “Distributed and coordinated processing relying on multiple cortical and subcortical brain regions suggests that white matter pathways connecting these regions play a crucial role. […] The striate cortex (V1), the prestriate visual area V2, the posterior parietal cortex and frontal eye fields, as well as the supplementary eye fields and the dorsolateral prefrontal cortex form a network which integrates vision, attention and eye-movements” (pag 2447). Further studies using voxel-based morphometry in a larger sample are needed to investigate this complex anatomical hypothesis (Salmond et al, 2002).

Overall, our results suggest that the presence of ND in USN patients may be due to the combination of two factors: a visuo-spatial disorder affecting the controlesional hemispace and a distorted oculomotor pattern generalized to the entire visual field. USN has a 40-80% incidence in acute stroke patients; in 40% of the cases patients are also affected by ND (Cappa et al., 2005; Lee et al., 2009). The large majority of studies on neglect dyslexia report results on this type of patient and our results account for their reading behavior. However, a few pure cases of ND and cases of double dissociations (left USN and right ND, and vice versa) have also been reported; the findings from the current study do not allow us to draw inferences about the reading behavior in these patients.

In a recent review of the literature on ND, Vallar et al. (2010) reported that patients who manifested ND without USN or an opposite lateralization in ND and USN deficit, had in common a lesion involving at least the left hemisphere or both (patient YM of Cohen & Dehaene, 1991; TB, Patterson & Wilson, 1990; JM, Katz & Sevush, 1989; RR, Caramazza & Hillis, 1990; Hillis & Caramazza 1995a and 1995b; Binder et al, 1992; Haywood & Coltheart, 2001; JOH, Costello & Warrington, 1987; RCG, Arduino, et al., 2005; RYT, Warrington 1991; Cubelli et al., 1991; Bisiach et al., 1986; 1990) or had right lesions but were left-handed (Miceli & Capasso, 2001). In agreement, both Katz and Sevush (1989) and Patterson and Wilson (1990) hypothesized a relationship between these patients and a certain degree of hemispheric asymmetry and defined this disorder as positional dyslexia. Similarly, Cubelli et al. (1991) described a right-handed left-brain-damaged patient with right visual unilateral spatial neglect, right-sided homonymous hemianopia and left neglect dyslexia and defined this reading disorder as "ipsilateral neglect" (Kwon & Heilman, 1991). In other cases, such as in MT reported in Bisiach et al.'s (1986) paper, ND without USN occurs in the presence of left hemianopia. In fact, MT might suffer from hemianopic dyslexia because her reported deep anosognosia prevents her from using a compensation strategy when reading. We acknowledge that these cases may be substantially different from the patients reported in the present study, and that this distinction may highlight important aspects of the information processing involved in reading.

Moreover, in interpreting these double dissociations it seems crucial to know the distribution of error types (omissions and substitutions) because, unlike substitutions that are evenly distributed over the string, omissions in ND patients are left-lateralized and positively correlated with the number of errors in line and letter cancellation tasks (Martelli et al., 2011). Furthermore, equating performance accuracy reveals that only USN patients produce omissions and that controls' performance is characterized by substitution errors (Weinzierl et al., 2012). The patients reported here have a reading behavior characterized by omission errors. RCG, an ND patient without USN described by Arduino et al. (2005), reads producing only substitution errors. We wonder whether measurement of error types may be crucial in understanding the pure ND cases and further studies are needed to better clarify the origins – and possibly the eye movement patterns - of patients who make lateralized reading errors in the absence of USN.

5. Impaired oculomotor behavior prevents both reading and scene perception in neglect patients

As described in the previous study, unilateral spatial neglect (USN) is the consequence of a right side brain lesion and most of the symptoms involves the left hemispace (Vallar, 2001; Halligan, Fink, Marshall, & Vallar, 2003; Verdon, Schwartz, Lovblad, Hauert, & Vuilleumier, 2010; Corbetta & Shulman, 2011). However it is worth noting that not all the neglect symptoms are lateralized in nature. Husain & Rorden (2003) pointed out that: "*The interaction of spatially lateralized mechanisms with non-lateralized components offers a different way of viewing the behaviour of neglect patients*" (page 29). The authors, indeed, highlighted the importance of studying lateralized and non-lateralized component of the deficit and their interaction in order to better understand the neglect symptoms. Husain et al. (1997), for example, examining the non-spatial temporal dynamics of attention, found that USN patients showed a protracted and abnormally severe attentional blink. The Authors used a letter identification task by the mean of a rapid serial visual presentation procedure (RSVP) where a sequence of letter is presented sequentially in the same spatial location. This procedure has the advantage that no directional shift of attention is required. In such a task, both controls and right side brain damaged patients without USN are at ceiling in discriminating a single letter. However, recognition of the subsequent letter was deeply impaired in USN patients that needed about a factor of three more time than controls to perform the task with low accuracy (Husain et al., 1997). In the same vein, Duncan et al. (1999) used a task where letters where briefly presented in arrays in both the left and right hemispaces. Letters could be red or green and patients' task was to report only the letters in the specified target colour. Results indicated that USN patients, although showing a worst performance in the left portion of the space, also show a very low accuracy level in the right side. Moreover results indicated that the maximum scores reached by each patient were similar for the two hemispaces. Globally, the results clearly indicate an overall loss of processing capacity in patients, stronger in the left portion of space but present also in the right, suggesting a major non-lateralized deficit in the USN patient group (Duncan et al., 1999). The presence of non-lateralized deficits in USN patients is not confined to the visual modality. Cusack et al. (2000) measured the auditory discrimination of sounds located centrally or in right side of space shifting their apparent position on the median plane by means of interaural time difference. USN patients, but not controls, were impaired in making comparisons between different sounds independently from their apparent spatial location (Cusack et al., 2000).

Investigations of the impairment in eye movement behaviour of USN patients also indicate the presence of non-lateralized deficits. Such studies have shown that some patients have an abnormal eye movement pattern not only in the left hemispace (toward which it is difficult to initiate saccades) but also in the right ipsilesional hemispace, where an over-fixation pattern has been described (Behrman, Watt, Black, & Barton, 1997; Behrmann, Black, McKeeff, & Barton, 2002; Zihl, & Hebel, 1997). Moreover, Niemeier & Karnath (2000), using a searching task, reported that, although neglect patients mostly explored the right hemispace, they also had significantly smaller amplitudes in all directions (leftward, rightward, upward and downward) as compared to controls. However, in agreement with the huge variability in symptoms described in literature, other studies described USN patients with an eye movement behaviour comparable to that of controls (Karnath, Niemeier, & Dichgans, 1998; Karnath, & Fetter, 1995; but see also Behrmann et al, 2002; Primativo, Arduino, De Luca, Daini & Martelli, 2013). Behrmann et al. (2002) and Primativo et al. (2013) focused on the association between eye movement disorders and neglect dyslexia (ND). Neglect dyslexia is an invalidating disturbance affecting a large part of neglect patients (40%, Lee et al., 2009) characterized by reading errors like omissions and substitutions (see chapter 4). ND patients may misread left sided letters in single word reading and usually omit or misread words in reading sentences or paragraphs. Behrmann et al. (2002) reported a direct correspondence between the oculomotor performance of patients with neglect dyslexia and their reading behaviour. In the cited study, patients with neglect and neglect dyslexia showed an over-fixation pattern to the right sided words, while left sided words are not fixated and were also verbally omitted. Crucially, another important finding of the study is that the eye movement pattern of USN patients without neglect dyslexia were shown to be completely comparable to that of controls in term of fixations number, duration and distribution (Behrmann et al., 2002). On the same vein, in characterizing the selectivity of the eye movement deficit, Primativo et al. (2013) showed that ND patients produce many inaccurate fixations while reading as well as in a saccadic task not involving orthographic material, where constrained eye movements were required in order to fixate a target moving horizontally in 5 different spatial positions. Since the eye movement disorder, not confined to the orthographic material, is not left lateralized, while reading errors are, it is argued that such a deficit interacts with the presence of unilateral spatial neglect, determining reading errors, and particularly letter omissions of left sided letters (Primativo et al., 2013). Regardless the notion that, for many years, the reading disorder has been attributed to a selective impairment at different stages of visual word processing (Caramazza & Hillis, 1990; Hillis, Rapp, Benzing, & Caramazza, 1998), the findings reported above, strongly support the notion that a subgroup of USN patients are compromised in eye-movements execution and that those patients, but not the others, produce left lateralized errors while reading. In the previous work of our research group (Primativo et al., 2013) we concluded that the eye movement deficit prevents the fine eye movements required in reading and cause the reading errors. In the present study we conjecture that this eye movement deficit reflects a more general oculomotor disorder that may also affect an ecological and less constrained task such as scene exploration. If this conjecture holds, we should be able to select two groups of USN patients on the basis of their exploratory eye movement pattern during a scene description and verify whether only patients that produce an abnormal oculomotor behaviour also show left lateralized errors in reading. Unlike reading, the description of a scene does not involve left-right scanning, but it requires fixations to be located on the relevant or more salient part of it (Henderson, 2003; Malcolm, Lanyon, Fugard, & Barton, 2008). It is known that USN patients typically explore preferentially the right side of the image to be described as compared to controls without USN (Datiè, Paysant, Destainville, Sagez, Beis, & André, 2006; Ptak, Golay, Müri, & Schnider, 2009). These same studies also indicated that USN patients preferentially report the right part of an image. Past investigations on this topic primarily focused on the effect of visual luminance, colour and edge information (Ptak et al., 2009), static and dynamic contrast (Ptak et al., 2009; Machner et al., 2012) colour and brightness (Machner et al., 2012), comparing the effects in the left and right sides of the stimulus. Also top-down effects, like the semantic continuity between left and right-sided parts of the image have been investigated (Karnath, 1994; Machner et al., 2012). In the present study we were interested in isolating and describing USN patients with a purely oculomotor deficit independently from the spatial asymmetry common to all neglect patients. Therefore, according to our conjecture, the presence of an abnormal oculomotor behaviour should predict the presence of neglect dyslexia and contribute to account for the USN symptoms variability. To this aim we adopted as a criteria to distinguish patients with and without an eye-movement deficit their oculomotor behavior during a scene description (Experiment 1). Furthermore, five saccadic tasks (from Experiment 2 to 6) have been used to further describe the eye movement pattern of these two groups of patients. We then explored patients' eye movements' behaviour and performance in reading single words and texts (Experiment 7). Our aim in this study is to provide a detailed description of the relationship between the oculomotor pattern and neglect dyslexia in USN patients. We suggest that oculomotor alteration is predictive of the occurrence of neglect dyslexia, and accounts, at least partially, for the large variability in neglect symptoms. This point is extremely relevant: The detection of a general eye movement disorder in some neglect patients, during the diagnostic phase, should address clinicians toward a specific rehabilitation strategy.

5.1 General method

5.1.1 Participants

Participants were recruited from the inpatient population of the I.R.C.C.S. Fondazione Santa Lucia (Scientific Institute for Research, Hospitalization and Health Care, Santa Lucia Foundation, Rome, Italy). Twenty consecutive right-hemisphere-damaged patients participated in the study. All patients had suffered a cerebrovascular ischemic stroke. Ten patients (six females and four males) suffered from unilateral spatial neglect (N+). Their mean age was 68 years (SD ±10.3; range 54–85), mean education was 10.5 years (SD ±4.4; range 5–17), and mean disease duration was 1.6 months (SD ±0.7; range 1–3). Ten right-hemisphere-damaged patients without neglect (N-) were matched for age (mean age = 71.2 years; SD = ±7.4 range = 61–83), education level (mean education = 11.9 years; SD = ±4.2;

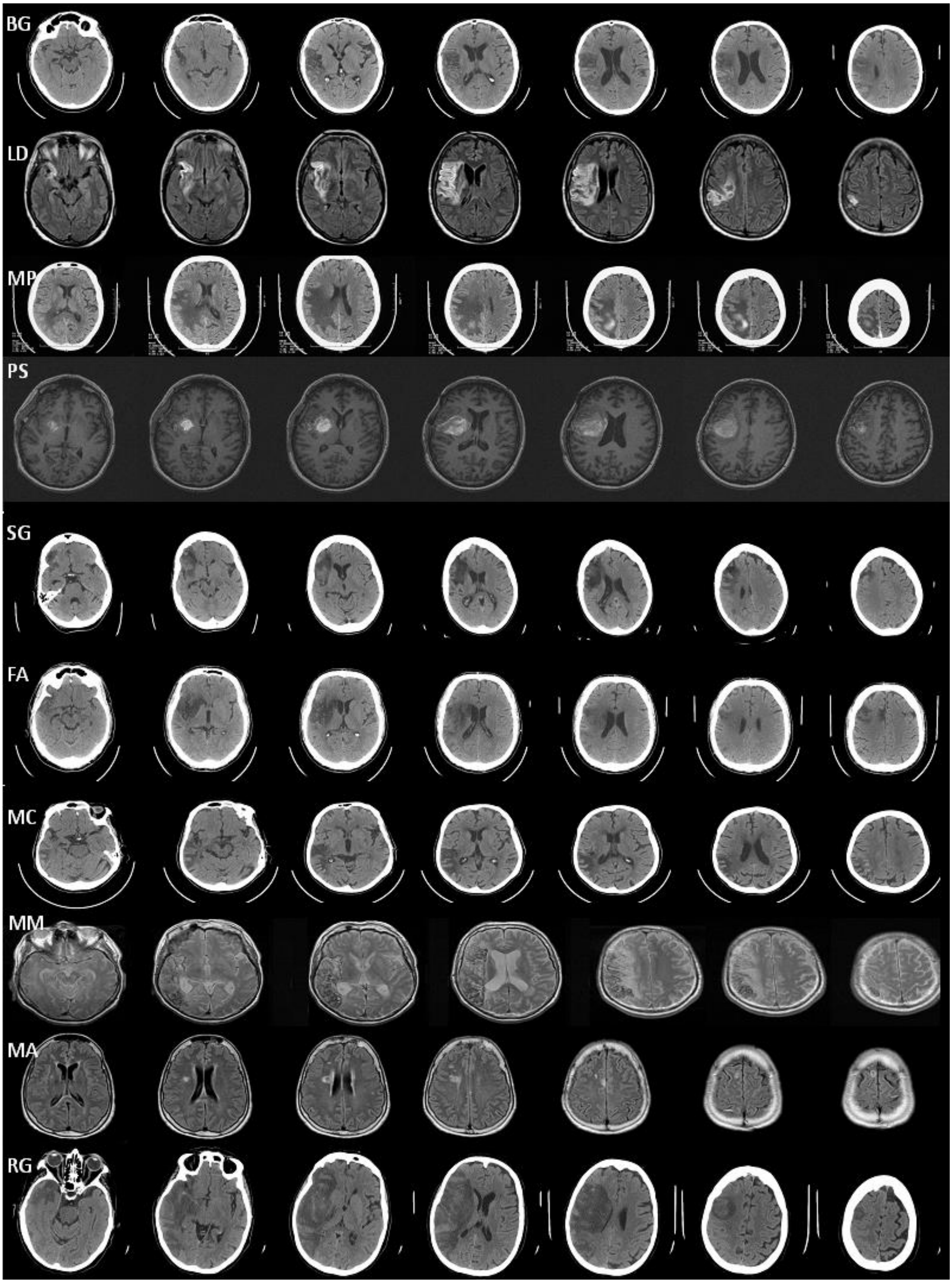
range = 5–18), and disease duration (mean duration = 1.6 months; SD = ±0.6; range = 1–2.5) and served as the control group. Demographic and neurological information are shown in Table 5.1. Lesion site, assessed by CT or MRI scan, are illustrated in Figure 5.1. All patients had normal or corrected-to-normal vision, preserved visual fields as assessed by Goldmann perimetry, and no history of previous neurological diseases. Informed consent was obtained from all participants prior to their participation.

Table 5.1. *Demographic features of the twenty right-brain-damaged patients*

	Sex/Age/Education	*Duration of disease (months)*	*Lesion site*	*Presence of USN**
Patients (N+)				
BG	M/69/16	1	F-T-P	Yes
LD	F/71/13	2,5	F-P	Yes
MP	F/60/17	1	F-T-P cs	Yes
PS	M/54/13	1.5	F	Yes
SG	F/74/8	1	F	Yes
FA	M/54/13	2	F-T-P cs	Yes
MC	F/85/5	1,5	P-T	Yes
MM	M/79/7	3	F-P	Yes
MA	F/62/8	1,5	F	Yes
RG	F/72/5	2	F-T-P	Yes
Controls (N-)				
ML	F/79/5	1	F-T-P	No
RE	M/65/13	2.5	F-T	No
GF	M/78/13	1.5	F	No
SM	M/62/8	2	s	No
IMA	F/72/10	1.5	s	No
DND	M/61/18	1	F	No
GN	F/74/13	1	s	No
ZR	M/83/18	1.5	s	No
CF	M/69/8	1	F	No
FL	F/69/13	2.5	ACM	No

Note. Lesion site: F: Frontal Lobe; P: Parietal Lobe; T: Temporal Lobe; c: cortical; s: subcortical; MCA: middle cerebral artery. M/F: male/female. *See the following section for the results of the baseline assessment for visual spatial neglect.

Figure 5.1. *Scan images for all 10 patients affected by unilateral spatial neglect.*



5.1.2 Baseline neuropsychological assessment

The presence and severity of unilateral spatial neglect were assessed using a diagnostic battery, which included the following tests:

a) *Letter cancellation* (Diller & Weinberg, 1977). The patient is asked to cross out all 104 letter H's printed on an A3 sheet of paper, that is, 53 on the left side and 51 on the right side. Targets are presented in alignment with other letter distractors. For healthy subjects, the maximum difference between omission errors on the two sides of the sheet is two (Vallar, Rusconi, Fontana, & Musicco, 1994).
b) *Line cancellation* (Albert, 1973). The task requires crossing out all 21 black lines (2.5 cm in length and 1 mm in width) printed on an A3 sheet of paper, that is, 11 on the left side and 10 on right side. Normal subjects make no errors on this task.
c) *Wundt-Jastrow Area Illusion test* (Massironi, Antonucci, Pizzamiglio, Vitale & Zoccolotti, 1988). The score is the number of responses (range 0-20) indicating that the patient do not show the illusory ("unexpected") effect arising from the left side of the stimulus. Patients with right brain damage and left neglect make errors only on stimuli with a left-sided illusory effect.
d) *Sentence reading* (Zoccolotti, Antonucci, Judica, Montenero, Pizzamiglio & Razzano, 1989). Patients have to read aloud six sentences (medium length 8.5 words, 31.8 letters; range 5-11 words, 20-41 letters) printed in uppercase on a horizontally placed A4 sheet of paper. The score is the number of reading errors (range 0-6, where 0 indicates no errors and 6 indicate that at least an error occurred in each sentence). Neurologically unimpaired subjects and right-hemisphere-damaged patients without neglect make no errors in this task.

Patients were considered affected by USN if they obtained pathological scores on at least two out of the four tests included in the diagnostic battery. Results of the assessment of visual spatial neglect are summarized in Table 5.2.

Table 5.2. *Baseline assessment for visual spatial neglect.*

	Letter Cancellation *(omissions)*		Line Cancellation *(omissions)*		Wundt-Jastrow *(unexpected responses)*		Sentence reading *(errors)*
	Left	*Right*	*Left*	*Right*	*Left*	*Right*	
Patients (N+)							
BG	53/53*	16/51	4/11*	0/10	0/20	0/20	1/6*
LD	11/53*	0/51	0/11	0/10	16/20*	0/20	0/6
MP	16/53*	2/51	0/11	0/10	3/20*	0/20	0/6
PS	53/53*	5/51	0/11	0/10	17/20*	1/20	1/6*
SG	29/53*	9/51	3/11	0/10	2/20*	0/20	1/6*
FA	53/53*	26/51	8/11*	0/10	11/20*	4/20	0/6
MC	7/53*	5/51	0/11	0/10	13/20*	0/20	4/6*
MM	43/53*	24/51	7/11*	3/10	15/20*	4/20	3/6*
MA	42/53*	21/51	3/11*	1/10	4/20*	2/20	6/6*
RG	53/53*	48/51	11/11*	8/10	0/20	0/20	6/6*
Controls (N-)							
ML	2/53	2/51	0/11	0/10	1/20	0/20	0/6
RE	0/53	0/51	0/11	0/10	0/20	0/20	0/6
GF	0/53	0/51	0/11	0/10	0/20	0/20	0/6
SM	1/53	0/51	0/11	0/10	0/20	0/20	0/6
IMA	0/53	0/51	0/11	0/10	0/20	0/20	0/6
DND	0/53	0/51	0/11	0/10	0/20	0/20	0/6
GN	1/53	0/51	0/11	0/10	0/20	0/20	0/6
ZR	1/53	0/51	0/11	0/10	0/20	0/20	0/6
CF	2/53	1/51	0/11	0/10	0/20	0/20	0/6
FL	6/53	5/51	0/11	0/10	0/20	0/20	0/6

Scores: (i) cancellation tasks: omission errors; (ii) Wundt-Jastrow Area Illusion test: "unexpected responses"; and (iii) Reading Task: the number of sentences in which patients showed left-sided errors. *Performance indicating the presence of unilateral spatial neglect. Pathological scores for Letter Cancellation (omissions = or > 5 and left/right omissions differences = or > 2), line cancellation (omissions = or > 2), Wundt-Jastrow (left/right unattended responses difference = or > 2) and sentence reading (errors = or > 1) are defined on the basis of the norms provided by the screening battery (Pizzamiglio, Judica, Razzano, & Zoccolotti, 1989).
Note: N+ and N- refer to patients with and without unilateral spatial neglect, respectively.

5.1.3 Eye movement recordings: apparatus, general procedure, and data analysis

Monocular eye movements were recorded in binocular vision via an SR Research Ltd. Eye Link 1000 eye tracker (SR Research Ltd., Mississauga, Ontario, Canada) sampling at 500 Hz, with spatial resolution of less than 0.04°. Head movements were avoided by using a headrest (and a chinrest for experiments where no verbal response was requested). Participants sat 57 cm away from a 17-in CRT Dell PC. A standard nine-point calibration procedure was run separately for each of the experiments before collecting the data. The calibration targets were presented randomly in nine different positions on the screen. Sometimes neglect patients had difficulty locating the targets on the left side of the screen, but all were able to shift their gaze toward the target when the experimenter specified its position verbally. Each experimental task started immediately after calibration.

When a verbal output was required, voice was digitally recorded by a system mounting a Shure microphone, a pre-amplifier, an E-MU sound card, and an ASIO driver, interfaced to the eye tracker by Eye Link Experiment Builder software.

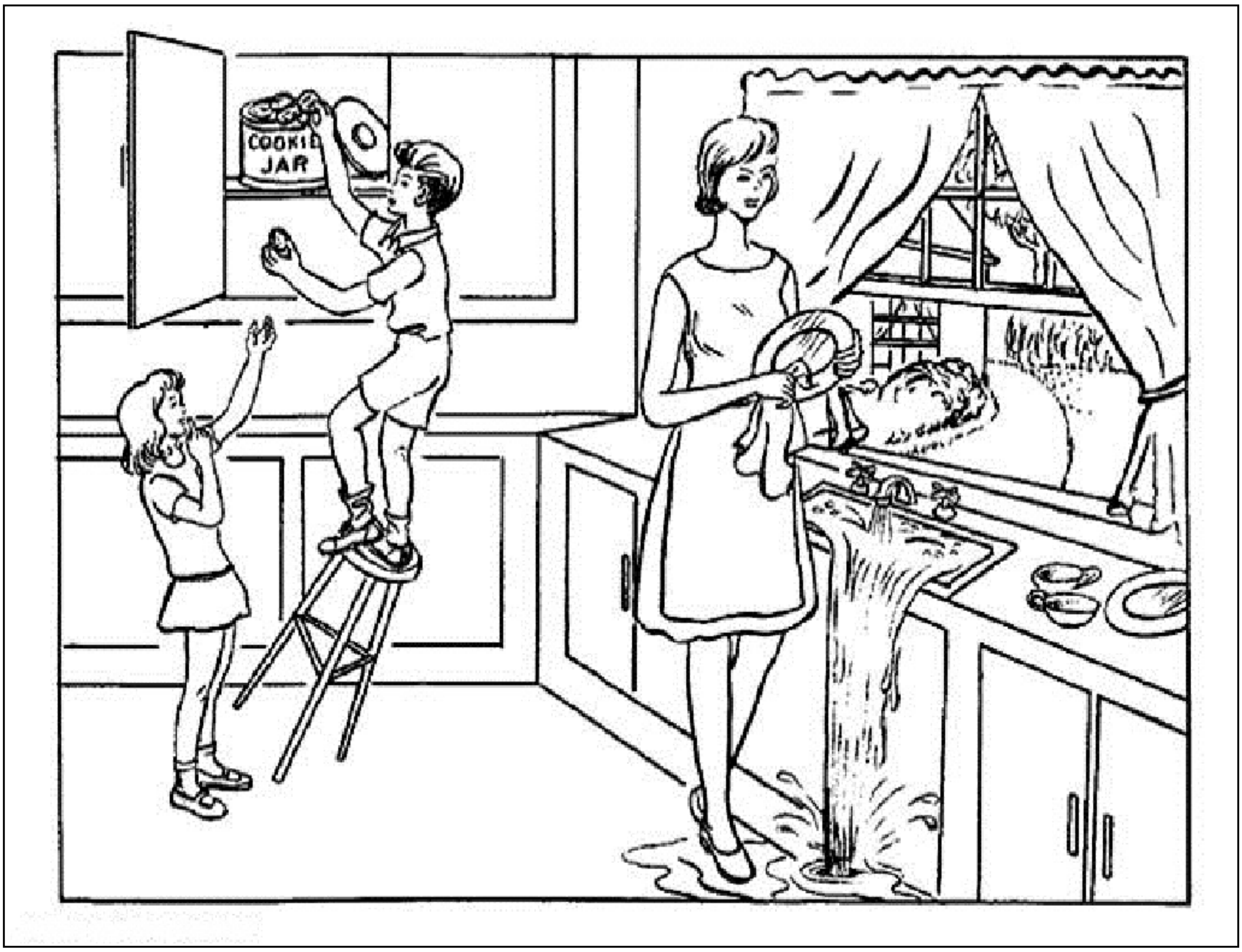
Eye movement data were pre-processed using EyeLink Data Viewer software (SR Research Ltd., Mississauga, Ontario, Canada). Fixation position, number, duration, and accuracy were analysed (see details in each of the Experiment sections below).

5.2 Experiment 1: Image exploration

Each patient was asked to look at and describe a line drawing (i.e., "Cookie theft picture", from the Boston Naming Test; Kaplan, Goodglass & Weintraub, 2001, see Figure 5.2) while their eye movements were recorded. Patients' task was to look at the picture and to describe everything they saw in the scene. They were also asked to say "finish" when they terminate describing the scene and did not desire to add any other detail. No time constraints were given. The image was displayed on the whole dimensions of the 17-in screen, subtending 32 deg on the horizontal and 24 deg on the vertical axis. Patients verbal description was digitally recorded and analysis were made offline.

Figure 5.2. *Experiment 1. Cookie theft picture (Kaplan et al., 2001). Patients were asked to look and describe this picture with no time constrains while their eye movements were*

recorded.



5.2.1 Data analysis

In order to establish if each element of the image belongs to the left or to the right, we drew a vertical line on the image so that it divided the image into two parts of equal size, left and right, respectively. We also selected an equal number of elements in the two sides. Eight salient elements in the scene were considered in the analysis, 4 belonging to the left and 4 to the right hand side of the stimulus. The elements we identified on the left are: little boy, little girl, biscuits and stool; on the right: mother, plates, water, window.

5.2.2 Results

5.2.2.1 Verbal description

Results for each patient and for each control subject, illustrated in Table 5.3, , indicated the percentage of elements reported in the left and in the right side on the scene. Controls report a mean of 3.8 and 3.5 elements on the left and the right, respectively. The verbal behaviour of N+ patients is heterogeneous: Some patients report many elements on both the left and the right side (BG, LD, SG, FA); others reports more elements on the right and few or none on the left (MP and PS); other reports few elements on both the left and the right side (MC, MM, MA and RG). A description limited to the right side is common in neglect patients and it can be attributed to the neuropsychological disorder itself which, by definition, causes difficulties in identifying and reporting objects in the contralesional hemispace. However, the poor object description on both the left and right sides is less common and it cannot be fully justified by the presence of the neglect disorder. The eye-movement analysis helped in clarifying this point (see below).

Table 5.3. *Experiment 1. Percentage of elements described on the left and on the right side of the image for each N+ patient and for each control.*

	% of object described on the left (N = 4)	**% of object described on the right (N = 4)**
Patients (N+)		
BG	100%	75%
LD	100%	100%
MP	0	100%
PS	50%	100%
SG	100%	75%
FA	100%	75%
MC	50%	25%
MM	50%	50%
MA	25%	50%
RG	0	50%
Controls (N-)		
ML	100%	75%
RE	100%	100%
GF	75%	75%
SM	100%	100%
IMA	100%	100%
DND	100%	75%
GN	100%	100%
ZR	100%	75%
CF	100%	100%
FL	75%	75%

5.2.2.2 Eye movements pattern

Basic eye movements information for each participant is reported in table 5.4.

Table 5.4. *Experiment 1. Basic eye movements information for each patient and each control subject during the scene exploration task.*

	Fixation Count	Average fixation duration	Average saccade amplitude	Total observation Time (ms)
Patients (N+)				
BG	356	326.2	2.6	129,140
LD	263	293.6	2.3	89,239
MP	132	495.9	2.3	66,839
PS	144	438.4	3.5	68,951
SG	146	313.4	4.3	53,930
FA	122	354.1	4.6	47,978
MC	103	337.6	4.9	34,419
MM	205	379.7	3.4	87,155
MA	188	375.4	3.7	81,303
RG	257	241.4	3.1	66,646
Controls (N-)				
ML	123	300.2	3.4	41,287
RE	326	313.1	3.8	123,838
GF	202	311.0	3.2	67,384
SM	187	325.3	4.6	70,698
IMA	178	307.2	4.4	62,453
DNA	125	331.8	3.8	44,665
GN	148	289.4	4.8	48,312
ZR	135	445.8	4.6	65,937
CF	96	379.6	3.6	38,931
FL	123	421.4	3.9	54,316

These eye movements parameters measured over discrete elements of the image do not highlight the difference in the verbal reports of N+ patients. We therefore looked at the fixations distribution over the image. This analysis aimed to identifying some interest areas on the basis of the controls performance (i.e. identify those areas where controls made a larger number of fixation and spent a longer total fixation time during the image exploration). Therefore we combined temporal and spatial features of the fixation distribution pattern over the image to obtain the cumulative contribution of fixation time of each patient. To this aim, a 2D matrix was created, i.e., a pixel map with a 1024 x 768 resolution. Then for each subject a 2D Gaussian has been applied to each fixation, where the

Gaussian centre is at the fixation location, the width of the Gaussian is set to an (adjustable) sigma value of 0.4 in degrees of visual angle, and the height of the Gaussian is proportional to fixation duration. This 2D Gaussian has been added to the subject's internal map by adding weight to that area of the map where a larger/longer number of fixations have been made. After the above process is applied for all fixations, the internal map shows the cumulative contribution of fixation time on each image pixel. The map activity has been summed based on trial count pooled across control subjects. We extracted a 3D image (see figure 5.3) on the basis of the control performance where peaks indicated higher fixation time. White areas in the image indicate those areas that have been fixated a time equal or smaller than the mean duration of fixations, while progressively colder colours indicate a longer duration of fixations. We selected those areas where the total fixation time is larger than the mean duration of fixations as interest areas. Afterwards, for each neglect patients and each control we measured the proportion of total fixation time spent within the interest areas. Results are reported in table 5.5. All controls had a proportion of fixations falling within the interest areas that ranges between 75 and 89%, indicating that all N- participants contributed to the creation the interest areas similarly. Among neglect patients, 6 (BG, LD, MP, PS, SG and FA) had a proportion of fixations within the interest areas similar to controls. Conversely 4 neglect patients (MC, MM, MA and RG) had a very small proportion of fixation time spent over the interest areas (ranging between 44 and 69%). On this basis we divided our original sample of neglect patients in two groups: those with a normal oculomotor pattern (from now on, NOP) and those with an abnormal oculomotor pattern (from now on, AOP). In Figure 5.4 an example of the exploration pattern, based on the fixation number and distribution, for a NOP and a AOP patients is shown. In this case progressively warmer colours indicate mostly fixated areas. From the Figure 5.4 it clearly emerges the difference between the two patients: It is evident that the NOP patient, but not the AOP, looks preferentially in the relevant parts of the image, as defined by the control patients performance.

Figure 5.3. *3D representation of the controls pattern of exploration during the scene exploration.*

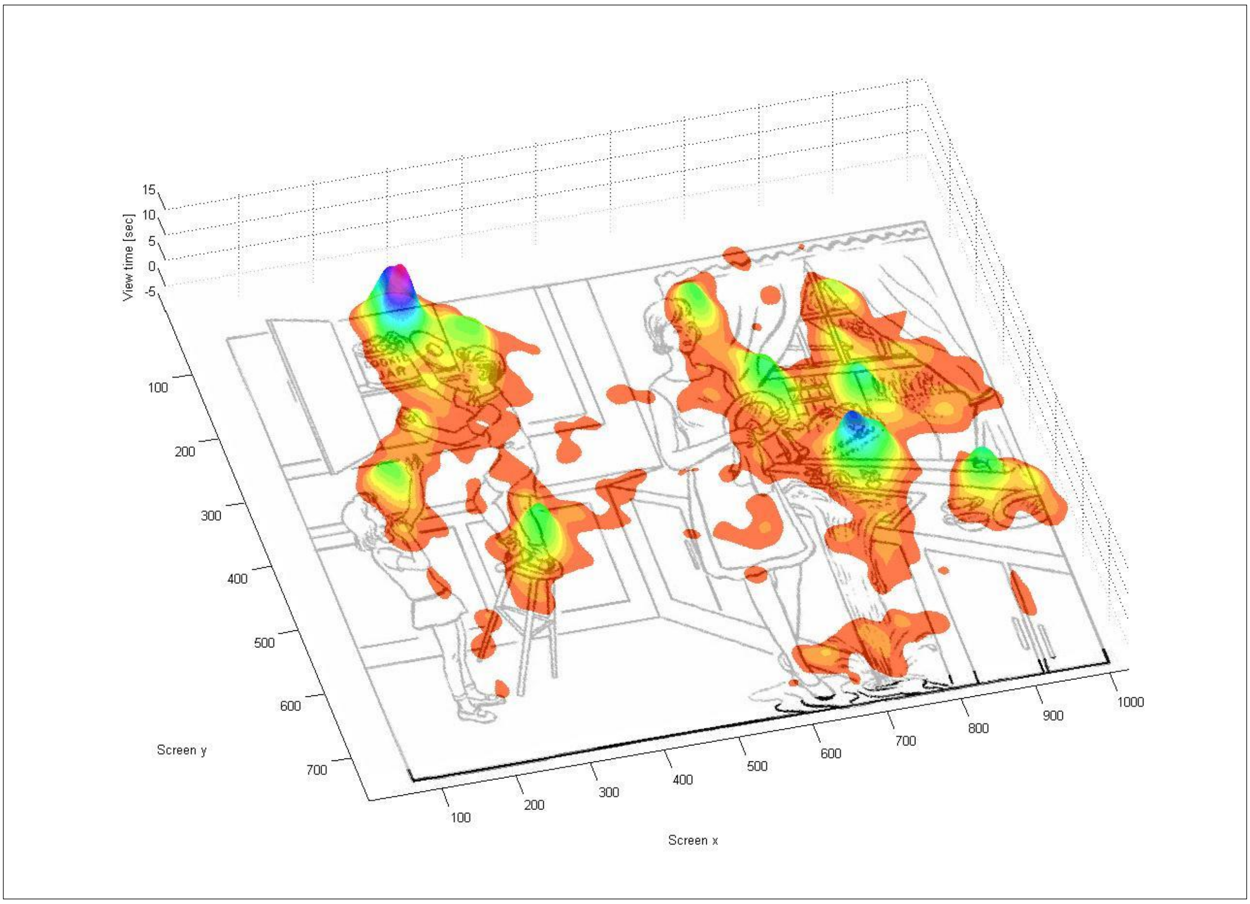
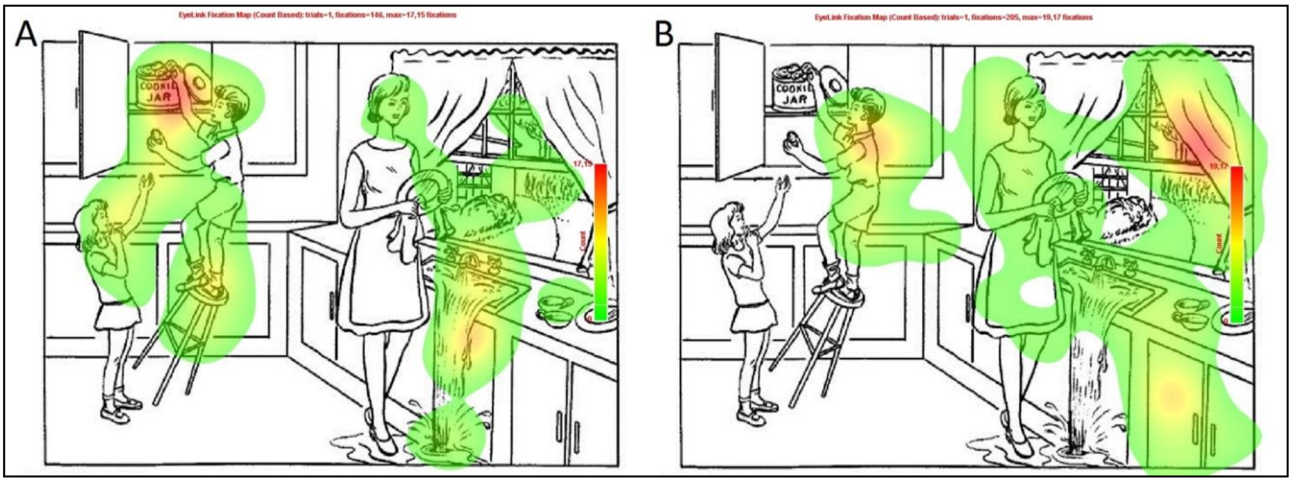

View time [sec]
15
10
5
0
-5
Screen y
100
200
300
400
500
600
700
Screen x
100
200
300
400
500
600
700
800
900
1000
COOKIE JAR

Table 5.5. *Proportion of fixation falling within the interest areas, as defined by the controls group performance, for each control and for each neglect patient.*

	Proportion of fixations falling within the interest areas
Patients (N+)	
BG	0.83
LD	0.80
MP	0.83
PS	0.83
SG	0.87
FA	0.86
MC	0.59
MM	0.44
MA	0.69
RG	0.58
Controls (N-)	
ML	0.88
RE	0.88
GF	0.78
SM	0.82
IMA	0.87
DND	0.89
GN	0.75
ZR	0.81
CF	0.84
FL	0.82

Figure 5.4. *Exploration pattern in a NOP (panel A) and in a AOP patient (panel B) during the image exploration task.*



5.2.3 Comments

Results of the present experiment have shown that 4 out of 10 neglect patients have an eye movement deficit which prevents them looking in the more salient parts of the image and to describe them. Conversely the other 6 N+ patients showed an eye movement pattern comparable to that of controls in terms of percentage of fixation within the interest areas. On this basis we divided our original sample of neglect patients in two groups: those with and eye movement deficit (AOP) and those with an intact eye movement pattern (NOP).

5.3 Experiment 2. Target steady fixation

In Experiment 2 patient’s ability to keep the fixation on a target has been evaluated in order to understand the nature and quality of this basic eye movement process in all the sample patients.

5.3.1 Material and procedure

A black dot subtending .2 deg of visual angle and displayed on a white background appeared in the middle of the screen for 10 seconds. Three trials were administered. Patients were required to fixate the target as accurately as possible trying not to move the eyes from it.

5.3.2 Results

We measured the distance between the target x coordinates and the patients eyes x coordinates both in pixel and in visual angle degrees for the entire duration of the target on the screen. An ANOVA with group (N-, NOP, AOP) as between factor and mean distance between patient's eye and target (expressed in visual deg) as dependent measure was run. No main effects of group emerged [$F(2, 17)=1.73$, $p=.21$; means: N- = -0.1 deg; NOP = 0.4 deg; AOP = 0.4 deg]. Results indicate that the three groups of patients were able to keep the fixation on a target.

5.3.3 Comments

Result of this experiment indicate that the basic ability of keeping fixation on a target is spared in controls and in patients with neglect, even in those patients who showed an eye movement deficit in scene exploration.

5.4 Experiment 3. Left-right and right-left saccade task

In the present experiment the horizontal component of the saccade programming and execution has been explored. To this aim we administered a rightward-leftward and leftward-rightward saccadic task.

5.4.1 Material and procedure

A black dot subtending .2 deg of visual angle and displayed on a white background appeared along the horizontal meridian in five consecutive positions, 4.0 deg away from each other according to a synchronous paradigm (i.e., no gap). The dot appeared sequentially in the five positions and stayed on for two seconds in the two extreme positions and one second in the three central ones. The sequence started with the extreme left dot and each dot appeared in turn until the extreme right dot appeared, then the reverse sequence took place. The rightward and leftward sequences were repeated twice in each trial. Three trials were administered and patients were required to follow the dot as quickly and as accurately as possible.

5.4.2 Results

Accuracy (percentage of fixations on the dot when it was on the screen) and saccade latencies (time elapsed from the appearance of the dot to the beginning of the saccade) were measured. We excluded analysis of fixations made on the first dot in the sequence and anticipatory saccades (i.e. saccades starting before the appearance of the following dot or earlier than 80 ms after it). We also excluded analysis of fixations that were far from the target with respect to its vertical axis (i.e. over 2 standard deviations calculated on the vertical fixation positions of the control group). The remaining fixations were considered “accurate” if they fell no more than 1 degree of visual angle away from the current target.

Figure 5.5. *Experiment 3: Percentage of accurate fixations (and standard errors) for N-, NOP and AOP in the five different dot positions where position 1 corresponds to the extreme left position and position 5 to the extreme right position reached by the moving dot .*

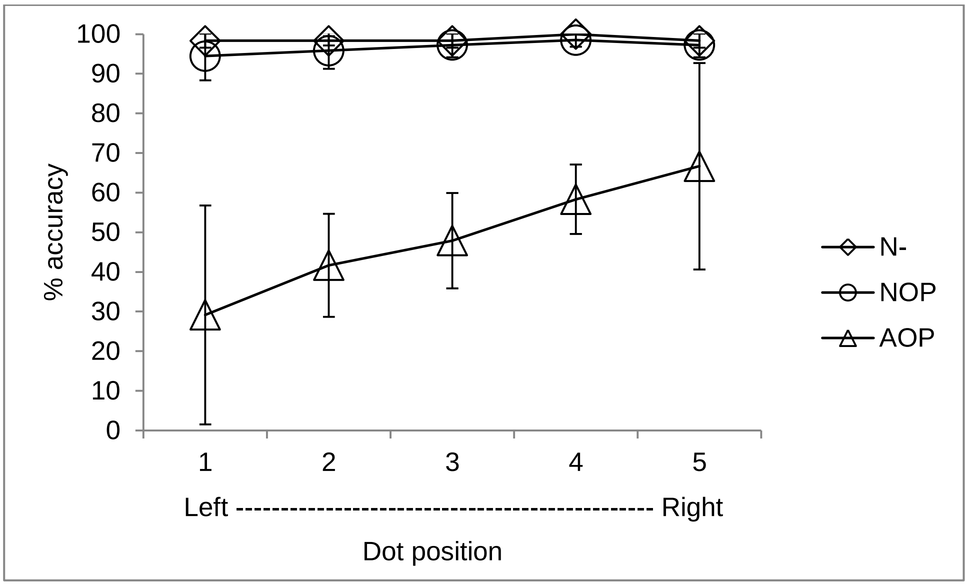
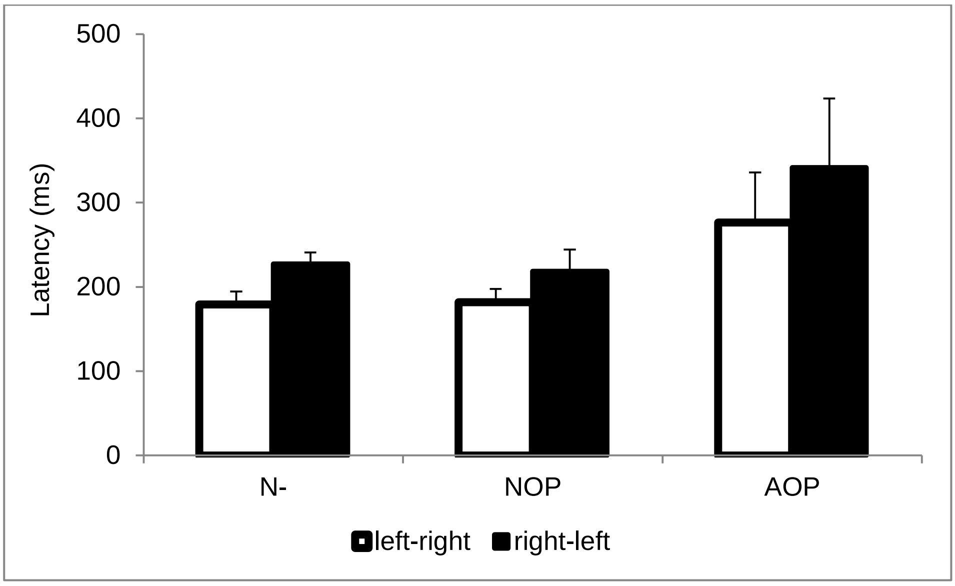


Figure 5.6. *Experiment 3: Saccade latencies (and standard errors) for N-, NOP and AOP patients in reaching the target when its direction was from left to right (white bars) and from left to right (black bars) .*



ANOVAs were carried out on percentages of accuracy (see Figure 5.5) and latencies (see Figure 5.6), with target direction (left-right *vs.* right-left) as repeated factors and group as fixed factor. The analyses of accuracy revealed main effects of group [F(2, 17)=30.9, p<.00001], target direction [F(1, 17)=17.3, p=.0007] and a statistically significant interaction group by target direction [F(2, 17)=9.19, p=.0019]. The Bonferroni post-hoc analysis of the group by target direction interaction indicated that AOP patients were significantly less accurate in both the left-right (69%) and right-left direction (34%) than both N- (left-right = 99%, right-left = 98%) and NOP patients (left-right = 99%, right-left = 95%) (all $p_s < .001$); the difference between N- and NOP patients was not significant in either direction.

An analysis of latencies indicated significant main effects of group [F(2, 17)=5.3, p=.016] and target direction [F(1, 17)=11.48, p=.003]. The interaction group by target direction was not statistically significant. A Bonferroni post-hoc analysis on the group effect indicated that AOP patients were significantly slower than both N- and NOP patients in both target directions (both p_s <.05). Controls were not significantly different from NOP patients in either direction (both $p_s > .1$). As shown in Figure 5.5, AOP patients were inaccurate in fixating the target regardless of whether it was in the left or the right position on the screen even if their performance was slightly better for the right sided targets.

To further investigate accuracy as a function of the position of the target on the screen, an ANOVA was carried out on percentages of accuracy with target position (1st, 2nd, 3rd, 4th and 5th, from left to right respectively) as repeated factor and group as fixed factor. Analyses revealed main effects of group [$F(2, 17)=27.63$, $p<.00001$], target position [$F(4, 68)=4.32$, $p=.0034$] and a statistically significant effect of group by target position [$F(8, 68)=2.65$, $p=.0136$]. The Bonferroni post-hoc analysis revealed that, compared to both N- and NOP groups, the AOP group of patients was significantly impaired in fixating the target in positions 1 to 4 (all $p_s < .005$) but the difference is not significantly different for position 5 (both $p_s > .1$). No difference in accuracy for the five targets was found between N- and NOP (all $p_s > .1$).

5.4.3 Comments

In the present saccadic task, results confirm the groups division as made by the eye movements pattern analysis in experiment 1. In fact in this saccade task only the group of patients who showed an abnormal pattern in the scene exploration showed also a low accuracy a longer saccade latencies in fixating the target. Conversely NOP patients showed a performance comparable to that of controls in term of both accuracy and saccade latencies.

5.5 Experiment 4. Vertical saccade test

In the present experiment the vertical component of the saccade programming and execution has been explored. We aimed at better understanding if the abnormal eye movement pattern is confined to the horizontal axis, or if it also extends to the vertical one.

5.5.1 Material and procedure

Material and procedure are the same as in Experiment 3. The only difference is represented by the vertical, instead of horizontal, movement of the target. In this case the sequence started with the target positioned on the top and each dot appeared in turn until target in the most bottom position appeared, then the reverse sequence took place. As in the previous experiments the top-down and bottom-up sequences were repeated twice in each trial and three trials were administered. Patients were required to follow the dot as quickly and as accurately as possible.

5.5.2 Results

As for Experiment 3, accuracy (see Figure 5.7) and saccade latencies (see Figure 5.8) were measured. Same saccade and fixation exclusion's criteria used in Experiment 3 were used in the present experiment. Also the same analysis on percentage of accuracy and saccade latencies were run.

Figure 5.7. *Experiment 4: Percentage of accurate fixations (and standard errors) for N-, NOP and AOP in the five different dot positions where position 1 corresponds to the topmost position and position 5 to the dot in the extreme bottom position.*

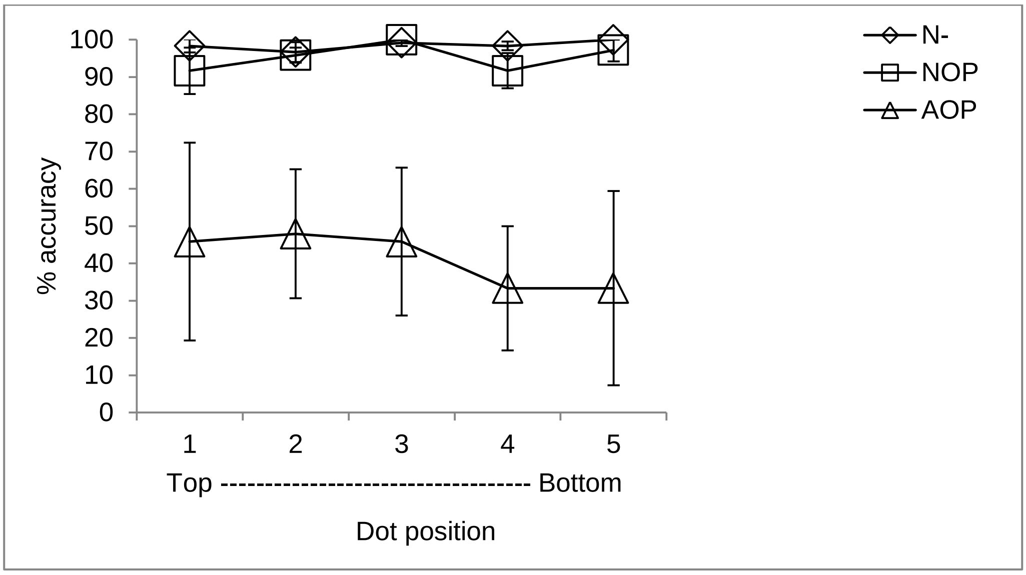
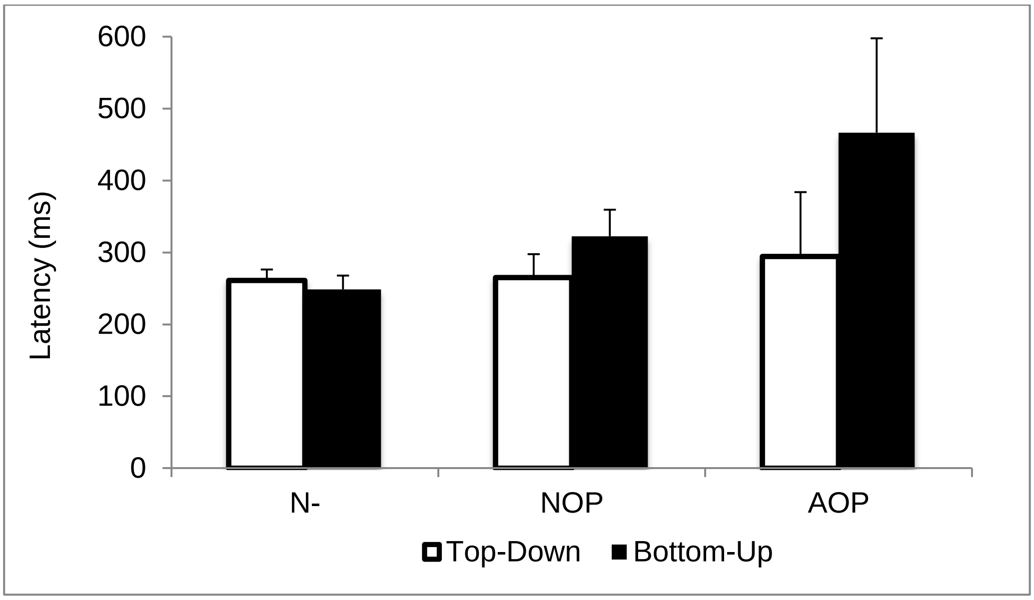


Figure 5.8. *Experiment 4: Saccade latencies (and standard errors) for N-, NOP and AOP patients in reaching the target when its direction was from left to right (white bars) and from left to right (black bars) .*



ANOVAs were carried out on percentages of accuracy and latencies, with target direction (top-down *vs.* bottom-up) as repeated factors and group as fixed factor. The analyses of accuracy revealed main effects of group [F(2, 17)=27.2, p=.00001], target direction [F(1, 17)=6.1, p=.02] and a statistically significant interaction group by target direction [F(2, 17)=6.04, p=.01]. The Bonferroni post-hoc analysis of the group by target direction interaction indicated that AOP patients were significantly less accurate in both the top-down (29%) and bottom-up direction (52%) than both N- (top-down = 99%, bottom-up = 98%) and NOP patients (top-down = 96%, bottom-up = 95%) (all $p_s < .05$); the difference between N- and NOP patients was not significant in either direction.

An analysis of latencies indicated significant main effects of group [F(2, 16)=6.27, p=.001] and dot direction [F(1, 16)=5.75, p=.029]. The group by dot direction interaction was not statistically significant. A Bonferroni post-hoc analysis on the group effect indicated that AOP patients were significantly slower than N- (p=.008) and marginally significantly slower than NOP patients (p=.07). The NOP group was not significantly different from controls (p=.76). The dot direction effect indicated that participants had lower latencies in reaching the target when it moves in the top-down (mean=274 ms) than in the bottom-up (mean=361 ms) direction.

In order to investigate if the AOP patients performance was better for some target as compared to others (see Figure 5.7), an ANOVA was carried out on percentages of accuracy with target position (1st, 2nd, 3rd, 4th and 5th, from top to bottom respectively) as repeated factor and group as fixed factor. Analyses revealed main effects of group [$F(2, 14)=119.07$, $p<.00001$], target position [$F(4, 56)=12.69$, $p<.00001$] and a statistically significant interaction of group by target position [$F(8, 56)=6.98$, $p<-00001$]. The Bonferroni post-hoc analysis revealed that, compared to both N- and NOP groups, AOP patients were significantly impaired in fixating the target in all positions (all p_s <.01). No difference in fixation accuracy for the five targets was found between N- and NOP groups (all p_s >.1).

5.5.3 Comments

Results of Experiment 4 confirm the groups division as made by the correlation analysis in Experiment 1 and establish that the eye movement impairment is not selective for the horizontal dimension but it also extends to the vertical one. In fact in the present saccade task only the group of patients who were classified as having an abnormal pattern in the scene exploration showed also a low accuracy a longer latencies in vertical saccade execution. Conversely NOP patients showed no differences with controls in term of both accuracy and saccade latencies.

5.6 Experiment 5. Overlap and gap saccadic tasks

To further investigate and better clarify the nature of the eye-movements deficit shown by AOP patients we managed three more specific saccadic tasks. Our aim was to understand the origin of such eye movement impairment, studying in detail fixation accuracy, saccade latency and amplitude. In Experiments 5a and 5b both the left and the right hemispace were tested. In Experiment 5c we presented the stimuli only in the right hemispace in order to study the eye movement pattern netted from the neglect symptoms that may negatively influence the performance of neglect patients when stimuli are presented in both hemispaces.

5.6.1 Participants

Due to the limited hospitalization time for some patients, a subgroup of the original sample took part in the three saccadic experiments. In particular 7 N- patients (GF, SM, IMA, DND, GN, ZR and CF), 4 NOP patients (MP, PS, SG and FA) and 2 AOP patients (MA and RG) completed the saccadic tasks described below.

5.6.2 Material and procedure

In the three saccadic tasks we adapted the procedure described in Walker & Findlay (1996). In Experiment 5a and 5b we administered the overlap and the gap condition, respectively, testing both the right and the left hemispace. Moreover, in a third Experiment (5c) we tested the patients' ability to make accurate saccadic movements exclusively in the right hemispace in order to study the nature of the eye movement pattern netted form the unilateral spatial neglect affecting the studied population of patients. In all three experiments, each trial started with a fixation cross subtending 1 deg and appearing in the centre of the screen. When the patients eye's converged on the fixation cross for 100 ms, immediately a red square (each side = 1 deg), was presented for 500 ms on a horizontal axis level. In the overlap condition (Experiment 5a) the fixation cross remained visible for the entire trial. In the gap condition (Experiments 5b and 5c) the target appearance was preceded by a 100 ms gap during which the fixation cross disappeared. In Experiments 5a and 5b, on each single trials a target could appear at one of six eccentricity locations (3 on the left: -12, -8, -4 deg and 3 on the right: 4, 8, 12 deg) in a randomized order. Sixty trials were administered, 10 for each eccentricity. In Experiment 5c, only the right hemispace was tested, using three eccentricities (4, 8 and 12 deg). In this case each participant saw ten trials for each eccentricity, for a total of 30 trials. The instructions for the participants were as follow: "Please look at the fixation cross. A small target square will then appear on the left or on the right side of the cross and you should move your eyes to the target as quickly as possible". In Experiment 5c patients were told that the target would have been presented only on the right side.

5.6.3 Data analysis

Accuracy, first saccade latency and amplitude were measured. Trials where the first saccade was in the opposite direction (or toward the top or the bottom) or saccades that did not start from the central fixation position (because of an eye movements made during the gap interval) were excluded from the analysis. A patient was considered accurate in each trial according to the ability of reaching the target (within 1 deg distance from the borders of the square target) while it was on the screen (i.e., 500 ms). For Experiments 5a and 5b three different 3x2 ANOVAs with group (N-, NOP, AOP) as between factor and target side as repeated factor (left and right) was performed on accuracy, saccade latency and amplitude. For Experiment 5c a 3x3 ANOVA with group (N-, NOP, AOP) as between factor and target eccentricity as repeated factor (4, 8 and 12 deg) was performed separately on accuracy, saccade latency and amplitude.

5.6.4 Results

5.6.4.1 Experiment 5a - Overlap condition: Targets in both left and right hemispaces

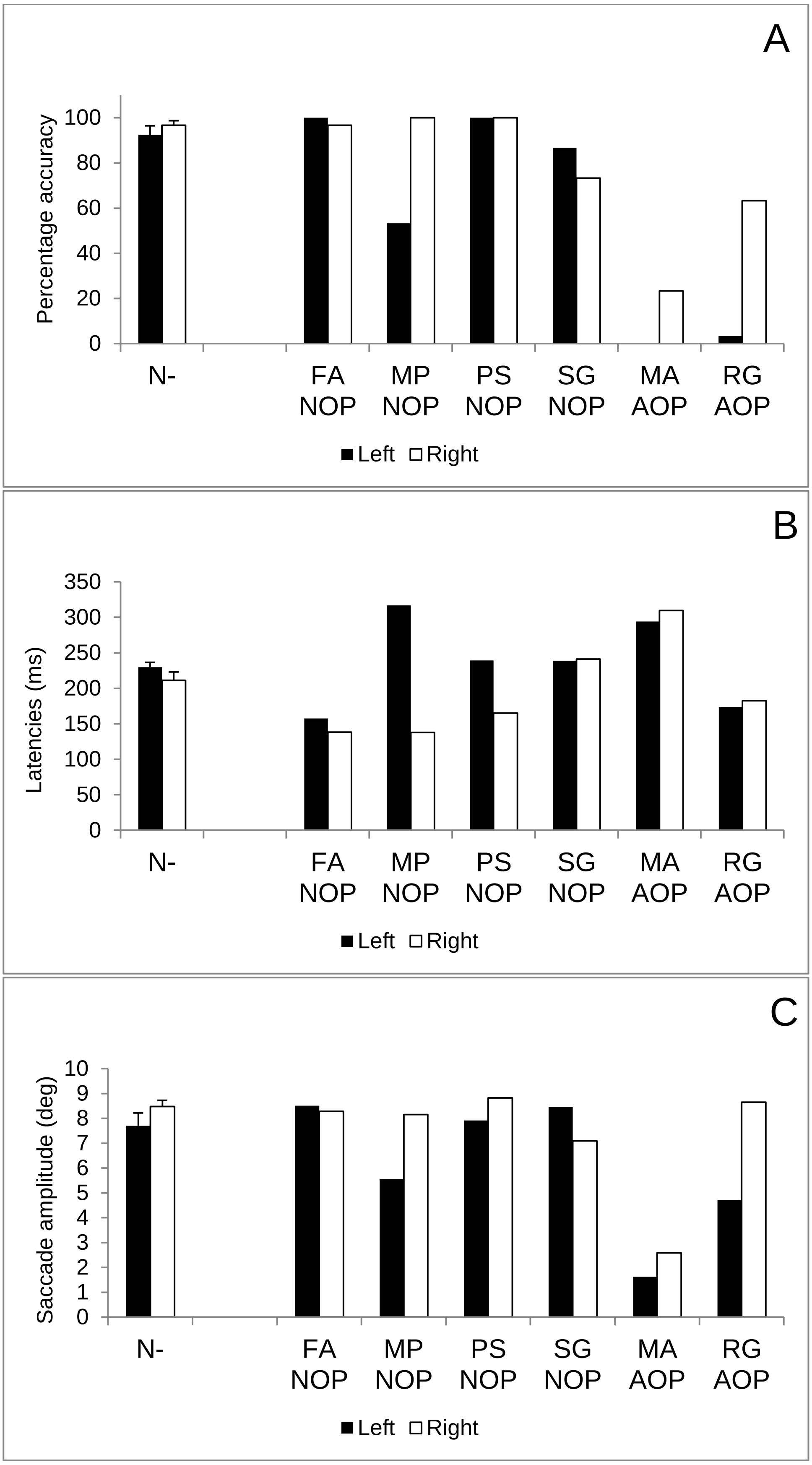
In the overlap condition 12.7% of the trials have been excluded from saccade analysis. In Figure 5.9 is reported the accuracy, latencies and saccade amplitude for controls and for each N+ patient (panels a, b and c, respectively). Analysis indicated that N- and NOP patients were at ceiling in this task. Conversely AOP patients showed a low proportion of accurate trials. Results on accuracy indicate a significant main effects of group [$F(2, 10)=45.5$, $p=.00001$], with AOP patients showing a worst performance than both N- and NOP patients (both ps $<.0001$) while the difference between these two groups is not significant ($p=1$). Also a significant main effect of target side emerged [$F(1, 10)=9.58$, $p=.01$] indicating a better performance on the right as compared to the left hemispace (78 vs 60% of accuracy, respectively). The interaction group by target side was not statistically significant.

Latencies of the first saccade towards the target after its onset were measured and are represented in Figure 5.9, panel b. No significant effects nor interaction emerged.

Saccade amplitude analyses (reported in Figure 9, panel c) revealed main effects of group [$F(2, 10)=6.86$, $p=.013$] and target side [$F(1, 10)=7.63$, $p=.02$]. The main effect of group revealed that AOP had a global smaller saccade amplitude (mean = 4.4 deg) as compared to

N- and NOP patients (8.1 and 7.8 deg, respectively), while the difference between these two groups is not statistically significant.

Figure 5.9. *Experiment 5a – Overlap saccadic task with target presented in the left and right hemispaces. Mean and standard errors for accuracy (a) saccade latency (b) and amplitude (c) for the control group (N-) and for each N+ patient.*


A
Percentage accuracy
0
20
40
60
80
100
N-
FA NOP
MP NOP
PS NOP
SG NOP
MA AOP
RG AOP
Left
Right
B
Latencies (ms)
0
50
100
150
200
250
300
350
N-
FA NOP
MP NOP
PS NOP
SG NOP
MA AOP
RG AOP
Left
Right
C
Saccade amplitude (deg)
0
1
2
3
4
5
6
7
8
9
10
N-
FA NOP
MP NOP
PS NOP
SG NOP
MA AOP
RG AOP
Left
Right

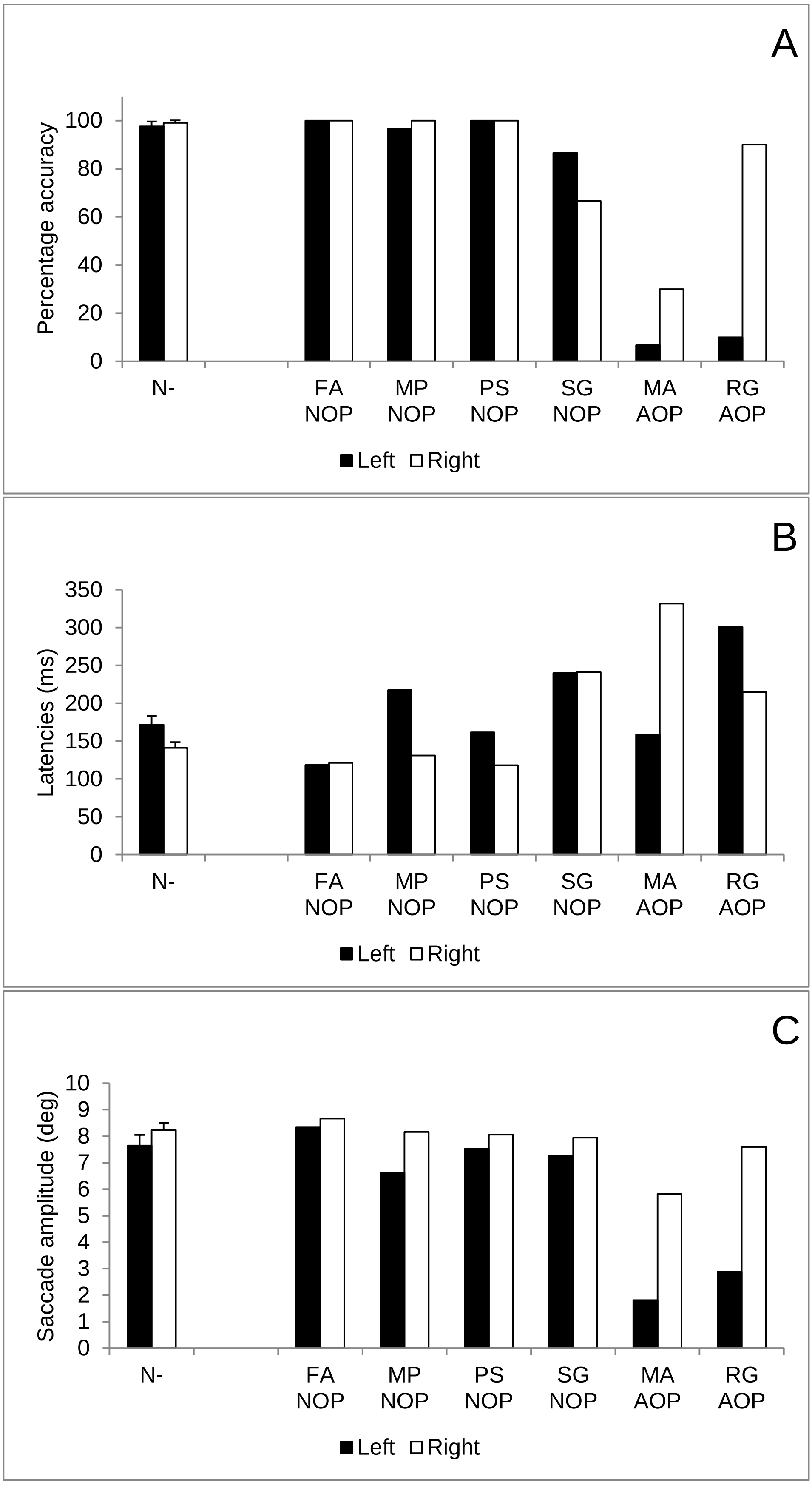
5.6.4.2 Experiment 5b - Gap condition: Targets in left and right hemispaces

In the gap condition 10% of the trials have been excluded from saccade analysis (latency and amplitude). Similarly to what seen in the previous condition, controls and NOP patients were at ceiling in this task. Conversely AOP patients showed a deficit in saccade execution (see Figure 5.10 panel A). The ANOVA analyses on accuracy indicates significant main effects of group [F(2, 10)=34.15, p=.00003], target side [F(1, 10)=13.48, p=.004] and a significant group by target side interaction [F(2, 10)=11.83, p=.002]. The interaction indicates that for left sided targets AOP patients are significantly less accurate than both N- and NOP patients (both p_s <.00001). For right sided targets AOP patients are significantly less accurate than N- (p=.012) while the difference between AOP and NOP patients is not significant (p=.1). The difference between N- and NOP is not significant for either left nor right-sided targets (both p_s = 1).

Latencies of the first saccade towards the target after its onset were measured and are represented in Figure 5.10 panel B. Only the significant main effect of group emerged [F(2, 10)=6.18, p=.018] indicating that AOP patients are slower (mean=252ms) than the others two groups of patients (N- mean = 156 ms, p =.017; NOP mean = 169 ms, p=.05) in making the first saccade toward the stimulus after its onset. No difference between N- and NOP patients emerged.

Finally the saccade amplitude analyses, reported in Figure 5.10, panel C, revealed significant main effects of group [F(2, 10)=22.4, p=.0002], target side [F(1, 10)=50.17, p=.00003] and significant group by target side interaction [F(2, 10)=15.99, p=.0008]. The Bonferroni post-hoc revealed that both N- and NOP patients made longer leftward saccades (mean = 8.24 and 8.21 deg, respectively) as compared to AOP patients (mean =2.3 deg, both p_s ps<.00001). The difference for rightward saccades is not statistically significant. No differences emerged between N- and NOP patients in either directions (both p_s =1).

Figure 5.10. *Experiment 5b – Gap saccadic task with targets presented in the left and right hemispaces. Mean and standard errors for accuracy (a) saccade latency (b) and amplitude (c) for controls (N-) and for each N+ patient.*


A
Percentage accuracy
0
20
40
60
80
100
N-
FA NOP
MP NOP
PS NOP
SG NOP
MA AOP
RG AOP
Left
Right
B
Latencies (ms)
0
50
100
150
200
250
300
350
N-
FA NOP
MP NOP
PS NOP
SG NOP
MA AOP
RG AOP
Left
Right
C
Saccade amplitude (deg)
0
1
2
3
4
5
6
7
8
9
10
N-
FA NOP
MP NOP
PS NOP
SG NOP
MA AOP
RG AOP
Left
Right

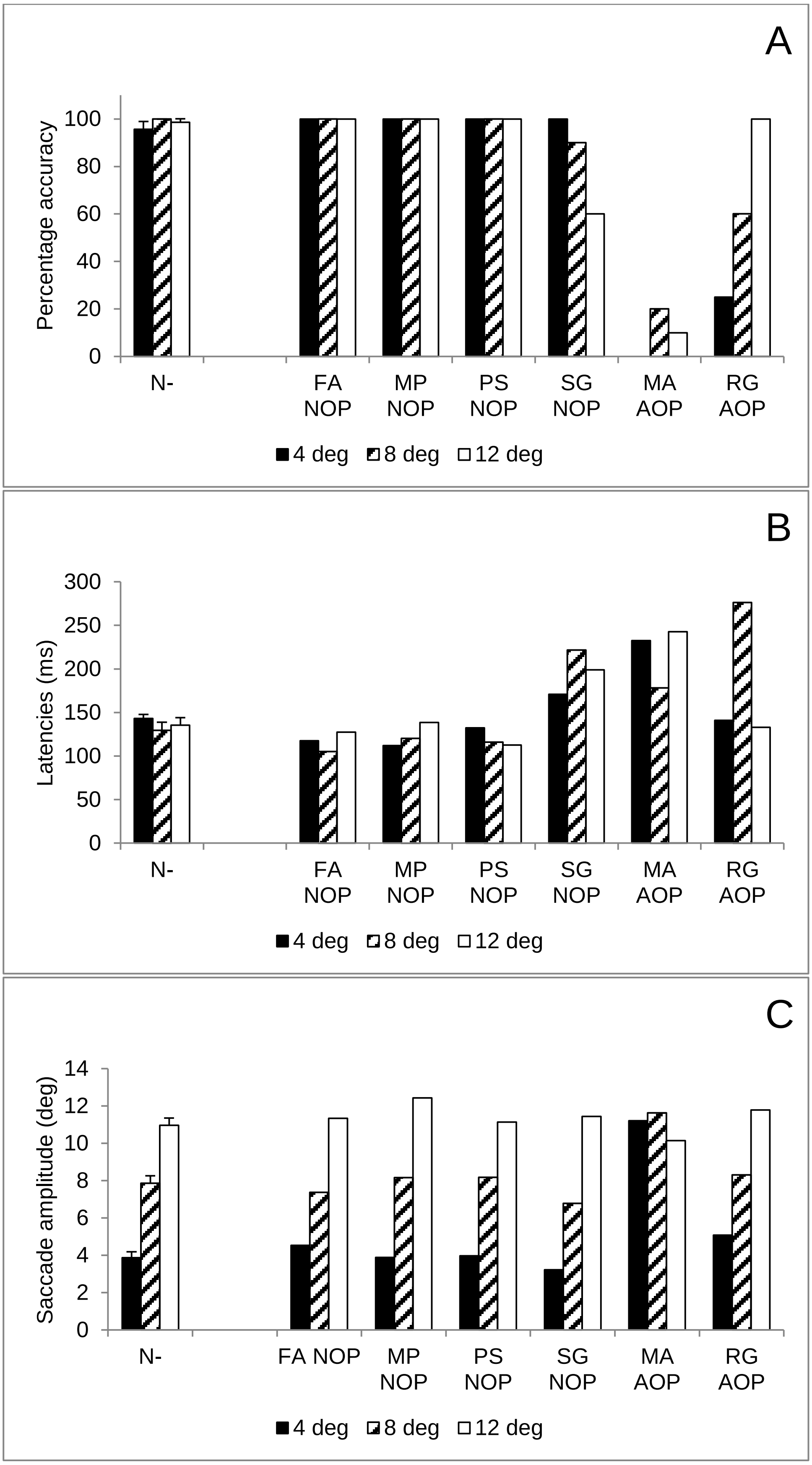
5.6.4.3 Experiment 5c: Gap condition: Targets presented in the right hemispace only

In this condition 8% of the trials have been excluded from analysis. Results are reported in Figure 5.11. Panel A indicates accuracy. Critically, AOP patients show an impaired eye movement pattern even in a condition in which the target appeared only in the right hemispace, this excluding hemispace uncertainty. The main effects of group [F(2, 10)=20.201, p=.0003], target eccentricity [F(2, 20)=3.74, p=.04] and the interaction group by target eccentricity [F(4, 20)=4.4, p=.01] are statistically significant. The Bonferroni post-hoc on the interaction indicates that N- and NOP patients are significantly more accurate than AOP at all eccentricities (all p_s <.005). The difference between N- and NOP is not statistically significant at any eccentricity (all p_s =1).

Latencies are reported in Figure 5.11, panel B. The ANOVA indicates a significant group effect [F(2, 10)=5.7, p=.02], with AOP patients significantly slower (mean=201 ms) than both N- (mean=136 ms, p=.024) and NOP (mean=139 ms, p=.048). Eccentricity effect and group by eccentricity interaction were not statistically significant.

Mean saccade amplitude for the three different eccentricities are reported in Figure 5.11, panel C. Statistics revealed significant effects of group [F(2, 10)=4.92, p=.03], target eccentricity [F(2, 20)=82.21, p<.00001] and a significant interaction group by target eccentricity [F(4, 20)=4.27, p=.012]. The Bonferroni post-hoc indicate that, for the less eccentric target (4 deg), both N- and NOP are significantly different from AOP (both p_s <.05) but not significantly different between each other (p=1). Interestingly, while for 8 and 12 deg targets, saccade amplitude in the three groups of patients is quite similar, when the target is presented at 4 deg of eccentricity, N- and NOP patients made saccades of the adequate amplitude (means=3.87 and 3.91 deg, respectively), while AOP patients made much larger (and inappropriate) saccade (mean=8.15 deg).

Figure 5.11. *Experiment 5b – Gap saccadic task with targets presented in the right hemispace only. Mean and standard errors for accuracy (a) saccade latency (b) and amplitude (c) for controls (N-) and for each N+ patient.*


A
Percentage accuracy
100
80
60
40
20
0
N-
FA NOP
MP NOP
PS NOP
SG NOP
MA AOP
RG AOP
4 deg
8 deg
12 deg
B
Latencies (ms)
300
250
200
150
100
50
0
N-
FA NOP
MP NOP
PS NOP
SG NOP
MA AOP
RG AOP
4 deg
8 deg
12 deg
C
Saccade amplitude (deg)
14
12
10
8
6
4
2
0
N-
FA NOP
MP NOP
PS NOP
SG NOP
MA AOP
RG AOP
4 deg
8 deg
12 deg

5.6.5 Comments

Results of the three saccadic tasks described represent a deepening on the oculomotor behaviour of neglect patients. Patients showing an abnormal oculomotor pattern in Experiment 1, also manifest a severe difficulty in executing the saccadic task. Conversely, USN patients with a normal oculomotor pattern show an eye movement behaviour very similar to that of controls. The low accuracy rate in AOP patients is paralleled by longer saccade latencies (in Experiments 5b and c) but also by saccades of inappropriate amplitude. It is worth noting that, although the performance is particularly impaired for the left contralesional hemispace, also the performance on the right side is affected. This is true not only when an hemispace uncertainty is present (Exps. 5a and b) but also when targets were presented in the right hemispace only (Exp. 5c).

5.7 Experiment 6: Eye movements pattern during a single word reading task

Eye movements were recorded during a reading aloud task of single words presented at the centre of the screen. Both reading responses and eye movement parameters were analysed.

5.7.1 Materials and procedure

We generated a list of 42 7-letter words (mean number of syllables = 2.95). The mean frequency of the words, selected from a corpus of Italian written language of 1.5 million tokens (Istituto di Linguistica Computazionale, CNR, 1989), was 96.1 (range 2–382). The mean summed number of neighbours was 2.24 with a mean summed frequency of 16.92 (Wagenmakers & Raaijmakers, 2006); bigram frequency was 16.92. Stimuli were written in capital Courier New font, which is characterized by consistent letter spacing. Letter size was kept constant (40 pt) and subtended 1.0 deg. Patients were shown two squared dots vertically displaced 1.5 deg apart in the centre of the screen; these fixation marks remained on the screen for the entire experimental session. Stimulus onset was triggered when the patient steadily fixated between the central marks for at least 50 ms. Each stimulus was presented at the centre of the screen between the fixation marks (i.e. the central letter of each stimulus was vertically aligned to the fixation marks) and remained on the screen until onset of the patient's response. There was no time constraint for responding. Patients were asked to read aloud each stimulus as accurately as possible. Words appeared in randomized order across participants. Patients' reading performance was digitally recorded and errors were scored offline.

5.7.2 Results

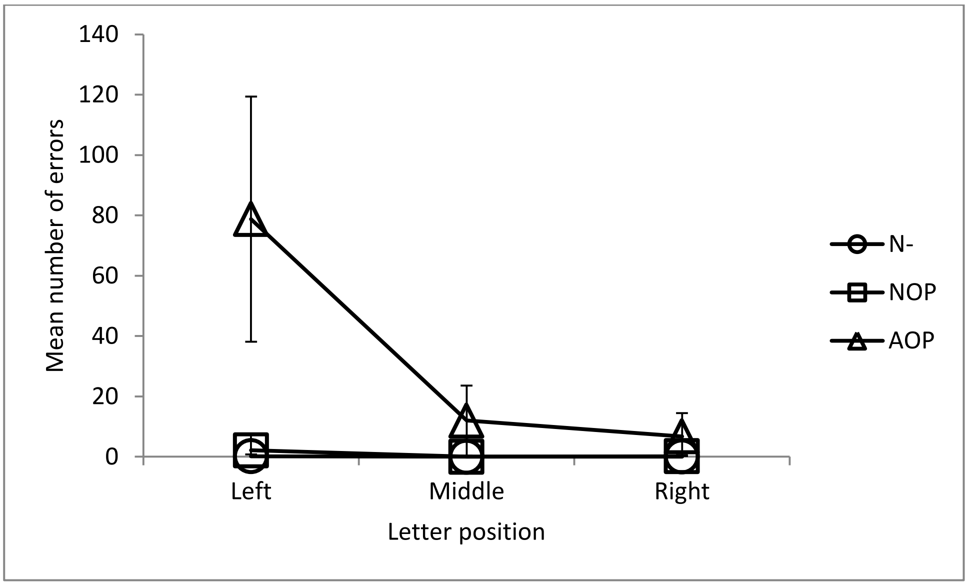
5.7.2.1 Reading performance

Reading errors (i.e. omitting or misreading the word) were classified as "neglect" errors, according to Ellis, Flude & Young (1987) neglect point measure. Table 5.6 reports the number and percentages of neglect errors made by the patients. Both N- and NOP patients made few errors in this task. By contrast, AOP patients made many errors, most of which were classified as neglect errors. Following a letter-based analysis (see Martelli et al., 2011), letter omissions and substitutions were also measured and presented separately for the left (composed of 2 letters), middle (1 letter) and right side (2 letters) of the stimulus in Figure 5.12. The Figure shows that in AOP patients the majority reading errors concerned the left portion of the stimuli, while in N- and in NOP patients the pattern of errors (although based on very few errors) was not left-lateralized. A 3x3 ANOVA with group (N-, NOP, AOP) as between factor and side of errors as repeated factor (left, middle and right) was performed. Analyses revealed significant main effects of group [$F(2, 17)=26.74$, $p=.00001$], and side [$F(2, 34)=44.89$, $p<.00001$]. The group by side interaction was also statistically significant [$F(4, 34)=34.02$, $p<.00001$]. The Bonferroni post-hoc revealed that AOP patients made a larger proportion of errors on the left side of the stimulus as compared to both N- and NOP patients (both $p_s <.0001$); the difference for errors on the middle and right-sided letters was not statistically significant (all $p_s >.1$). No difference emerged between N- and NOP groups.

Table 5.6. *Experiment 6. Percentage and number (in parentheses) of neglect errors on the 42 words with respect to the total number of reading errors made by NOP, AOP patients and controls (N-)*

	Neglect errors
Patients (NOP)	
BG	0 (0/0)
LD	0 (0/0)
MP	0 (0/0)
PS	.75 (3/4)
SG	0 (0/0)
FA	0 (0/0)
Patients (AOP)	
MC	.58 (24/41)
MM	.67 (25/37)
MA	.90 (37/41)
RG	.64 (9/14)
Controls (N-)	
ML	0 (0/1)
RE	0 (0/0)
GF	0 (0/0)
SM	0 (0/0)
IMA	.5 (1/2)
DND	0 (0/0)
GN	0 (0/0)
ZR	0 (0/0)
CF	0 (0/0)
FL	0 (0/0)

Figure 5.12. *Experiment 6: Mean number (and standard errors) of letters omitted or substituted in the left, middle and right portion of the stimuli by N-, NOP and AOP groups of participants.*

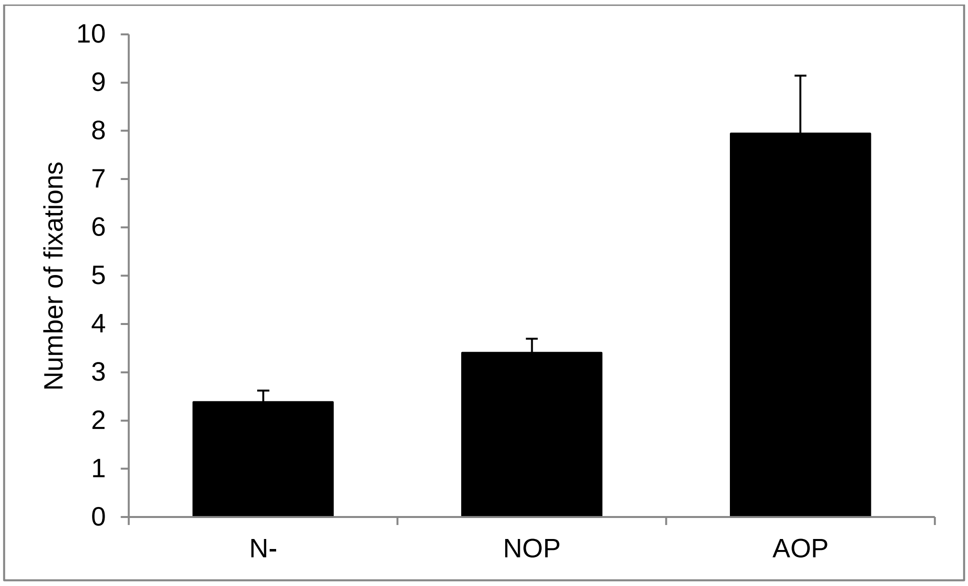


5.7.2.2 Eye movements

Four eye movement parameters were measured separately for each participant: mean number of fixations per item, first fixation position, distribution of fixations on the left- and right-sided group of letters of the stimulus and mean fixation duration per item.

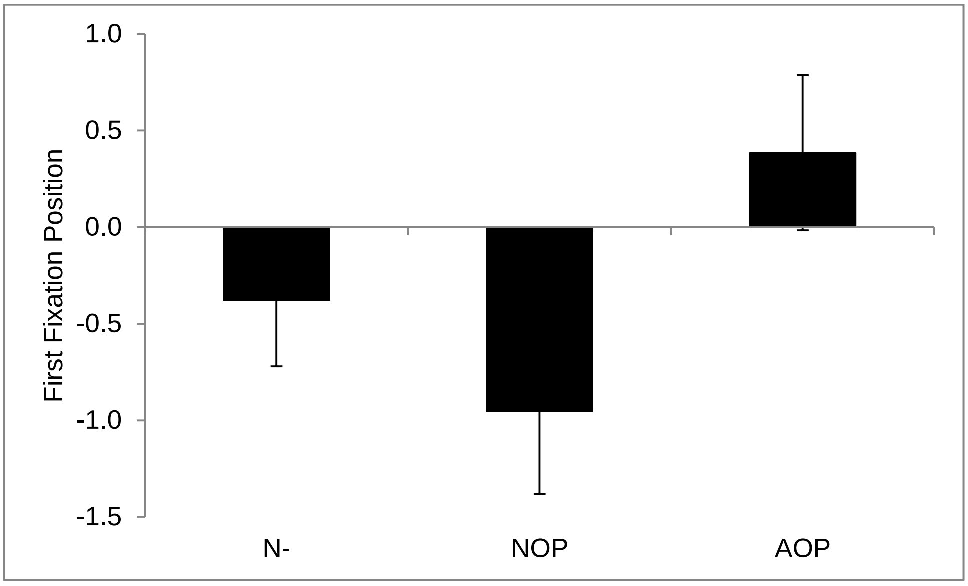
Number of fixations. Mean number of fixations was computed separately for each item and was based on all fixations performed after the stimulus onset and prior to the verbal response. In Figure 5.13, the mean number of fixations for each group of participants is shown. An ANOVA with group (N-, NOP, AOP) as fixed factor and number of fixations as dependent measure was run and revealed a main effect of group [$F(2, 17)=38.44$, $p<.00001$]. Controls made a mean of 2.4 fixations, NOP patients made a mean of 3.4 fixations. The difference between the two groups is not statistically significant. Vice versa AOP patients made more fixations (mean = 7.9) than both N- and NOP groups (both $p_s<.001$).

Figure 5.13. *Experiment 6. Mean number of fixations and standard errors for each group of participants (N-, NOP, AOP).*



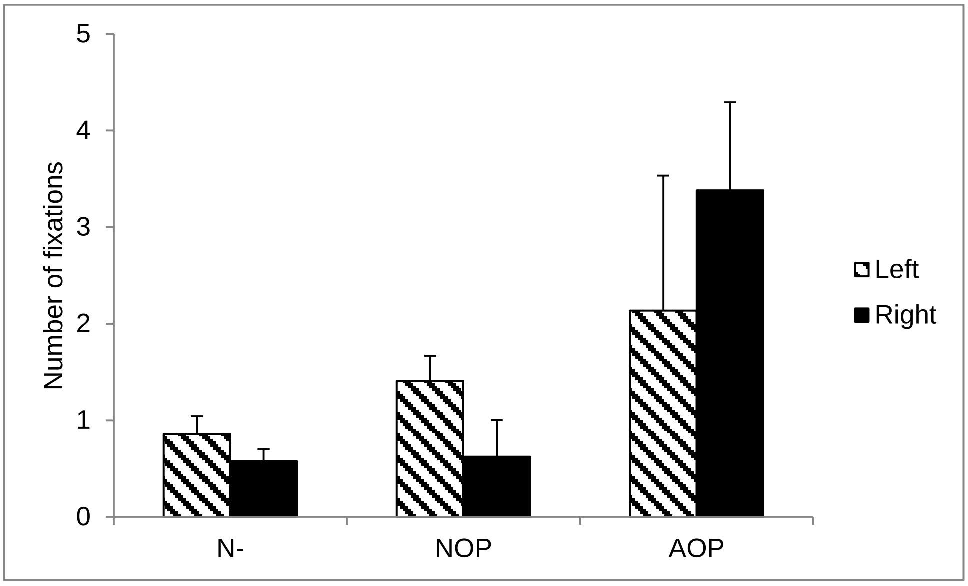
First fixation position. For each item, letter positions were coded by attributing a zero value to the central letter, negative values to the letters on the left (i.e., the letter adjacent to the left of the central letter was coded as -1, etc.), and positive values to letters on the right; first fixation position value was determined using these values. An ANOVA with group (N-, NOP, AOP) as factor and first landing position as dependent measure was run. Although N- and NOP had a similar leftward first fixation position (N- = -0.4; NOP = -0.6) while AOP showed a rightward first fixation position (0.4), the group effect is not statistically significant. Figure 5.14 shows the mean first fixation position after stimulus onset separately for each group of participants.

Figure 5.14. *Experiment 6. Mean position (and standard errors) of the first fixation after the word appearance for each group of patients (N-, NOP, AOP).*



Distribution of fixations on the left- and right-sided letters. The distribution of fixations on the left- and right-sided letters for the three groups of patients is shown in Figure 5.15. A 3x2 ANOVA with group (N-, NOP, AOP) as between factor and side of fixations as repeated factor (left and right) was performed. The main effect of group is statistically significant [$F(2, 17)=48.49$, $p<.00001$] indicating that the AOP group made more fixations than both the N- and the NOP groups (both $ps<.00001$), while the difference between the N- and the NOP is not statistically significant. The other effects and interactions are not statistically significant.

Figure 5.15. *Experiment 6. Mean fixations number and standard errors for left- and right-sided letters of the words separately for each group of participants (N-, NOP, AOP).*



Mean fixation duration. Mean fixation duration of was computed separately for each item and was based on all fixations performed after the stimulus onset and prior to the verbal response. The mean fixation durations were: 415, 372 and 426 ms for the N-, NOP and AOP groups, respectively. An ANOVA with group (N-, NOP, AOP) as fixed factor and fixation duration as dependent measure was run. No significant effects nor interactions emerged.

5.7.3 Comments

Recently, it has been demonstrated that neglect patients who exhibit a reading disorder also have an eye movement deficit (Primativo et al., 2013). Accordingly, results of the present study indicate that those patients who have an oculomotor impairment, as defined using a scene description task (see Experiment 1), also made many reading errors. Conversely, those neglect patients who have a spared eye movement behaviour, are errorless in the reading task. These results thus indicate that an intact eye movement pattern is necessary to correctly read, but also that when it is altered, it causes, in neglect patients, left lateralized reading errors.

5.8 Experiment 7: eye movement pattern in paragraph reading

To further investigate the eye movement pattern and its relation the reading difficulties shown by some neglect patients, in Experiment 7 we adopted a paragraph reading task. This is a very ecological test and it is often part of the screening battery for neglect evaluation (e.g., BIT battery, Wilson, Cockburn, & Halligan, 1987; Pizzamiglio et al., 1989). During text reading, neglect patients may show whole word omissions on the contralesional side of the text, and word-based errors like omission or substitutions of left sided letters within single words (Kerkhoff, Keller, Ritter, & Marquardt, 2006; Friedmann, Tzailer-Gross & Gvion 2011; Rehinart, Keller & Kerkhoff, 2010, Rehinart, Schindler & Kerkhoff, 2011). Here we aim at clarifying the reading pattern, in terms of both errors and eye movements, in neglect patients with and without an eye movement deficit as identified in Experiment 1.

5.8.1 Material and procedure

We generated 5 texts containing an average 21 words each (sd=0.89; range = 20 - 22), and arranged on 5 lines. The 5 texts were matched for length (i.e. number of words), number of syllables and frequency of substantives. The substantives of the text were matched with the words of Experiment 1 for the frequency of use (mean frequency of the texts substantives = 128.1, all p_s>.1). As in Experiment 6 Courier New font and 40 pt letter size were used. After the calibration procedure texts appeared on the screen one at the time. The same order was used for all the participants. Patients were asked to read each paragraph as accurately as possible.

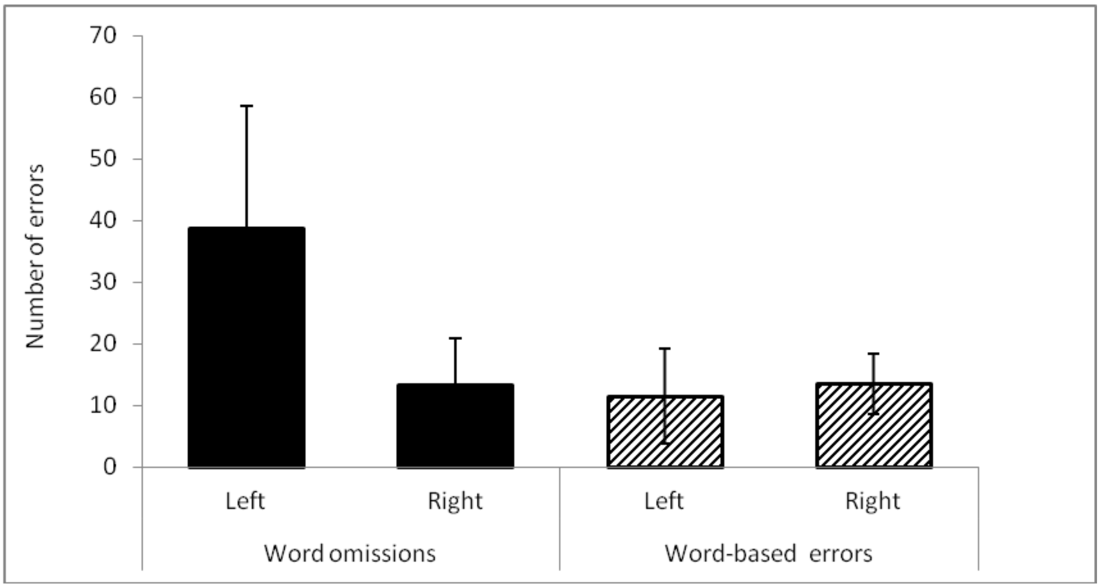
5.8.2 Results

5.8.2.1 Reading errors

We scored errors as omission errors (i.e. whole word omission) and word-based errors (i.e. omission or substitutions of letters within the word). Controls did not omit any words. Only one N- patient (ML) did 4 word-based errors. NOP patients read the paragraphs mostly errorless: only patient BG made one omission error, while all the other patients performed the task at ceiling. AOP patients did many reading errors. Specifically patients

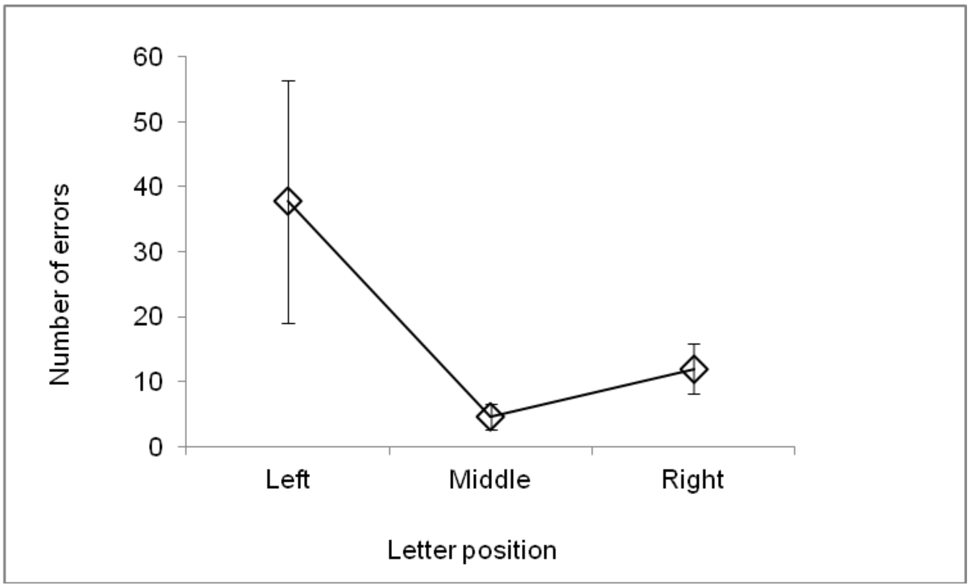
MC, MM, MA and RG made 15, 9, 93 and 98 word omissions, respectively; they also made 57, 14, 16 and 14 word-based errors, respectively. In Figure 5.16 is reported the mean number of text-based and word-based errors in the right and left side of the paragraph for the AOP patients. As shown in the figure, text-based errors are left lateralized (X^2= 98.09, p<.0001) while word-based errors are similarly distributed on the left and right side of the paragraphs (X^2=.98, p =.32).

Figure 16. *Mean number and standard errors of text- and word-based errors on the left and right side of the paragraphs for the four AOP patients.*



To further investigate the word-based errors we made a letter-based analysis, where letter omissions and substitutions were measured separately for the left, middle and right side of the misread stimulus (as we did for the reading errors in Experiment 6). Results are shown in Figure 5.17. As can be seen, the great majority of errors affects left-sided as compared to right sided letters (X^2= 96.55, p<.00001).

Figure 5.17. *Experiment 7: Mean numbers (and standard errors) of letters omitted or substituted in the left, middle and right portion of the words within the paragraphs by the AOP group of patients.*



5.8.2.2 Eye movements

Fixation number, distribution and duration and the number of fixations made for correctly read words was analysed. In the AOP group patients only (since it was the only one making reading errors) the number of fixations made on omitted words (i.e., text-based words) and on misread words (i.e., word-based errors) was separately computed.

Number of fixations. For each patient the mean number of fixations made while reading the five paragraphs has been measured (mean values for each group are shown in table 5.7). Also fixations' distribution has been evaluated. A fixation was considered falling on the left or the right of the text according to its position on the screen as compared to the central pixel coordinate. All fixation having a x coordinate <512 (which was the central pixel in the monitor used for the experiments) where considered on the left, while all fixations having coordinate >512 was considered on the right. A 3x2 ANOVA with group (N-, NOP and AOP) as between factor and number of fixations on the left and the right as repeated factor was performed. A significant main effect of group emerged [$F(2, 17)=11.66$, $p=.0007$] indicating a larger number of fixations made by AOP patients as compared to both N- and NOP patients (both $p_s<.01$). Controls and NOP groups did not show any significant difference ($p=1$). No main effect of fixations' side nor interaction emerged.

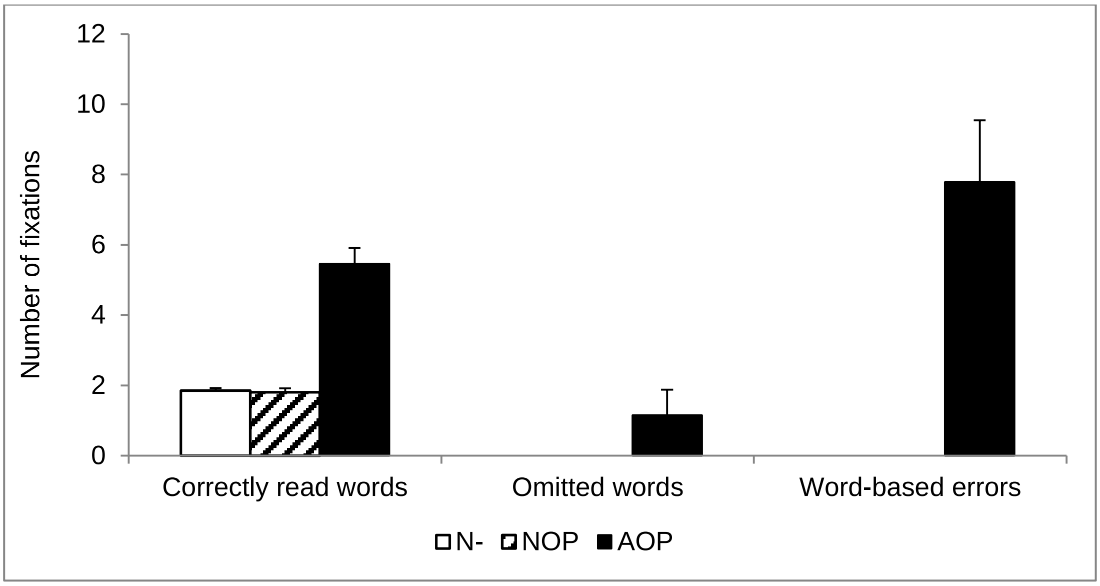
Fixation duration. Mean fixations duration for each group of participants has been measured (see table 5.7). Also fixation duration distribution (left and right) has been evaluated according to the same criteria applied for fixation number. A 3x2 ANOVA with group (N-, NOP and AOP) as between factor and fixation duration on the left and the right as repeated factor was performed. Significant main effects of group [$F(2, 17)=8.18$, $p=.003$], side [$F(1, 17)=10.01$, $p=.006$] and a significant group by side interaction [$F(2, 17)=5.8$, $p=.012$] emerged. The Bonferroni post-hoc indicates that AOP patients had longer fixation duration on the right side of the texts as compared to both N- and NOP patients (both ps<.01). No difference emerged between N- and NOP groups (all p_s >.1).

Table 5.7. *Experiment 7. Mean values (and standard deviations) of fixation number (global, on the left and right) and fixation duration (global, on the left and right) for the three group of patients during text reading.*

Group	Global fixation number	Number of fixations on the left	Number of fixations on the right	Global fixation duration	Fixation duration on the left	Fixation duration on the right
N-	50.7 (7.5)	28.5 (4.0)	22.1 (4.7)	243 (52)	245 (55)	240 (56)
NOP	55.4 (4.2)	31.8 (3.2)	23.6 (2.3)	240 (26)	231 (22)	250 (31)
AOP	118.7 (56.8)	51.6 (46.2)	67.1 (16.3)	360 (46)	305 (44)	374 (43)

Number of fixations on correctly read, omitted and misread words. We measured the number of fixations done by N-, NOP and AOP patients for correctly read words. As shown in Figure 5.18, N- and NOP patients did a similar number of fixations on correctly read words (mean number of fixations: N- = 1.9; NOP = 1.8) Vice versa AOP patients did many more fixations on correctly read words (mean number of fixations = 5.5). The ANOVA analyses confirmed this result, showing a significant main effect of group [$F(2, 17)=137.7$, $p<.00001$]. Differently, omitted words are not fixated by AOP patients (mean number of fixation = 0.5), indicating a direct correspondence between the eye-movement pattern and the [absent] verbal report in AOP patients. Finally we investigated what happens, from an eye-movement point of view, when words are read incorrectly. As shown on the right side of Figure 5.18, in this case words are over-fixated by AOP patients (mean number of fixations = 7.8).

Figure 5.18. Mean number of fixation (and standard errors) for correctly read, omitted and misread words in the three groups of patients.



5.8.3 Comments

Results of the present experiment indicate that the eye movement impairment described in four USN patients during image exploration and during the execution of different saccadic tasks, also determines the two most common types of text reading errors: entire word omissions and letter omissions and substitutions within words. Omitted words are prevalently on the left side of the texts and are not fixated by patients, confirming their difficulty, also seen in Experiments 5a and b, of initiating saccades towards the left. Patients also made a remarkable number of word based errors which are equally distributed on the left and right side of the text and are paralleled by an over-fixation pattern, confirming their difficulty in programming and executing saccade of the correct amplitude (see also Experiments 5a, b and c) which prevent them in accurately extract the needed orthographic information.

5.9 General discussion

In the present paper we deeply investigated the eye movements pattern of 10 patients with neglect and 10 right-side-brain-damaged subjects who served as controls. Firstly we showed that a large part of USN patients (about 40%) have an eye movement deficit. Secondly we demonstrated that the presence of the eye movement deficit is predictive of the reading impairment.

The neglect patients group has been split in two groups according to the oculomotor pattern's similarity (or deviation) from the controls performance during a scene exploration task (Exp. 1). This analysis indicated that 4 out of 10 neglect patients have an eye movement deficit. These same patients, although being able to keep the fixation on a target, are not able to accurately execute horizontal and vertical saccadic tasks (Exp. 3 and 4), or saccadic tasks where target side and eccentricity is manipulated (Exps. 5a and b). Critically, also in the condition where the right hemispace only is tested (Exp. 5c, no side uncertainty), these patients fail in accurately executing the task. Moreover, patients with an eye movement deficit also show a severe reading disorder, making errors in both single words and paragraphs reading. This is in line with what recently found by our research group and reported in the previous study: Neglect dyslexia is the outcome of the concomitant presence of both neglect and a non-lateralized eye movements deficit (Primativo et al., 2013).

Classical theories of neglect dyslexia attributed the reading disorder to a selective impairment in the orthographic representation of words (Caramazza & Hillis, 1990; Hillis et al., 1998). However the eye movements deficit in ND patients described in previous studies (Behrmann et al., 2002, Primativo et al., 2013) and in the present research, support the notion that USN patients who produce left-lateralized reading errors, mainly omissions, have an additional deficit involving the saccade planning and execution. Here we demonstrate that the oculomotor deficit, when present, is generalized and is not task- or stimulus-dependent: It manifests itself in saccadic tasks, reading single words and texts and exploring scenes.

The presence of an eye movement deficit in USN patients apparently contradicts the results obtained by Ptak and colleagues (2009) where the eye movement pattern of USN patients was recorded during an image exploration task. Ptak et al. (2009) reported that, although looking preferentially toward the right hemispace, USN patients' fixations were accurate, falling on the relevant part of the image. Our previous investigation (Primativo et al., 2013) and the present study indicate that out of the 21 USN patients tested, 38% of them showed an eye movements impairment. These patients are also those who suffer from neglect dyslexia and, given the big effort made during the calibration phase, we are aware that these are not the best candidates for eye-tracker studies. Ptak et al. (2009) tested 7 USN patients and the reading performance of the tested patients is not reported, so it is possible that the included patients fall within the USN group of patients without ND. The absence of an eye movement deficit in Ptak et al.'s results (2009) may be due to the low sample size or to the intrinsic difficulty in testing these patients with the eye-tracker.

Why do some USN patients show an eye movement disorder while others do not? Although we believe that an anatomical study is required, some speculations are possible. In 1998, Leibovitch, Black, Caldwell, Ebert, Ehrlich and Szalai have shown that the inferior parietal cortex, which contains the parietal eye fields, is compromised in 38% of the patients with USN. This area is involved in integrating visual information from both the dorsal and the ventral stream with motor information (Fogassi & Luppino, 2005). A central part of its activity is dedicated to the orienting and maintenance of spatial attention and the generation and control of saccadic eye movements (Goldberg, Bisley, Powell, & Gottlieb, 2006; Bisley 2011; Ptak & Muri, 2013). However, when considering the cortical gaze control, it is fundamental to consider that not only some specific brain areas are involved, but a large sub-cortical network also plays an important role (Anderson, Jones, O'Gorman, Leemans, Catani, & Husain, 2012). Anderson and colleagues (2012), indeed, combined the fMRI technique - which gives a very good idea of the brain areas involved during a saccadic task - and a MRI-based tractography - which enables researchers to visualize large-scale connectivity maps. This technique helped in clarifying not only the role played by frontal, supplementary and parietal eye fields, but also the white matter pathways connections between these areas. Specifically, Authors described a connection between the frontal and the supplementary eye fields, and another connection between the frontal eye fields and inferior parietal lobe; both connections have also shown to be right hemisphere dominant (Anderson et al., 2012).The 38% of USN patients have a lesion involving the inferior parietal lobe as described by Leibovitch et al. (1998). This alone may explain the presence of an eye movement deficit in 40% of the USN patients (Lee et al., 2009). However, it is highly plausible that different brain lesions, involving not only the cortical areas controlling the planning and execution of saccadic eye movements, but also the fibre bundles connecting these areas (Anderson et al., 2012) may be at the origin of the eye movement disorder found in a large percentage of neglect patients.

Such a large number of patients with an eye movement deficit needs to be clearly diagnosed and differentiated from others patients who do not have the disturbance. While patients with neglect without an eye movement deficit may benefit from a training in visuo-spatial conscious strategies, this may not work when an additive eye movement deficit is present. A specific rehabilitation may thus be taken into account. For example, Daini, Albonico, Malaspina, Martelli, Primativo, & Arduino, (2013), used the optokinetic stimulation (OKS) in a patient affected by USN and an eye movement deficit, which caused her letter omissions in a single word reading task. The OKS technique, having the advantage of acting directly on the oculomotor exploration behaviour, actually reduced the number of errors in this patient (Daini et al., 2013). A similar result has been reported for entire word omissions in texts reading, significantly reduced after OKS (Kerkhoff et al., 2006; Reihnart et al., 2011). This results are also in accordance with meta-analytic approaches aiming at evaluating the rehabilitation effects (Rohling, Faust, Beverly, & Demakis, 2009) which showed that gains are moderate and domain specific, calling for selective deficit that specifically need to be taken into account in designing the treatment (see also Rossetti & Rode, 2002; Luauté, Halligan, Rode, Rossetti, & Boisson, 2006; Kerkhoff & Schenk, 2012).

In conclusion, in the present study, we claim that some neglect patients (roughly 40%) have an eye movement deficit, which impairs both reading and scene exploration and needs to be carefully taken into account during the diagnostic and rehabilitation phases.

6. General conclusion

In the present PhD thesis my focus has been on reading, one of the highest cognitive functions belonging exclusively to humans. Using psychophysical and eye-tacking paradigms I investigated normal and impaired mechanisms contributing to the reading process. In the first part of the thesis normal readers have been studied in order to better understand the role exerted by different factors in modulating reading rate. It has been demonstrated the enormous limit exerted by visual factor, like visual masking, and the bottleneck represented by the necessity of executing eye-movements while reading. Also, the role of other higher-level cognitive factors have been proven to increase reading rate, like the presence of a context, or to decrease it, like the number of words exceeding the working memory span. Overall, results from the first study reconcile the differences in reading speed measures obtained from different laboratories providing an estimate of the weight of the various cognitive components and provide suggestions for targeting different components that contribute to reading rate.

In the second part of the thesis, the focus has been on a reading disorder, i.e., neglect dyslexia. Specifically the role of eye movements in interaction with unilateral spatial neglect has been deeply studied in order to understand basic components of the reading disorder. To this aim and throughout many reading, saccadic, and scene exploration experiments, it has been systematically shown that the reading disorder in neglect patients is the outcome of the presence of a specific damaged mechanism: an eye-movement deficit. Such a deficit prevents neglect patients in accurately read words, pseudo-words and texts, but also in adequately explore and describe an image. The importance of taking into account such an additive deficit for the diagnostic and rehabilitation phases has been presented.

7. References

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