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HELLO FROM THE OTHER SIDE:

A NEUROPSYCHOLOGICAL, BEHAVIORAL AND COMPUTATIONAL EXPLORATION OF HEMISPHERIC ASYMMETRIES IN READING.

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A mio padre.

Abstract

The dominance of the left cerebral hemisphere (LH) over the right one (RH) for reading is widely recognized in the domain of cognitive neuroscience. However, it is still not clear whether such dominance is underlaid by a complete word blindness of the RH (*absolute* LH dominance) or by poorer/weaker lexical representations in the RH than in the LH (*relative* dominance). According to the first account, reading should be impossible when the visual word form system of the LH is lesioned and both afferent and efferent connections with the rest of the LH are interrupted by the lesion. Also, according to this account, hemispheric differences in lateralized reading in healthy subjects are explained by greater sensitivity of the RH than the LH to pre-lexical orthographic processing factors. According to the framework advocating a *relative* LH dominance for reading and suggesting poorer lexical orthographic abilities of the RH than the LH, reading should be possible even in case of lesion and disconnection of the LH reading system, although limited to frequent and/or concrete words. Accordingly, hemispheric differences in lateralized reading in healthy subjects should be explained by lexical-semantic factors.

The predictions of these models were tested by means of a behavioral and structural disconnectome study on a patient with Pure Alexia, and two divided visual field reading studies (conducted on healthy right-handed and left-and right-handed subjects, respectively) in which pre-lexical and lexical factors were manipulated. Evidence of residual reading abilities in case of a LH visual word form system lesioned with both afferent and efferent connections with the rest of the LH being interrupted, together with evidence of a lexical effect accounting for visual field/hemisphere differences in lateralized reading supported the view of a *relative* LH dominance, according to the idea of the existence of a poorer/weaker orthographic lexicon in the RH. A computational modelling study conducted to simulate the development of orthographic representations in the two hemispheres suggested that weaker orthographic representations in the RH than in the LH -giving rise to such *relative* LH advantage for reading-could be due to inefficient consolidation of orthographic knowledge in the RH.

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Chapter 1

Is the dominance of the left hemisphere for reading *absolute* or *relative*?

The dominance of the left cerebral hemisphere over the right one for reading has become apparent since the first anatomo-clinical descriptions of the late XIX century. However, it is still not clear whether this dominance is *absolute* (i.e. the right hemisphere does not contain any orthographic representation), or *relative* (i.e. the right hemisphere contains fewer and/or weaker orthographic representations than those of the left hemisphere). In this opening chapter, I will describe how the dominance of the left hemisphere over the right one for reading has been defined through anatomo-clinical descriptions, divided visual field methodologies, and contemporary neuroimaging techniques.

Finally, two neurocognitive models of reading in the two hemispheres supporting either the *absolute* or the *relative* view of left hemisphere dominance in reading will be described and discussed.

The dominance of left hemisphere for reading: classical and modern neuropsychological evidence.

The dominance of the left cerebral hemisphere (LH) over the right hemisphere (RH) for reading has become apparent since the earliest breakthroughs of the cognitive neuroscience of reading (for a historical perspective, see Henderson, 2019). However, while the efficiency of the LH in providing an interface between printed words, linguistic sounds and meanings has not been challenged during the history of cognitive neuroscience, there has been much less consensus on the role played by the RH in this LH dominance. One possibility is that the RH is completely "word blind", i.e., it completely lacks representations of orthographic stimuli. In this case, to use a wording borrowed from Rutherford & Lutz (2004)[1], LH dominance would be *absolute* (see also Coltheart, 1980). Alternatively, the RH could contain a limited and/or weaker set of orthographic representations. In this case, LH dominance over the RH for reading would be *relative*.

In what follows, the neural correlates of reading will be reviewed in a historical perspective and discussed according to the *absolute* vs. *relative* frameworks of LH dominance.

Early anatomo-clinical correlations.

In the XIX century, Jean-Baptiste Bouillaud introduced the anatomo-clinical neuropsychological paradigm, that allowed to infer the association between specific brain areas and high order psychological functions through the joint observation of specifically impaired aspects of cognition and brain lesions (Graves, 1997). This localizationist approach allowed Nadine Skwortzoff (1881) to associate word blindness to lesions of the angular gyrus of the left hemisphere. In line with Skwortzoff's intuition, Dejerine (1891) revealed (in a post-mortem examination) tissue softening at level of the left angular gyrus in a case of a 63-year-old man who had lost the ability to read and write. One year later (1892), Dejerine described the case of a 68-year-old man who had 2 strokes: the first one caused "pure alexia" (without agraphia),

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[1] This dichotomy has been introduced by Rutherford & Lutz (2004) as a framework to interpret the greater processing costs for orthographic stimuli initially targeting the RH, as compared to those initially targeting the LH. In this thesis, the concepts of "absolute" and "relative" dominance will be generalized, in order to indicate a LH dominance model based on the complete inability of the RH to read, and a LH dominance model based on poorer reading abilities in the RH, respectively.

while the second one caused alexia with agraphia. The first lesion involved the cuneus, the lingual gyrus, the fusiform gyrus and the posterior part (splenium) of the corpus callosum. The second stroke caused a lesion involving the left angular gyrus. Dejerine concluded that a lesion involving the left angular gyrus disrupts the “visual images of the letters”, causing alexia with agraphia. Conversely, a lesion involving a “common visual region” does not cause a loss of the “visual images of the letters”, that can be effectively retrieved in the voluntary act of writing. Rather, this lesion disconnects the angular gyrus from visual input, so that the “visual images of the letters” simply cannot be activated. The result is pure alexia (without agraphia). According to Dejerine (1892), at the level of primary visual cortices (in both hemispheres), written letters are not different from any other generic pictorial stimulus (such as a drawing). For this generic pictorial stimulus to activate the “idea of a word”, transfer of information to the left angular gyrus (likely mediated by white matter tracts) is necessary, at least in right-handed subjects.

In these descriptions, the sufficiency of a LH brain lesion to cause reading deficits was apparent, whereas no critical role in reading seemed to be played by the RH. Indeed, the sparing of the right hemisphere was clearly indicated in Dejerine’s 1892 report. However, despite its sparing, the RH could not compensate for the reading impairment due to the LH lesion in Dejerine’s patient. The emerging picture from these anatomo-clinical accounts is thus that of an *absolute* dominance of the LH over the RH for reading, whereby the RH would not play any role in reading.

From split-brain patients to the “right-hemisphere hypothesis” in deep dyslexia and pure alexia.

The introduction of commissurotomy as a surgical treatment for drug-resistant epilepsy in the 60s (Bogen, Fisher & Vogel, 1965) opened a new era for the neuropsychology of hemispheric differences in cognition. The introduction of the “divided visual field” or “half-field” paradigm (reviewed in detail below) allowed to take advantage of the crossed projections from the visual fields to the primary visual cortices (Figure 1.1) to target each disconnected cerebral hemisphere separately (Gazzaniga, Bogen & Sperry, 1965).

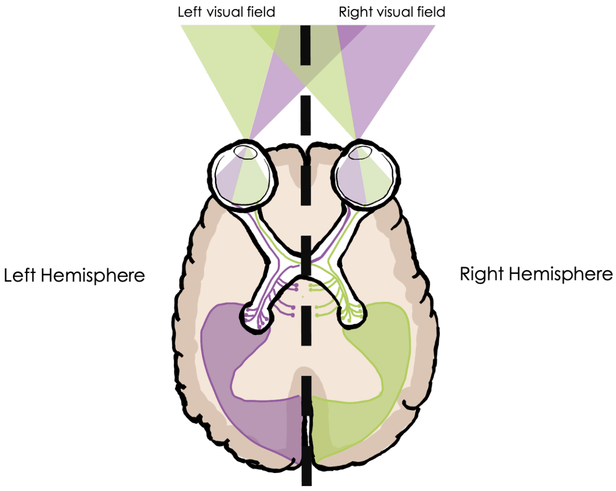

Figure 1.1 | Schematic representation of the crossed arrangement of the visual system.

These pioneering studies confirmed the dominance of the LH over the RH for reading and language in general (Gazzaniga & Sperry, 1967). Remarkably, they also suggested that the RH may not be completely "word-blind". Indeed, these studies highlighted that although the RH has poorer phonological and semantic abilities than those of the LH (Levy & Trevarthen, 1977), it can recognize nouns (Gazzaniga & Hillyard, 1971) and provide lexical decisions (i.e. deciding whether an incoming orthographic stimulus is a word, e.g.: "HOME" or not, e.g: "HOFE") significantly better than chance level (Baynes, Tramo & Gazzaniga, 1992). The RH would rely on an "orthographic vocabulary" different from that of the LH (Reuter-Lorenz & Baynes, 1992). More in general, according to Zaidel & Peters (1981), the RH would process orthographic input in a holistic manner and -differently from the LH- without any phonological mediation.

These features of RH reading described in split-brain patients suggested that reading attempts of the RH might also underlie the (limited) reading abilities of patients with acquired "deep dyslexia". This syndrome is characterized by a severe impairment of reading via association between print and sound (phonological route; Coltheart et al., 2001), to such an extent that reading unknown words (pseudowords) is impossible. Remarkably, reading can be spared for concrete nouns (Marshall & Newcombe, 1973). A peculiar feature of this reading syndrome is that it is also frequently associated with semantic *paralexias* (e.g.: reading "violin" when the target word is “saxophone”). Given the vast LH lesion causing this syndrome[2] and thus the unlikely contribution of the LH in the spared reading abilities of patients with deep dyslexia, Coltheart (1980; 2000; see also Saffran et al., 1980) suggested that the reading phenomena described in deep dyslexia arise from the RH attempting to read[3]. Similarly, Landis and colleagues (1983) interpreted the emergence of semantic errors as due to a lesion-based reduction of the interhemispheric inhibition exerted by the LH towards the RH.

The RH has also been hypothesized to mediate implicit reading phenomena in pure alexia. In brief (this topic will be explored in detail in the next chapter), patients with pure alexia show a selective reading impairment due to a posterior LH brain lesion. These patients, that may be fully unable to recognize even single letters or -in some cases- be characterized by the use of an extremely effortful and time-consuming letter-by-letter reading strategy, often show the surprising ability to classify orthographic input above chance level according to lexical (i.e. lexical decision) or semantic (i.e. semantic decision) features (Coslett & Saffran, 1989). In line with the “right hemisphere hypothesis” of deep dyslexia, it has been proposed that such implicit reading abilities in pure alexia could be a manifestation of the RH reading abilities (Coslett & Saffran, 1989, 1994; Saffran & Coslett, 1998).

The scenario portrayed by this set of studies thus tips in favor of a *relative* dominance of the LH over the RH for reading: the LH would normally overshadow the RH in reading due to a combination of poorer (although existing) orthographic processing abilities of this latter and a direct inhibition from the LH to the RH (Landis et al., 1983; see also Cook, 1984 and Van der Knaap & Van der Ham, 2011).

However, in case of a brain lesion impairing the LH, the limited RH reading abilities would be the only set of available cognitive resources to process orthographic information, giving rise to the reading phenomena described in deep dyslexia and pure alexia.

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[2] Anatomical descriptions of brain lesions were obtained through Computerized Tomography and structural Magnetic Resonance Imaging (MRI).

[3] For a critical analysis of this approach, see Patteron & Besner, 1984.

Divided visual field studies and the lateralization of reading in healthy subjects.

Divided visual field techniques, massively adopted for the study of the lateralization of cognitive processes in split-brain patients, have been used to explore laterality also in healthy subjects. This set of methods takes advantage of the fact that neural projections from the nasal hemi-retinae cross at the level of the optic chiasm, and therefore a stimulus projected to one half of the visual field is first processed by the contralateral hemisphere (Bourne, 2006). Inferences on lateralization of a cognitive process are done basing on the behavioral differences evoked by stimuli presented in the two opposite hemifields (see Figure 1.2 for an example of divided visual field paradigm).

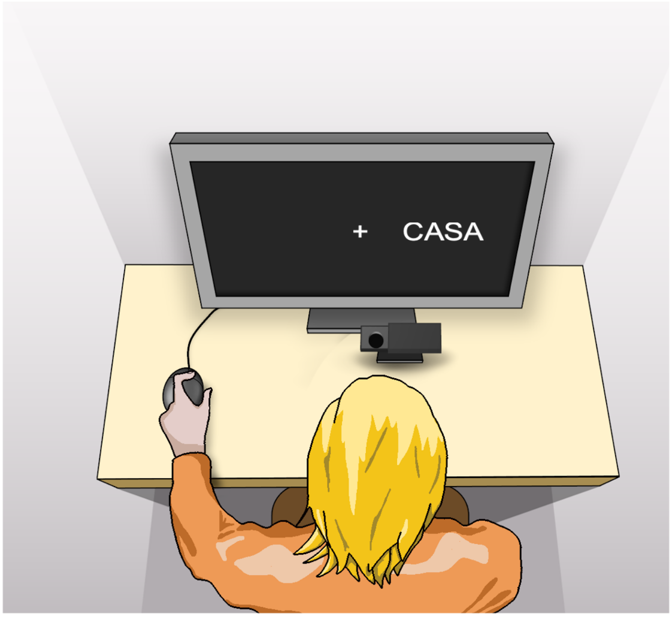

Figure 1.2 | Example of divided visual field paradigm applied to reading. If the central cross is being fixated, a stimulus presented in the RVF is projected in the right nasal hemiretina and in the left temporal hemiretina. Due to decussation of the nasal hemiretinae, visual information of the stimulus targets the left visual cortex.

Given that most of the empirical work developed in this thesis relies on divided visual field techniques, in what follows the technical features of divided visual field paradigms will be briefly reviewed and results on divided visual field studies of reading will be summarized. As the reader will notice, these extensively adopted paradigms have provided promising yet inconclusive evidence on the reading capabilities of the RH in healthy participants.

Key features of divided visual field paradigms

Given the necessity of targeting the two different cerebral hemispheres through visual stimulation, the first crucial requirement in divided visual field studies is lateralized projection of visual stimuli, in order to avoid targeting (at least in the earliest phases of processing) both hemispheres during a given experimental trial. It has been considered "safe" to present stimuli with their internal edge located 2.5°-3° laterally from the vertical midline (Bourne, 2006)[4].
Of course, if volunteers move their eyes to fixate the target at the center of their visual field, the target can become available to both hemispheres, thus making it impossible to explore any laterality effect. Therefore, minimizing eye-movements is fundamental as well. For this reason, stimuli are typically presented briefly enough to avoid saccades[5]. The use of short presentation times does not, however, rule out the possibility that subjects can -by chance- produce eye movements before stimuli presentation. For this reason, eye-fixation-control approaches have been developed. The so-called "indirect" techniques for fixation control involve the introduction of a secondary task that requires the subject to verbally report a digit or a number flashed at the center of the screen prior to presentation of the lateralized stimulus (Belger & Banich, 1998; Bourne & Hole, 2006; Leehay et al., 1978; Luh & Levy, 1995). As an alternative, "direct" techniques involve monitoring the participant's eyes and presenting the test stimulus when the participant's eyes are in a desired location. This monitoring can be accomplished either via experimenters' inspection (e.g., Deruelle & de Schonen, 1998; Marzi & Berlucchi, 1977; Mohr et al., 1994), or via eye-tracking (e.g., Christman, 1990; Hardycket al., 1985, Jordan & Patching, 2003). A more general requirement of divided visual field studies, which is reasonably common to all studies targeting laterality, is to limit the experimental sample to

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[4] Early reports suggested the existence of an area of bi-hemispheric projection close to the midline (Stone, Leicester, & Sherman, 1973), estimated between 0.5° (Wyatt, 1978) to 3° of the visual field (Bunt, Minckler, & Johanson, 1977). More recent data have suggested that the fovea could be split vertically in two halves, with each half projecting to the contralateral hemisphere (Lavidor & Ellis, 2003). However, this proposal has been criticized by evidence of bi-hemispheric projection of stimuli presented foveally (Lindell & Nicholls, 2003).

[5] Saccadic latencies have been estimated between 150 ms and 200 ms (Carpenter, 1988). Although stimuli presentation for 200ms in divided visual field paradigms has been considered acceptable in the past (Young, 1982), it has been more recently proposed that stimuli should not be present on the screen for more than 180 ms (Bourne, 2006).

subjects characterized by an overall comparable hemispheric dominance pattern (Bourne, 2006) to avoid that hemispheric differences in a specific cognitive function could be modulated by subjects' overall functional lateralization pattern (unless the specific goal of the study is precisely comparing populations characterized by different laterality patterns). One practical, although not necessarily accurate, way to accomplish this is to consider hand preference: it was observed that over 95% of right-handed subjects show a LH lateralization for language, whereas such percentage is about 76% in left-handed subjects (Pujol et al., 1999; see also Branch, Milner & Rasmussen, 1964).

Divided visual field paradigms and reading in healthy subjects

The combination of reading tasks with the divided visual field approach has provided a promising tool for the study of the lateralization of reading and the reading capabilities of the RH in healthy subjects. The face validity of this methodology has been proved by the fact that, consistently with the LH dominance for reading described in the neuropsychological domain, the vast majority of lateralized reading studies on healthy subjects has converged in identifying an advantage for word stimuli projected to the Right Visual Field (RVF), and therefore, first processed by the LH, compared to stimuli projected to the Left Visual Field (LVF) and first processed by the RH (see for instance Leiber, 1976; Babkoff & Ben-Uriah, 1983; Chiarello, Senehi & Soulier , 1986; Hernandez, Nieto & Barroso, 1992; Chiarello et al., 2005; Willemin et al., 2016; De Clercq & Brysbaert, 2020). However, unlike divided visual field data obtained from split-brain patients, the interpretation of an RVF/LH reading advantage on the LVF/RH for data obtained from healthy controls is not straightforward, as at least two different functional brain models could generate this pattern.

Indeed, healthy subjects -unlike split-brain patients- do not have their hemispheres structurally and functionally separated from each other. Hence, worse performance for stimuli presented to the LVF/RH (compared to those presented to the RVF/LH) could either be explained by a *direct access* to a poor reading system in the RH, or by a *callosal relay model*, whereby the RH provides no contribution in reading and performance worsening is due to inter-hemispheric transfer via the corpus callosum (Eviatar, Menn & Zaidel, 1990)[6]. These two frameworks assume a *relative* and an *absolute* LH dominance for reading, respectively. However, although a *relative* LH dominance model has been extensively adopted in the literature (explicitly or implicitly) as a functional brain model underlying the RVF advantage (e.g., Day, 1977; Babkoff & Ben-Uriah, 1983; Chiarello, Senehi & Soulier, 1986; Waldie & Moseley, 2000; De Clercq & Brysbaert, 2020), divided visual field reading data have also been provided in support to an *absolute* account of LH dominance in reading (see for instance Ellis, Young & Anderson, 1988; Olk & Hartje, 2001;Whitney & Lavidor, 2005). Interestingly, contemporary studies suggest that a divided visual field reading tasks can be effectively adopted to measure functional hemispheric dominance for reading and language in general, as laterality estimations obtained with this set of techniques correlate with those obtained by more complex and expensive functional brain imaging methods (e.g., Hunter & Brysbaert, 2008; Van der Haegen et al., 2011; Haussmann et al., 2019). However, somewhat surprisingly, most of the studies advocating the extensive use of divided visual field techniques to measure hemispheric asymmetries in reading and in language do not overtly indicate the functional brain model meant to generate the RVF/LH advantage.

To sum up, divided visual field techniques provide a method for the behavioral exploration of laterality effects in reading. However, despite a RVF/LH advantage over the LVF/RH has been consistently described, both a functional brain model supporting an *absolute* LH dominance and a model supporting a *relative* advantage have been adopted to explain this effect. This topic will be discussed in Chapter 3.

The contribution of functional neuroimaging.

The introduction of functional neuroimaging techniques has allowed fine-grained localization of cognitive functions in healthy subjects, thus providing a link between cognitive psychology

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[6] See Whitney (2001) for an interpretation of the locus of hemispheric differences in lateralized reading still not involving direct access to RH word representations but emphasizing, rather than the costs of inter-hemispheric transfer, a greater cost of letter position encoding for stimuli falling in the LVF/RH than for stimuli falling in the RVF/LH.

and neuropsychology. Also, by studying healthy subjects, such localization effort was not hampered by the presence of confounding effects such as possible functional brain reorganization due to lesions (Price, 2012). In what follows, the main contributions of functional neuroimaging towards the definition of the functional anatomy of the "visual word form system" will be reviewed. Earlier studies tipped in favor of an *absolute* LH dominance. More recent studies have partially reconsidered this position.

A "visual word form system" in the brain

In 1988, Petersen and colleagues observed that perception of visual word forms was associated with cerebral blood flow (after subtraction of the response evoked by the presentation of a fixation point) in extrastriate regions of both hemispheres. In 1990, the same group (Petersen et al., 1990) observed that the activity of the left medial extrastriate cortex was associated with the processing of words and pronounceable pseudowords (i.e., obeying to grapheme-phoneme conversion rules), and not with unpronounceable strings of letters or strings of letter-like forms. In addition, the left frontal cortex was described as more active during word reading, if compared to pseudoword reading. Subsequent studies proposed a greater functional brain network involved in reading, including the posterior portion of the left middle and superior temporal gyri (Howard et al., 1992; Small et al., 1996), the left angular gyrus (Menard et al., 1996) and the left ventral regions located at the interface between occipital and temporal areas (Kiyosawa et al., 1995). A few years later, a strong functional association between orthographic processing and the activity of a left ventral occipito-temporal complex was proposed (Cohen et al., 2000). The authors presented word reading and non-word detection tasks to healthy controls and to patients with a disconnection of the posterior part of the callosum with a divided visual field presentation, during functional Magnetic Resonance Imaging (fMRI) scanning and Electroencephalography (EEG). Activation in the left middle portion of the left fusiform gyrus identical for stimuli projected in the LVF and RVF was detected, together with a left unilateral infero-temporal negative electrophysiological component peaking 180-200ms after stimulus presentation. At the same time, in patients with posterior callosal disconnection this set of areas was only activated by RVF stimulation. This set of observations led the authors to identify this left ventral occipito-temporal complex as the "visual word form area" (see also Cohen et al., 2002). Although the functional specificity of this "visual word form area" has been questioned (see for instance Price & Devlin, 2003), a considerable amount of converging evidence has brought support to the idea that this set of regions is a crucial hub for orthographic processing (Paulesu et al., 2000; Dehaene et al., 2002; Kronbichler et al., 2004; Devlin et al., 2006; Dehaene et al., 2010) and in particular for the extraction of the statistical regularities of the word forms (Wandell. 2011), with a posterior-anterior hierarchy of responsiveness towards letters, orthographically regular letter strings and pseudowords, and whole words (Dehaene et al. 2005; Vinckier et al., 2007; Glezer et al., 2009).

At the same time, functional neuroimaging studies also allowed the description of the neural correlates of accessing the lexical orthographic and semantic representations of a known word, and of reading unknown words through grapheme-to-phoneme mapping rules (reading via a lexical-semantic reading route, and via a phonological decoding route, respectively; see for instance Herbster et al., 1997; Paulesu et al., 2000; Mechelli et al., 2005; Danelli et al., 2015).

As neuroimaging-based meta-analytical techniques became available, from this wide set of findings, a clearer overall picture was described. In a meta-analytical work on 35 neuroimaging studies of reading, Jobard and colleagues (2003) dissociated (a) a lexical-semantic reading route involving the anterior portion of the left ventral occipito-temporal complex, the posterior middle temporal gyrus, and the triangular part of inferior frontal gyrus, and (b) a non-semantic route directly binding orthography and phonology, involving left-lateralized superior temporal areas, the supramarginal gyrus, and the opercular part of the inferior frontal gyrus. In a similar vein, the meta-analytical work by Taylor, Rastle & Davis (2013) revealed clusters associated with orthographic analysis in left occipito-temporal regions, lexical-semantic processing (also known as the "ventral-route") in the anterior fusiform and middle temporal gyri, grapheme-phoneme conversion in the inferior parietal cortex (the so-called "dorsal route"), and phonological output resolution in the inferior frontal gyrus (see Figure 1.3).

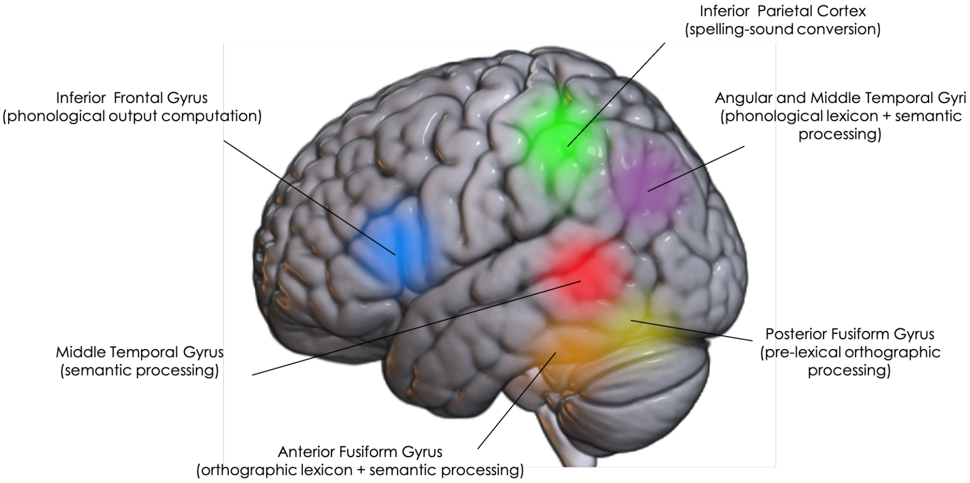

Figure 1.3 | Meta-analytical functional anatomy of the reading network. Adapted from Taylor, Rastle & Davis (2013).

Functional neuroimaging and reading in the right hemisphere

No significant role in functional brain models for reading is seemingly played by the RH (Jobard et al., 2003; Taylor, Rastle & Davis, 2013). Accordingly, the picture portrayed by the seminal works on the functional neural correlates of the "visual word form system" (Cohen 2000, 2002) is that of a strongly *absolute* dominance of the LH over the RH for reading. Also, the "visual word form area" has been described as responsive for orthographic stimuli projected to either visual field. This latter evidence tips in favor of a *callosal relay* explanation of divided visual field studies of reading (Cohen et al., 2002), with the RH being substantially word-blind. However, in the neuroimaging literature, it is not uncommon to come across some RH activation foci in reading experiments, although their functional significance is not clear (Turkeltaub et al., 2002; Taylor, Rastle & Davis, 2013; Cattinelli et al., 2013). Activation foci located in the RH can also be observed by running an automated meta-analysis using Neurosynth (Yarkoni et al., 2011) using the keyword "reading" (see Figure 1.4)

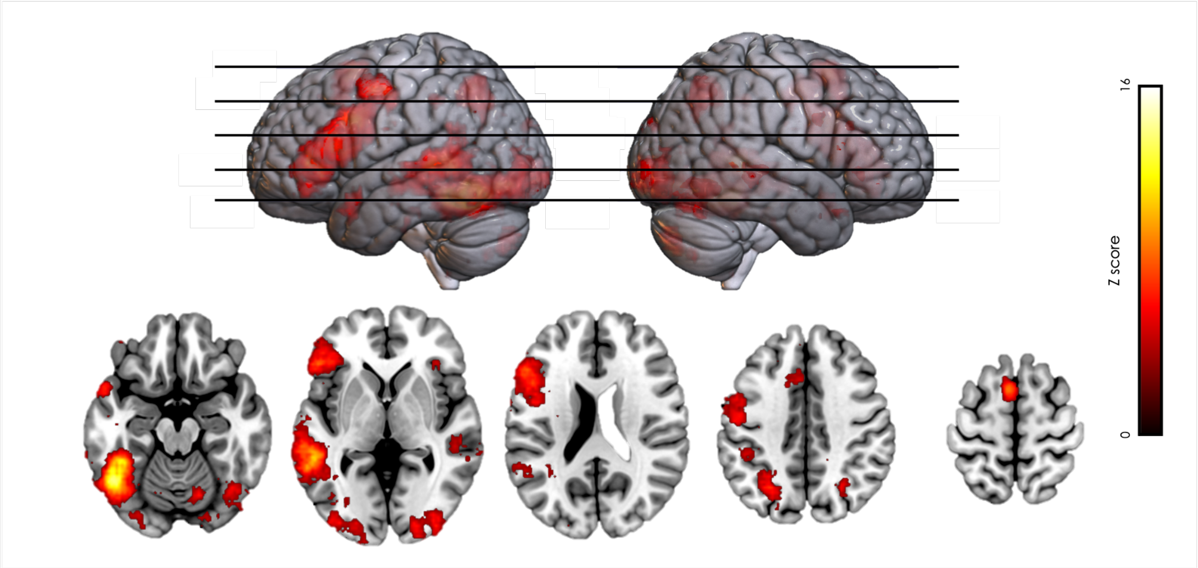

Figure 1.4 | Results of an automated meta-analysis (association test, $p < 0.01$ FDR-corrected) conducted with Neurosynth (Yarkoni et al., 2011, https://neurosynth.org/) using the “reading” keyword. The colour bar indicates z scores.

It is worthy to note that, at least to some extent, an *absolute* LH dominance for reading could be explained by statistical power and thresholding in neuroimaging studies: the RH, being less active than the LH during reading tasks, may simply not succeed in “surviving” statistical thresholding (for a similar interpretation of threshold-dependent functional laterality patterns, see Cabeza, 2002), and this could be particularly true in experimental designs involving samples with low numerosity.

On the other hand, the same principle of interhemispheric cross-inhibition derived from the neuropsychological domain (Landis et al., 1983; see also Patterson & Besner, 1984; Cook, 1984 and Van der Knaap & Van der Ham, 2011) could also apply to functional imaging: the activity of a healthy LH could inhibit the activity of the RH for reading. Accordingly, it was shown that in a patient who underwent surgical removal of a left occipito-temporal neoplasm, the intact RH homologue of the “visual word form area” showed an activation pattern similar to that of the “visual word form area” proper, such as stronger activation for alphabetic strings than for chequerboards (Cohen et al., 2004; see also Cohen et al., 2003 and Henry et al., 2005), suggesting that orthographic stimuli (at least letters) are processed in high-level ventral visual cortices devoted to object recognition also in the RH. According to Cohen and colleagues

(2004), a LH dominance would emerge as such processing is contrasted with visual stimuli of increasing complexity.

Also, from a methodological point of view, targeting the activity of the RH may require the use of divided visual field techniques. Indeed, Rauschecker and colleagues (2012) observed that the "visual word form area" and its RH homologue are both more active for lateralized stimuli presented contralaterally than for stimuli presented ipsilaterally (although the left visual word form area is also active for ipsilateral stimuli). The authors proposed that two hemispheres independently process orthographic input coming from opposite hemifields from primary visual cortices to the two contralateral visual word form areas, and then information reaches language regions[7]. In case of RH processing, this pathway could include either direct connections to language areas, or indirect connections mediated by the left visual word form area.

This interpretation suggests that LH dominance for reading could be an emerging property, resulting from the interaction between visual decoding and more general processes (e.g. spoken language) whose lateralization develops prior to that of reading. Accordingly, it was shown that the neural correlates of reading co-lateralize with those of spoken language (Cai et al., 2008), and have opposite lateralization relative to those of face processing (see for instance Brederoo et al., 2020; Gerrits et al., 2019). In particular, based on the similarities between the neurofunctional underpinnings of word (left fusiform gyrus, see for instance Cohen et al., 2000) and face processing (typically localized in the right fusiform gyrus, see for instance Kanwisher & Yovel, 2006; see also Sorger et al., 2007), it was proposed that words and faces compete for representational space in high-order visual areas as reading skills are being acquired, and -to minimize connection length with language areas (which are already lateralized prior to schooling; see for instance Sowman et al., 2014)- LH ventral occipito-temporal areas become tuned to represent words (Plaut & Behrmann, 2011; Behrmann & Plaut, 2015). Due to competition with word representations in the left occipito-temporal region, face representations, that were initially bilateral, become more lateralized to the right fusiform region. Accordingly, lateralization for word processing, would be *graded*, triggered by the necessity of connecting visual and linguistic processes, with regions being "optimized for" -rather than "dedicated to"

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[7] Data from the magnetoencephalographic study by Chu & Meltzer (2019) have provided partial support for this claim, by suggesting that intra-hemispheric information transfer in divided visual field reading tasks takes place both at very early stages of visual processing and at the level of the left visual word form area and its right homologue.

orthographic processing (Plaut & Behrmann, 2011; Behrmann & Plaut, 2015; see also Dehaene & Cohen, 2007; Taylor, Davis & Rastle, 2019).

In conclusion, contemporary neuroimaging data suggest that LH dominance over the RH for reading could be more *relative* than anticipated by earlier studies, resulting as the outcome of a learning process progressively wiring visual and linguistic processing mechanisms. Nevertheless, the neurofunctional (not to mention the cognitive and behavioral) correlates of an alleged "right visual word form system" remain elusive.

Does the RH have lexical orthographic representations?

Neuropsychological, behavioral, and neurofunctional studies all suggest that the RH could be involved in reading, at least in case of a brain lesion involving the LH. This raises the question of whether the RH contains (just as the LH) a set of proper stored orthographic representations (a "vocabulary").

What is an (orthographic) lexicon?

In psycholinguistics and neurolinguistics, this "vocabulary" is named *lexicon* (for a historical perspective, see Coltheart et al., 2001). According to Coltheart (2004), a lexicon is "*a system of local mental representations, the elements in such a system representing stimulus forms in one particular representational domain*", with these "representational domains" being phonological, pictorial, and orthographic. The idea of a neurocognitive "dictionary" containing representations for words is traced back to Wernicke (1874), who assumed the existence of a component referred to as the "*wortschatz*" ("treasury of words"). In the 20th century, this idea was reintroduced by Anne Treisman (1961), and refined by Morton (1961), who distinguished between a "cognitive system" and a system of knowledge about word forms "logogen system". According to Morton, the logogen system is composed by a set of mechanisms (*logogens*) collecting evidence from visual or auditory input. When evidence collected by a word's logogen exceeds its specific threshold, higher-order information about that word is accessed in the cognitive system. This mechanism is meant to be word-frequency dependent: the higher the frequency of a given word, the lower the evidence required to reach the activation threshold. In a final version of the model (1980), Morton included input and output logogen systems separate for visual and auditory modalities, and a grapheme-phoneme conversion system to accommodate the reading of unknown words. This architecture is identical to that later proposed by Patterson (1986). However, Patterson, instead of *logogens*, used the more generic term *lexicons*, which does not imply that entries within it are evidence-gathering mechanisms. For what concerns reading aloud, Coltheart and colleagues (2001) provided a computational framework of this architecture, involving a lexical-semantic reading route and a grapheme-phoneme conversion unit (Marshall & Newcombe 1973). The former entails visual analysis (that according to Ellis, Young & Anderson (1988) basically involves abstract recognition of letters), access to the orthographic visual lexicon, access to semantic representations[8], output phonemic representations, and a phonemic buffer. Conversely, the second binds visual analysis to the output buffer via a grapheme-to-phoneme conversion routine. On the one hand, a "lexical route" explains why reading frequent words is easier than reading infrequent words (Forster & Chambers, 1973). On the other hand, it explains why patients with phonological dyslexia (who cannot read through the grapheme-to-phoneme route) show better performance for concrete than for abstract words (Funnell, 1983; Hamilton & Coslett, 2008; Ripamonti et al., 2014), being concreteness a semantic feature.

More recently, consolidation and activation of lexical-semantic units (*lexomes*) has been simulated through the Naïve Discriminative Reader model, according to which the development (and subsequent) retrieval of lexical-semantic knowledge depends on how easily lexical-semantic representations can be discriminated (Baayen et al., 2011; see also Milin et al., 2017), basing on the distinctiveness of the associations between sub-lexical cues and whole words. Noteworthy, simulations based on this learning approach effectively mimicked word frequency effects obtained in real lexical decision tasks. This approach will be presented in detail in Chapter 5.

In general terms, an orthographic input lexicon (1) allows words to be recognized as distinctive units (at a more general level as compared to that of recognition of single letters); (2) provides an interface with the semantic system, so that the meaning of the perceived word can be extracted. For these reasons, for the purpose of this thesis, the existence vs. non-existence of an

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[8] Although included in the theoretical description of the model, the semantic component was not formally implemented in Coltheart et al. (2001).

orthographic input lexicon in the RH will be taken as the crucial criterion to assess whether the RH is able or not able to read. In other words, the existence of RH orthographic lexical representations will be taken as the critical test to define the *absolute*, rather than *relative* dominance of the LH over the RH for reading.

According to the framework advocating an *absolute* LH dominance for reading, because an absolute dominance implicates that the RH is word-blind, no orthographic lexicon[9] should exist in the RH. Conversely, a RH orthographic lexicon could be expected in the *relative* LH dominance framework. In what follows, two models (proposing either the existence of one single left-lateralized lexicon, or the co-existence of two orthographic lexicons with different capabilities in the two hemispheres) will be presented, and their implicit and explicit predictions on behavior and brain functioning will be discussed.

A "single- lexicon" framework

Ellis, Young, and Anderson, (1988) (see also Ellis, 2004, see Figure 1.5) introduced a model aiming at describing lateralized reading patterns in the healthy brain. The background of this model is constituted by divided visual field studies of reading in healthy subjects, that highlighted a seemingly consistent length-by-visual field interaction effect, indicating that, while the RVF/LH is only mildly sensitive to stimuli length (i.e. number of letters), the LVF/RH is associated with lower performance as word length increases (Young & Ellis, 1985; Brysbaert & d'Ydewalle, 1990).

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[9] Here and henceforth, by "orthographic lexicon", I indicate an "orthographic input lexicon" (Coltheart et al., 2001), unless otherwise specified.

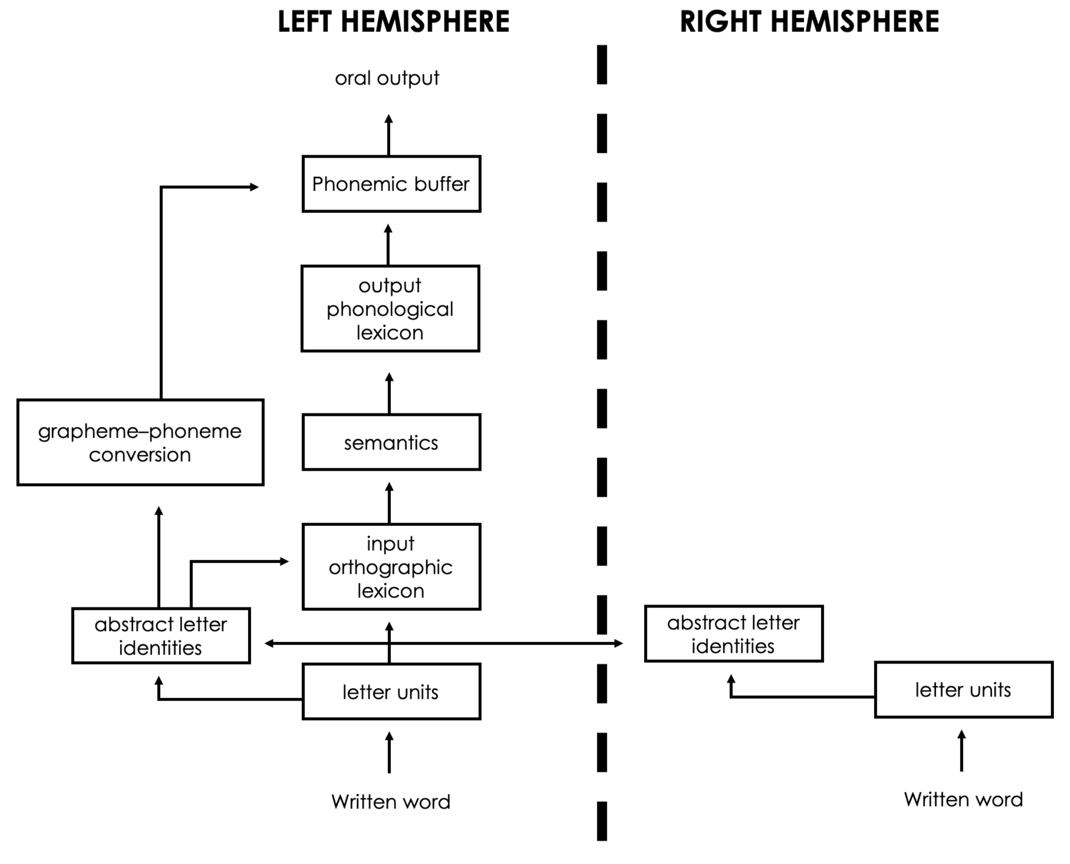

Figure 1.5 | A "single orthographic lexicon" model (Adapted from Ellis, 2004).

In other words, the greater the amount of orthographic information to process, the larger the behavioral difference among hemispheres. These findings have suggested that visual field/hemispheric differences in reading could depend on factors preceding lexical access, making the existence of a RH orthographic lexicon an unnecessary assumption. The model proposed by Ellis, Young & Anderson (1988) and by Ellis (2004) assumes that the LH contains an orthographic lexical store and a grapheme-to-phoneme conversion system, while the RH has none of these modules. Conversely, both hemispheres contain a single-letter processor and a module that converts single letters into abstract letter units, with these latter modules being connected across hemispheres. The model suggests two ways along which a word presented to the RVF/LH can reach the LH lexicon in order to be read: via a fast, direct, "parallel" pathway from a "letter units" module to the lexicon, or via an indirect, step-by-step (letter-by-letter)[10]

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[10] It is worthy to note that by "stepwise" does not imply "in a left-to-right fashion". As Ellis and colleagues acknowledge (1988; 2004), evidence has suggested that such cognitive operation is indeed likely to happen in a "ends-in" manner (Bradshaw et al., 1977; Jordan et al., 2000, 2003).

conversion from “letter units” into “abstract letter identities”, prior to lexical activation. Stepwise reading is meant to be slower than the parallel procedure and to be sensitive to word length (longer words are processed more slowly). For these reasons, the parallel strategy is the preferred one for processing words projected to the LH. When a pseudoword is presented to the RVF/LH, any attempt of finding a lexical representation is ineffective, as no representation of the stimulus exists in the lexicon. To be read aloud, a pseudoword needs to be converted letter-by-letter from “letter units” into “abstract letter identities”, and then to be processed by means of the grapheme-to-phoneme conversion unit.

When a lateralized verbal stimulus (either word or pseudoword) is presented to the LVF/RH, due to the lack of both a lexicon and a grapheme-to-phoneme conversion system in the RH, it has to be transferred to the LH after stepwise (length-dependent) conversion into abstract letter identities. A word will then reach the lexicon via the indirect pathway, while a pseudoword will reach the grapheme-to-phoneme conversion system. Hence, according to the model, there is one single lexicon (the LH one), differently accessed by the two hemispheres: the LH would use a rapid “parallel” mode, while the RH would necessarily use a word-length-dependent “stepwise” mode[11].

From this model, a set of neurolinguistic and psycholinguistic predictions can be derived:

(1) Reading should be impossible if a lesion impairs the LH visual word form system. Residual reading abilities in case of a LH lesion must be explained by partial sparing and activation of the LH reading system, as well as by sparing of connections between the LH visual word form system and the rest of the LH (a partially active LH visual word form system unable to communicate with the rest of the brain would be ineffective). (2) Hemispheric differences in lateralized reading should vary according to variables accounting for pre-lexical computations, such as word-length-dependent processes subtending abstract recognition of letters and/or stepwise information transfer from the RH to the LH. No effects of lexical/semantic variables should emerge without sizeable effects of pre-lexical variables[12].

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[11] For a different pre-lexical interpretation of the RVF/LH advantage over the LVF/RH, see (Whitney, 2001).

[12] If we assume that activation of the single-LH orthographic lexicon could be lower for stimuli initially presented in the RH than for those initially targeting the LH (Lambon Ralph, Hesketh & Sage, 2004), differences among hemispheres could arise also at a lexical level (e.g. hemispheric differences in the size of a word frequency effect). However, these lexical effects should not emerge without pre-lexical effects.

A “two orthographic lexicons” framework

The idea of the existence of a RH orthographic lexicon stemmed from research on neuropsychological patients, and in particular from the observation of spared reading abilities in patients with deep dyslexia (Coltheart 1980, 2000; Saffran et al., 1980) and implicit reading in pure alexia (Coslett & Saffran, 1989, Saffran & Coslett, 1998). In line with Coltheart's proposal, the orthographic lexical abilities of the RH would be mostly rough and limited to high-frequency concrete nouns (Patterson, 1979; Saffran, Bogyo, Schwartz, & Marin, 1980). For this reason, the RH orthographic lexicon does not succeed in fully compensating for a LH reading deficit. A functional brain model involving the existence of a (limited) orthographic lexicon in the RH was proposed by Coslett & Safran (1994, see also Saffran & Coslett, 1998) and integrated by Luzzatti (2003; Luzzatti, Rumiati & Ghirardi,1998; see Figure 1.6). This model suggests that the RH possesses a rough lexical route, whose modules partially mirror those of the LH one (namely visual analysis, orthographic input lexicon and conceptual knowledge). The main difference among hemispheres (apart from the lack of, or impoverished, phonemic representations in the RH) would be the limitation of the RH lexical abilities only to high-frequency concrete nouns. The basic predictions of this model are that:

(1) The RH can account for residual reading abilities after a LH lesion, even in case of a complete disconnection between the left visual word form system and the rest of the brain. (2) Lexical-semantic factors, more than pre-lexical factors, should explain hemispheric differences in reading performance.

In the following chapters, the two presented models will be used to guide the interpretation of empirical and computational data and to compare the *absolute* and *relative* frameworks of LH dominance over the RH for reading.

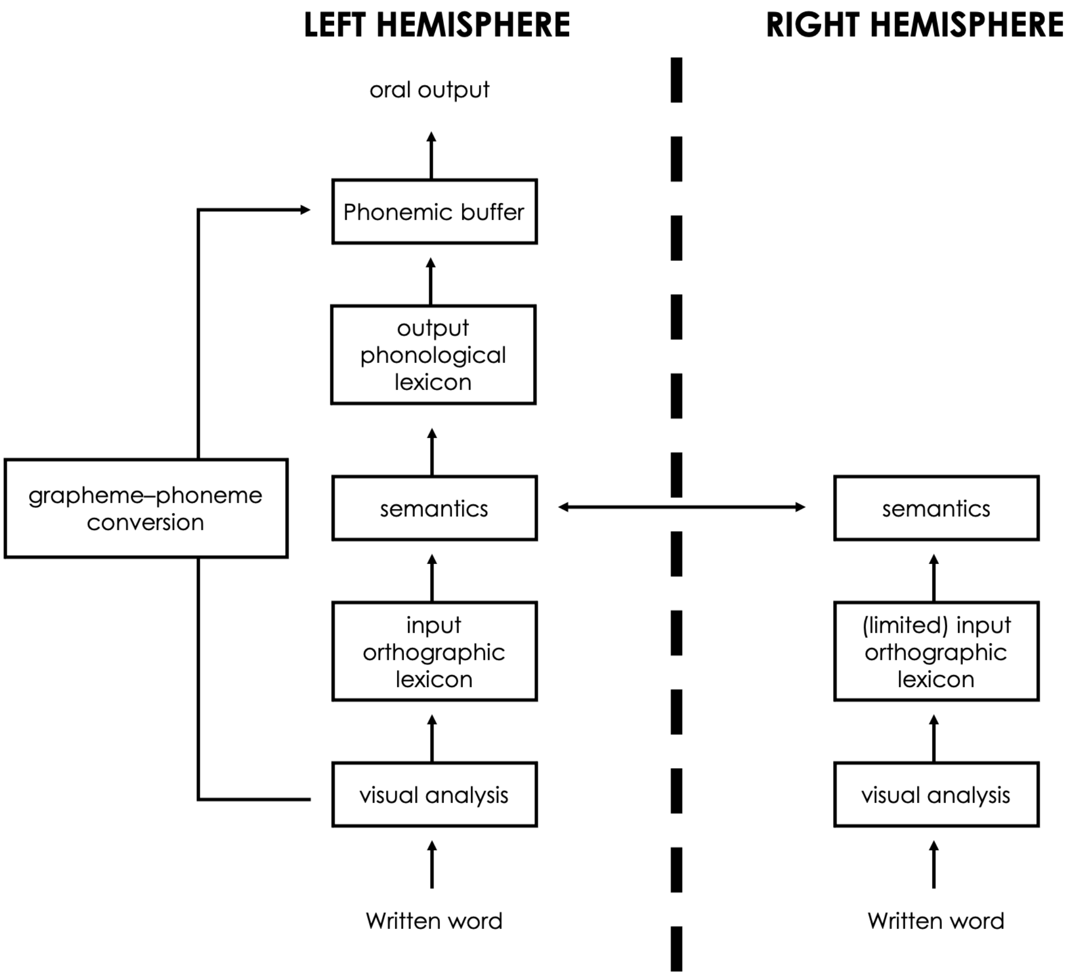

Figure 1.6 | A "two orthographic lexicons" model (Adapted from Luzzatti, Rumiati & Ghirardi 1998; Luzzatti, 2003).

References

Baayen, R. H., Milin, P., Đurđević, D. F., Hendrix, P., & Marelli, M. (2011). An amorphous model for morphological processing in visual comprehension based on naive discriminative learning. *Psychological Review, 118*(3), 438.

Babkoff, H., & Ben-Uriah, Y. (1983). Lexical decision time as a function of visual field and stimulus probability. *Cortex, 19*(1), 13-30.

Baynes, K., Tramo, M. J., & Gazzaniga, M. S. (1992). Reading with a limited lexicon in the right hemisphere of a callosotomy patient. *Neuropsychologia, 30*(2), 187-200.

Behrmann, M., & Plaut, D. C. (2015). A vision of graded hemispheric specialization. *Annals of the New York Academy of Sciences, 1359*(1), 30-46.

Belger, A., & Banich, M. T. (1998). Costs and benefits of integrating information between the cerebral hemispheres: a computational perspective. *Neuropsychology, 12*(3), 380.

Bogen, J. E., Fisher, E. D., & Vogel, P. J. (1965). Cerebral commissurotomy: A second case report. *Jama, 194*(12), 1328-1329.

Bourne, V. J. (2006). The divided visual field paradigm: Methodological considerations. *Laterality, 11*(4), 373-393.

Bourne, V. J., & Hole, G. J. (2006). Lateralized repetition priming for familiar faces: Evidence for asymmetric interhemispheric cooperation. *Quarterly Journal of Experimental Psychology, 59*(6), 1117-1133.

Bradshaw, J. L., Bradley, D., Gates, A., & Patterson, K. (1977). Serial, parallel, or holistic identification of single words in the two visual fields?. *Perception & Psychophysics, 21*(5), 431-438.

Branch, C., Milner, B., & Rasmussen, T. (1964). Intracarotid sodium amytal for the lateralization of cerebral speech dominance: observations in 123 patients. *Journal of Neurosurgery, 21*(5), 399-405.

Brederoo, S. G., Van der Haegen, L., Brysbaert, M., Nieuwenstein, M. R., Cornelissen, F. W., & Lorist, M. M. (2020). Towards a unified understanding of lateralized vision: A large-scale study investigating principles governing patterns of lateralization using a heterogeneous sample. *Cortex, 133*, 201-214.

Branch, C., Milner, B., & Rasmussen, T. (1964). Intracarotid sodium amytal for the lateralization of cerebral speech dominance: observations in 123 patients. *Journal of Neurosurgery*, *21*(5), 399-405.

Brysbaert, M., & D'Ydewalle, G. (1990). Tachistoscopic presentation of verbal stimuli for assessing cerebral dominance: Reliability data and some practical recommendations. *Neuropsychologia, 28*(5), 443-455.

Bunt, A. H., Minckler, D. S., & Johanson, G. W. (1977). Demonstration of bilateral projection of the central retina of the monkey with horseradish peroxidase neuronography. *Journal of Comparative Neurology, 171*(4), 619-630.

Cabeza, R. (2002). Hemispheric asymmetry reduction in older adults: the HAROLD model. *Psychology and Aging, 17*(1), 85.

Cai, Q., Lavidor, M., Brysbaert, M., Paulignan, Y., & Nazir, T. A. (2008). Cerebral lateralization of frontal lobe language processes and lateralization of the posterior visual word processing system. *Journal of Cognitive Neuroscience, 20*(4), 672-681.

Carpenter, R. H. S. (1988). *Movements of the eyes*. London: Pion

Cattinelli, I., Borghese, N. A., Gallucci, M., & Paulesu, E. (2013). Reading the reading brain: a new meta-analysis of functional imaging data on reading. *Journal of Neurolinguistics, 26*(1), 214-238.

Chiarello, C., Senehi, J., & Soulier, M. (1986). Viewing conditions and hemisphere asymmetry for the lexical decision. *Neuropsychologia, 24*(4), 521-529.

Chiarello, C., Shears, C., Liu, S., & Kacinik, N. A. (2005). Influence of word class proportion on cerebral asymmetries for high-and low-imagery words. *Brain and Cognition, 57*(1), 35-38.

Christman, S. (1990). Effects of luminance and blur on hemispheric asymmetries in temporal integration. *Neuropsychologia, 28*(4), 361-374.

Chu, R. K., & Meltzer, J. A. (2019). Interhemispheric connectivity during lateralized lexical decision. *Human Brain Mapping, 40*(3), 818-832.

Cohen, L., Dehaene, S., Naccache, L., Lehéricy, S., Dehaene-Lambertz, G., Hénaff, M. A., & Michel, F. (2000). The visual word form area: spatial and temporal characterization of an initial stage of reading in normal subjects and posterior split-brain patients. *Brain, 123*(2), 291-307.

Cohen, L., Henry, C., Dehaene, S., Martinaud, O., Lehéricy, S., Lemer, C., & Ferrieux, S. (2004). The pathophysiology of letter-by-letter reading. *Neuropsychologia, 42*(13), 1768-1780.

Cohen, L., Lehéricy, S., Chochon, F., Lemer, C., Rivaud, S., & Dehaene, S. (2002). Language-specific tuning of visual cortex? Functional properties of the Visual Word Form Area. *Brain, 125*(5), 1054-1069.

Cohen, L., Martinaud, O., Lemer, C., Lehéricy, S., Samson, Y., Obadia, M., ... & Dehaene, S. (2003). Visual word recognition in the left and right hemispheres: anatomical and functional correlates of peripheral alexias. *Cerebral cortex, 13*(12), 1313-1333.

Coltheart, M. (1980). Deep dyslexia: a right-hemisphere hypothesis. In Coltheart, M., Patterson, K., & Marshall, J.C. (Eds.), *Deep Dyslexia*. London: Routledge and Kegan Paul.

Coltheart, M. (2000). Deep dyslexia is right-hemisphere reading. *Brain and Language, 71*(2), 299-309.

Coltheart, M. (2004). Are there lexicons?. *The Quarterly Journal of Experimental Psychology Section A, 57*(7), 1153-1171.

Coltheart, M., Rastle, K., Perry, C., Langdon, R., & Ziegler, J. (2001). DRC: a dual route cascaded model of visual word recognition and reading aloud. *Psychological Review, 108*(1), 204.

Cook, N. D. (1984). Homotopic callosal inhibition. *Brain and Language*, *23*(1), 116-125.

Coslett, H. B., & Saffran E. M. (1989). Evidence for preserved reading in 'pure alexia'. *Brain, 112*(2), 327-359.

Coslett, H. B., & Saffran, E. M. (1994). Mechanisms of implicit reading in alexia. In M. Farah & G. Ratcliff (Eds.), *The neuropsychology of high-level vision* (pp. 299–330). Lawrence Erlbaum Associates.

Danelli, L., Marelli, M., Berlingeri, M., Tettamanti, M., Sberna, M., Paulesu, E., & Luzzatti, C. (2015). Framing effects reveal discrete lexical-semantic and sublexical procedures in reading: an fMRI study. *Frontiers in Psychology, 6,* 1328.

Day, J. (1977). Right-hemisphere language processing in normal right-handers. *Journal of Experimental Psychology: Human Perception and Performance, 3*(3), 518.

De Clercq, P., & Brysbaert, M. (2020). The influence of word valence on the right visual field advantage in the VHF paradigm: time to adjust the expectations. *Laterality,* 1-23.

Dehaene, S., & Cohen, L. (2007). Cultural recycling of cortical maps. *Neuron*, 56(2), 384-398.

Dehaene, S., Cohen, L., Sigman, M., & Vinckier, F. (2005). The neural code for written words: a proposal. *Trends in Cognitive Sciences, 9*(7), 335-341.

Dehaene, S., Le Clec'H, G., Poline, J. B., Le Bihan, D., & Cohen, L. (2002). The visual word form area: a prelexical representation of visual words in the fusiform gyrus. *Neuroreport, 13*(3), 321-325.

Dehaene, S., Pegado, F., Braga, L. W., Ventura, P., Nunes Filho, G., Jobert, A., ... & Cohen, L. (2010). How learning to read changes the cortical networks for vision and language. *Science, 330*(6009), 1359-1364.

Déjerine, J. (1891). Sur un cas de cécité verbale avec agraphie suivi d'autopsie. *Mémoires de la Société de Biologie*, *3*, 197-201.

Dejerine, J. (1892). Contribution à l'étude anatomopathologique et clinique des différents variétés de cécité verbale. *Mémoires de la Société de Biologie, 4*, 61-90.

Deruelle, C., & de Schonen, S. (1998). Do the right and left hemispheres attend to the same visuospatial information within a face in infancy?. *Developmental Neuropsychology, 14*(4), 535-554.

Devlin, J. T., Jamison, H. L., Gonnerman, L. M., & Matthews, P. M. (2006). The role of the posterior fusiform gyrus in reading. *Journal of Cognitive Neuroscience, 18*(6), 911-922.

Ellis, A. W. (2004). Length, formats, neighbours, hemispheres, and the processing of words presented laterally or at fixation. *Brain and Language, 88*(3), 355-366.

Ellis, A. W., Young, A. W., & Anderson, C. (1988). Modes of word recognition in the left and right cerebral hemispheres. *Brain and Language, 35*(2), 254-273.

Eviatar, Z., Menn, L., & Zaidel, E. (1990). Concreteness: Nouns, verbs, and hemispheres. *Cortex, 26*(4), 611-624

Forster, K. I., & Chambers, S. M. (1973). Lexical access and naming time. *Journal of Verbal Learning and Verbal Behavior, 12*(6), 627-635.

Funnell, E. (1983). Phonological processes in reading: New evidence from acquired dyslexia. *British Journal of Psychology, 74*(2), 159-180.

Gazzaniga, M. S., & Hillyard, S. A. (1971). Language and speech capacity of the right hemisphere. *Neuropsychologia, 9*(3), 273-280.

Gazzaniga, M. S., & Sperry, R. W. (1967). Language after section of the cerebral commissures. *Brain, 90*(1), 131-148.

Gazzaniga, M. S., Bogen, J. E., & Sperry, R. W. (1965). Observations on visual perception after disconnexion of the cerebral hemispheres in man. *Brain, 88*(2), 221-236.

Gerrits, R., Van der Haegen, L., Brysbaert, M., & Vingerhoets, G. (2019). Laterality for recognizing written words and faces in the fusiform gyrus covaries with language dominance. *Cortex, 117*, 196-204.

Glezer, L. S., Jiang, X., & Riesenhuber, M. (2009). Evidence for highly selective neuronal tuning to whole words in the “visual word form area”. *Neuron, 62*(2), 199-204.

Graves, R. E. (1997). The Legacy of the Wernicke-Lichtheim Model. *Journal of the History of the Neurosciences, 6*(1), 3-20.

Hamilton, A. C., & Coslett, H. B. (2008). Role of inflectional regularity and semantic transparency in reading morphologically complex words: Evidence from acquired dyslexia. *Neurocase, 14*(4), 347-368.

Hardyck, C., Chiarello, C., Dronkers, N. F., & Simpson, G. V. (1985). Orienting attention within visual fields: How efficient is interhemispheric transfer?. *Journal of Experimental Psychology: Human Perception and Performance, 11*(5), 650.

Hausmann, M., Brysbaert, M., Van der Haegen, L., Lewald, J., Specht, K., Hirnstein, M., ... & Roch, M. (2019). Language lateralisation measured across linguistic and national boundaries. *Cortex, 111*, 134-147.

Henderson, V. W. (2019). Alexia and Agraphia from 1861 to 1965. In J. Bogousslavsky, F. Boller, & M. Iwata (Eds.), *A history of neuropsychology* (Vol. 44, pp. 39–52). Karger Publishers.

Henry, C., Gaillard, R., Volle, E., Chiras, J., Ferrieux, S., Dehaene, S., & Cohen, L. (2005). Brain activations during letter-by-letter reading: A follow-up study. *Neuropsychologia, 43*(14), 1983-1989.

Herbster, A. N., Mintun, M., Nebes, R. D., & Becker, J. T. (1997). Regional cerebral blood flow during word and nonword reading. *Human Brain Mapping, 5*(2), 84-92.

Hernandez, S., Nieto, A., & Barroso, J. (1992). Hemispheric specialization for word classes with visual presentations and lexical decision task. *Brain and Cognition, 20*(2), 399-408.

Howard, D., Patterson, K., Wise, R., Brown, W. D., Friston, K., Weiller, C., & Frackowiak, R. (1992). The cortical localization of the lexicons: Positron emission tomography evidence. *Brain, 115*(6), 1769-1782.

Hunter, Z. R., & Brysbaert, M. (2008). Visual half-field experiments are a good measure of cerebral language dominance if used properly: Evidence from fMRI. *Neuropsychologia, 46*(1), 316-325.

Jobard, G., Crivello, F., & Tzourio-Mazoyer, N. (2003). Evaluation of the dual route theory of reading: a metanalysis of 35 neuroimaging studies. *Neuroimage, 20*(2), 693-712.

Jordan, T. R., Patching, G. R., & Milner, A. D. (1998). Central fixations are inadequately controlled by instructions alone: Implications for studying cerebral asymmetry. *The Quarterly Journal of Experimental Psychology Section A, 51*(2), 371-391.

Jordan, T. R., Patching, G. R., & Milner, A. D. (2000). Lateralized word recognition: Assessing the role of hemispheric specialization, modes of lexical access, and perceptual asymmetry. *Journal of Experimental Psychology: Human Perception and Performance, 26*(3), 1192.

Jordan, T. R., Patching, G. R., & Thomas, S. M. (2003). Assessing the role of hemispheric specialisation, serial-position processing, and retinal eccentricity in lateralised word recognition. *Cognitive Neuropsychology, 20(*1), 49-71.

Kanwisher, N., & Yovel, G. (2006). The fusiform face area: a cortical region specialized for the perception of faces. *Philosophical Transactions of the Royal Society B: Biological Sciences, 361*(1476), 2109-2128.

Kiyosawa, M., Itoh, M., Nakagawa, Y., Kobayashi, N., & Tamai, M. (1995). Effect of kanji and kana reading on cerebral blood flow patterns measured by PET. *Japanese Journal of Ophthalmology, 39*(2), 198-205.

Kronbichler, M., Hutzler, F., Wimmer, H., Mair, A., Staffen, W., & Ladurner, G. (2004). The visual word form area and the frequency with which words are encountered: evidence from a parametric fMRI study. *Neuroimage, 21*(3), 946-953.

Lambon Ralph, M. A., Hesketh, A., & Sage, K. (2004). Implicit recognition in pure alexia: The Saffran effect—a tale of two systems or two procedures? *Cognitive Neuropsychology, 21*(2–4), 401–421.

Landis, T., Regard, M., Graves, R., & Goodglass, H. (1983). Semantic paralexia: A release of right hemispheric function from left hemispheric control?. *Neuropsychologia, 21*(4), 359-364.

Lavidor, M., & Ellis, A. W. (2003). Interhemispheric integration of letter stimuli presented foveally or extra-foveally. *Cortex, 39*(1), 69-83.

Leehey, S., Carey, S., Diamond, R., & Cahn, A. (1978). Upright and inverted faces: The right hemisphere knows the difference. *Cortex, 14*(3), 411-419.

Leiber, L. (1976). Lexical decisions in the right and left cerebral hemispheres. *Brain and Language, 3*(3), 443-450.

Levy, J., & Trevarthen, C. (1977). Perceptual, semantic and phonetic aspects of elementary language processes in split-brain patients. *Brain, 100*(1), 105-118.

Lindell, A. K., & Nicholls, M. E. (2003). Cortical Representation of the Fovea: Implications for Visual Half-Field Research. *Cortex, 39*(1), 111-117.

Luh, K. E., & Levy, J. (1995). Interhemispheric cooperation: Left is left and right is right, but sometimes the twain shall meet. *Journal of Experimental Psychology: Human Perception and Performance, 21*(6), 1243.

Luzzatti, C. (2003). Optic aphasia and pure alexia: contribution of callosal disconnection syndromes to the study of lexical and semantic representation in the right hemisphere. In Zaidel, E., & Iacoboni, M. (Eds.), *The Parallel Brain: The Cognitive Neuroscience of the Corpus Callosum* (pp. 479-499). Cambridge, MA: MIT Press.

Luzzatti, C., Rumiati, R. I., & Ghirardi, G. (1998). A functional model of visuo-verbal disconnection and the neuroanatomical constraints of optic aphasia. *Neurocase, 4*(1), 71-87.

Marshall, J. C., & Newcombe, F. (1973). Patterns of paralexia: A psycholinguistic approach. *Journal of Psycholinguistic Research*, 2(3), 175-199.

Marzi, C. A., & Berlucchi, G. (1977). Right visual field superiority for accuracy of recognition of famous faces in normals. *Neuropsychologia, 15*(6), 751-756.

Mechelli, A., Crinion, J. T., Long, S., Friston, K. J., Ralph, M. A. L., Patterson, K., ... & Price, C. J. (2005). Dissociating reading processes on the basis of neuronal interactions. *Journal of Cognitive Neuroscience, 17*(11), 1753-1765.

Menard, M. T., Kosslyn, S. M., Thompson, W. L., Alpert, N. M., & Rauch, S. L. (1996). Encoding words and pictures: a positron emission tomography study. *Neuropsychologia, 34*(3), 185-194.

Milin, P., Feldman, L. B., Ramscar, M., Hendrix, P., & Baayen, R. H. (2017). Discrimination in lexical decision. *PloS one, 12*(2), e0171935.

Mohr, B., Pulvermüller, F., Rayman, J., & Zaidel, E. (1994). Interhemispheric cooperation during lexical processing is mediated by the corpus callosum: Evidence from the split-brain. *Neuroscience Letters, 181*(1-2), 17-21.

Morton, J. (1961). *Reading, context and the perception of words.* Unpublished PhD thesis, University of Reading, Reading, England.

Morton, J. (1980). The logogen model and orthographic structure. In U. Frith (Ed.), *Cognitive processes in spelling.* London: Academic Press.

Olk, B., & Hartje, W. (2001). The bilateral effect: Callosal inhibition or intrahemispheric competition?. *Brain and Cognition, 45*(3), 317-324.

Patterson, K. (1986). Lexical but nonsemantic spelling?. *Cognitive Neuropsychology, 3*(3), 341-367.

Patterson, K., & Besner, D. (1984). Is the right hemisphere literate?. *Cognitive Neuropsychology, 1*(4), 315-341.

Paulesu, E., McCrory, E., Fazio, F., Menoncello, L., Brunswick, N., Cappa, S. F., ... & Pesenti, S. (2000). A cultural effect on brain function. *Nature Neuroscience, 3*(1), 91-96.

Petersen, S. E., Fox, P. T., Posner, M. I., Mintun, M., & Raichle, M. E. (1988). Positron emission tomographic studies of the cortical anatomy of single-word processing. *Nature, 331*(6157), 585-589.

Petersen, S. E., Fox, P. T., Snyder, A. Z., & Raichle, M. E. (1990). Activation of extrastriate and frontal cortical areas by visual words and word-like stimuli. *Science, 249*(4972), 1041-1044.

Plaut, D. C., & Behrmann, M. (2011). Complementary neural representations for faces and words: A computational exploration. *Cognitive Neuropsychology, 28*(3-4), 251-275.

Price, C. J. (2012). A review and synthesis of the first 20 years of PET and fMRI studies of heard speech, spoken language and reading. *Neuroimage, 62*(2), 816-847.

Price, C. J., & Devlin, J. T. (2003). The myth of the visual word form area. *Neuroimage, 19*(3), 473-481.

Pujol, J., Deus, J., Losilla, J. M., & Capdevila, A. (1999). Cerebral lateralization of language in normal left-handed people studied by functional MRI. *Neurology, 52*(5), 1038-1038.

Rauschecker, A. M., Bowen, R. F., Parvizi, J., & Wandell, B. A. (2012). Position sensitivity in the visual word form area. *Proceedings of the National Academy of Sciences, 109*(24), E1568-E1577.

Reuter-Lorenz, P. A., & Baynes, K. (1992). Modes of lexical access in the callosotomized brain. *Journal of Cognitive Neuroscience, 4*(2), 155-164. doi: 10.1162/jocn.1992.4.2.155.

Ripamonti, E., Aggujaro, S., Molteni, F., Zonca, G., Frustaci, M., & Luzzatti, C. (2014). The anatomical foundations of acquired reading disorders: a neuropsychological verification of the dual-route model of reading. *Brain and Language, 134*, 44-67.

Rutherford, B. J., & Lutz, K. T. (2004). Conflicting strategies and hemispheric suppression in a lexical decision task. *Brain and Cognition, 55*(2), 387-391.

Saffran, E. M., & Coslett, H. B. (1998). Implicit vs. letter-by-letter reading in pure alexia: A tale of two systems. *Cognitive Neuropsychology, 15*(1-2), 141-165.

Saffran, E. M., Bogyo, L. C., Schwartz, M. F., & Marin, O. S. M. (1980). Does deep dyslexia reflect right-hemisphere reading? In Coltheart, M., Patterson, K., & Marshall, J.C. (Eds.), *Deep Dyslexia* (pp. 381-406) London: Routledge and Kegan Paul.

Skwortzoff N: *De la Cécité et de la Surdité des Mots dans l'Aphasie*. Paris, Delahaye et Lecrosnier, 1881.

Small, S. L., Noll, D. C., Perfetti, C. A., Hlustik, P., Wellington, R., & Schneider, W. (1996). Localizing the lexicon for reading aloud: replication of a PET study using fMRI. *Neuroreport, 7*(4), 961-965.

Sorger, B., Goebel, R., Schiltz, C., & Rossion, B. (2007). Understanding the functional neuroanatomy of acquired prosopagnosia. *Neuroimage*, *35*(2), 836-852.

Sowman, P. F., Crain, S., Harrison, E., & Johnson, B. W. (2014). Lateralization of brain activation in fluent and non-fluent preschool children: a magnetoencephalographic study of picture-naming. *Frontiers in Human Neuroscience, 8,* 354.

Stone, J., Leicester, J., & Sherman, S. M. (1973). The naso-temporal division of the monkey's retina. *Journal of Comparative Neurology, 150*(3), 333-348.

Taylor, J. S. H., Davis, M. H., & Rastle, K. (2019). Mapping visual symbols onto spoken language along the ventral visual stream. *Proceedings of the National Academy of Sciences, 116*(36), 17723-17728.

Taylor, J. S. H., Rastle, K., & Davis, M. H. (2013). Can cognitive models explain brain activation during word and pseudoword reading? A meta-analysis of 36 neuroimaging studies. *Psychological Bulletin, 139*(4), 766.

Treisman, A. M. (1961). *Attention and speech*. Unpublished doctoral thesis, Oxford University.

Turkeltaub, P. E., Eden, G. F., Jones, K. M., & Zeffiro, T. A. (2002). Meta-analysis of the functional neuroanatomy of single-word reading: method and validation. *Neuroimage, 16*(3), 765-780.

Van der Haegen, L., Cai, Q., Seurinck, R., & Brysbaert, M. (2011). Further fMRI validation of the visual half field technique as an indicator of language laterality: A large-group analysis. *Neuropsychologia, 49*(10), 2879-2888.

Van der Knaap, L. J., & Van der Ham, I. J. (2011). How does the corpus callosum mediate interhemispheric transfer? A review. *Behavioural Brain Research, 223*(1), 211-221.

Vinckier, F., Dehaene, S., Jobert, A., Dubus, J. P., Sigman, M., & Cohen, L. (2007). Hierarchical coding of letter strings in the ventral stream: dissecting the inner organization of the visual word-form system. *Neuron, 55*(1), 143-156.

Waldie, K. E., & Mosley, J. L. (2000). Hemispheric specialization for reading. *Brain and Language, 75*(1), 108-122.

Wandell, B. A. (2011). The neurobiological basis of seeing words. *Annals of the New York Academy of Sciences, 1224*(1), 63.

Wernicke, C. (1874). *Der aphasische symptomenkomplex* Breslau, Germany: Cohn and Weigart.

Whitney, C. (2001). How the brain encodes the order of letters in a printed word: The SERIOL model and selective literature review. *Psychonomic Bulletin & Review, 8*(2), 221-243.

Whitney, C., & Lavidor, M. (2005). Facilitative orthographic neighborhood effects: The SERIOL model account. *Cognitive Psychology, 51*(3), 179-213.

Willemin, J., Hausmann, M., Brysbaert, M., Dael, N., Chmetz, F., Fioravera, A., ... & Mohr, C. (2016). Stability of right visual field advantage in an international lateralized lexical decision task irrespective of participants' sex, handedness or bilingualism. *Laterality: Asymmetries of Body, Brain and Cognition, 21*(4-6), 502-524.

Wyatt, H. J. (1978). Nasotemporal overlap and visual field sparing. *Investigative Ophthalmology & Visual Science, 17*(11), 1128-1130.

Yarkoni, T., Poldrack, R. A., Nichols, T. E., Van Essen, D. C., & Wager, T. D. (2011). Large-scale automated synthesis of human functional neuroimaging data. *Nature Methods, 8*(8), 665-670.

Young, A. W. (1982). Methodological theoretical bases. In J. G. Beaumont (Ed.), *Divided visual field studies of cerebral organisation* (pp. 11- 27). London: Academic Press.

Zaidel, E., & Peters, A. M. (1981). Phonological encoding and ideographic reading by the disconnected right hemisphere: Two case studies. *Brain and language, 14*(2), 205-234.

Chapter 2

A behavioral and structural disconnectome study of implicit reading in a patient with Pure Alexia.

In the last chapter, I described the dominance of the LH over the RH for reading, and I presented two models, advocating the existence of a "single LH orthographic lexicon" (in line with the idea of an *absolute* LH dominance) and "two orthographic lexicons" in the brain (one for each hemisphere, in line with a *relative* account of LH dominance), respectively. From a neural point of view, the first model suggests that reading should be impossible if a lesion impairs and disconnects the LH visual word form system. Residual reading abilities must be explained by partial sparing and activation of the LH reading system as well as sparing of connections between the LH visual word form system and the rest of the brain. Conversely, a "two orthographic lexicons" framework anticipates that the RH can account for residual reading abilities after a LH lesion, even in case of a disconnection between the left visual word form system and the rest of the brain. In this chapter, these neural predictions will be tested through the behavioral and structural disconnectome description of a patient with pure alexia who showed signs of implicit reading.

Introduction

As anticipated in the previous chapter, it has been suggested that the RH might perform some reading operations, although with poorer lexical, semantic, or phonological proficiency than the LH (Coslett & Saffran, 1989; 1994; Ellis & Shepherd, 1974; Hines, 1977; Rutherford & Mathesius, 2012; Saffran & Coslett, 1998). Accordingly, the extensively documented LH dominance for reading would be *relative*. However, a complete incapability of the RH to process orthographic stimuli has also been proposed (see for instance Ellis, 2004; Ellis, Young, & Anderson., 1988). In this perspective (*absolute* LH dominance for reading), the RH would be word blind, i.e., it only would be a relay station for orthographic information before being transferred to the LH for orthographic lexical processing. Accordingly, if the LH neural centers devoted to reading are disrupted by a brain insult, reading should become utterly impossible. Within this framework, patients with a posterior LH lesion and pure alexia constitute a critical clinical condition. According to the recent definition provided by Starrfelt and Shallice (2014), pure alexia is a selective impairment of reading in the absence of other language deficits, occurring as a consequence of brain injury in previously literate individuals. These patients typically perform very poorly in overt reading tasks and they fail in identifying even single letters, and in some cases use an extremely effortful letter-by-letter reading strategy (for recently described cases refer to Cohen et al., 2016; Hansen & Starrfelt, 2019; Huang, Baskin & Fung, 2016; Rodríguez-López, Molina & Salio, 2018; Rosazza et al., 2018; Sabsevitz et al., 2020; Veldsman et al., 2017). Lesions associated with pure alexia typically involve the territory of the left posterior cerebral artery and they either impair the left visual word-form system directly, or damage the LH primary visual areas disconnecting the preserved visual word form system from visual input (Cohen et al., 2000; 2003). However, despite their inability to explicitly recognize printed stimuli, patients with pure alexia have often been associated with surprising above chance-level performance in "implicit" word recognition tasks, such as lexical decision and/or semantic judgment in tachistoscopic modality[1] (e.g.: McKeeff & Behrmann, 2004; Saffran & Coslett, 1998; Shan et al., 2010).

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[1] If the presentation time is excessively long, patients rely on a letter-by-letter reading strategy and refrain from "guessing" whether the stimulus is a word or not (Coslett & Saffran, 1994). Tachistoscopic presentation is meant to be necessary for observing implicit reading in pure alexia, by discouraging letter-by-letter reading and forcing the appreciation of the letter string as a whole.

Two explanations of implicit reading in pure alexia

There is no agreement in the literature on the functional brain architecture giving rise to implicit reading in pure alexia (Coltheart, 1998). Indeed, the phenomenon may be explained either as due to partial LH sparing and its consequent partial activation ("LH hypothesis"; Lambon Ralph, Hesketh & Sage, 2004; Roberts, Lambon Ralph & Woollams, 2010; see also Mayall & Humphreys, 1996), or as a sign of RH reading ("RH hypothesis"; Coslett & Monsul, 1994; Coslett & Saffran, 1989, 1994; Saffran & Coslett, 1998; Shan et al., 2010): the RH would contain an orthographic lexicon limited to high-frequency concrete nouns, independent from the LH one, which would try to compensate for the LH damage and consequent reading impairment (e.g., Coltheart, 1980, 2000; Saffran et al., 1980; Luzzatti, 2003; Luzzatti et al., 1998). The former account complies with an *absolute* view of LH dominance for reading, while the second one is in line with a *relative* LH dominance.

Psycholinguistic predictions

The RH hypothesis assumes that the RH reading system is an imperfect orthographic processor only containing representations for frequent and highly imageable words (Coltheart, 1980, 2000; Saffran et al., 1980). Accordingly, when the LH visual word-form system is damaged, reading is mediated by the emergence of RH abilities, and thus performance can only be accurate for frequent imageable words. Therefore, lexical-semantic effects in residual reading abilities are expected.

Conversely, the LH hypothesis suggests that the RH is completely word blind. In order to explain residual reading abilities after a brain lesion at the level of the left visual word form system, the LH assumes that impairment may not be necessarily complete. Accordingly, some orthographic input may still yield partial, degraded activation of the visual word-form system (Lambon Ralph, Hesketh & Sage, 2004). This would imply that some orthographic representations could be successfully activated despite the LH lesion. This would happen more likely for frequent and/or concrete words, as they would be more efficiently represented in the lexical/semantic system than infrequent and/or abstract words. In their computational model, Mayall and Humphreys (1996) trained and tested a single visual word-form system (not implying the existence of two symmetrical reading systems in the brain). When hidden units were (partially) damaged to simulate pure alexia, performance in a simulated lexical decision task was still above chance level. When simulated damage affected input units, lexical-semantic effects were obtained. Therefore, a mere psycholinguistic account of performance is not sufficient to conclusively point to either the "LH hypothesis" or the "RH hypothesis" as the best interpretation of implicit reading in pure alexia, as lexical-semantic effects (although meant to be generated by different functional brain mechanisms) are predicted by both the LH and the RH interpretations of implicit reading in pure alexia.

Testing the two hypotheses

Given the relative non-informativity of psycholinguistic data, in order to test which framework best accounts for implicit reading in pure alexia, it may be important to differentiate the two hypotheses basing on their predictions at the neural level.

Remarkably, making a decision on either lexical or semantic features of an incoming orthographic stimulus requires -at least- orthographic processing and formulation and implementation of the decision. As far as lexical decision is concerned, information has to flow from the primary visual areas to the LH visual word-form system through the inferior longitudinal fasciculus (ILF; Catani & Thiebaut de Schotten, 2008; Epelbaum et al., 2008). However, orthographic information not only has to be processed by the visual word-form system: it must also stream from LH posterior regions to frontal and/or pre-frontal cortices (such as the middle frontal gyrus/Brodmann area 6: see Cattinelli et al., 2013) for the decision to be formulated and implemented. The inferior fronto-occipital fasciculus (IFOF), the superior longitudinal fasciculus (SLF), and the arcuate fasciculus (AF) are among the candidate white-matter tracts for this intra-hemispheric connection. The IFOF connects the posterior portion of the visual word form system to the superior temporal pole and to the orbitofrontal cortex (Bouhali et al., 2014). Although it is not directly connected to the visual word form area (it streams dorsally), the SLF connects posterior regions to frontal areas, and one of its branches (SLF II) is connected with Brodmann area 6 (Thiebaut de Schotten et al., 2012). A role for the SLF in lexical decision has been suggested by the correlation between its fractional anisotropy and the speed of responses in this task (Gold et al., 2007). The AF, instead, connects Brodmann area 37 – which is involved in the visual word-form system (McCandliss, Cohen & Dehaene, 2003) – to Brodmann area 6, as well as posterior regions of the middle and inferior frontal gyrus (Brodmann areas 8, 9, 44, and 45).

Therefore, for the LH to be able to perform lexical decision in pure alexia, the sparing and activation of some LH neural centers involved in visual perception and reading may not be sufficient: connectivity between LH centers involved in visual perception, orthographic processing, and decision/motor implementation must not be affected by the lesion. Conversely, such assumption is not required by the RH account, since according to this view information would be processed by RH neural centers completely unaffected by the lesion. Therefore, testing the sparing of intra-hemispheric connections from the visual word form system in the LH can be useful to compare the validity of the LH and RH accounts of implicit reading in pure alexia.

In the present study, I describe the case of a patient with LH occipital lesion and pure alexia showing partially preserved implicit reading abilities. I propose that a structural disconnectome analysis may help unveiling the specific role of the two hemispheres in mediating lexical decision abilities in the patient. In particular, if the lesion does not involve the LH white-matter tracts meant to be necessary for lexical decision, then the LH could still mediate implicit reading. On the contrary, if the lesion disconnects these intra-hemispheric tracts, then an RH contribution to implicit reading is most plausible.

Case Report

AA, an 81-year-old right-handed woman with 8 years of education, was hospitalized for a stroke at the level of the left temporooccipital inferior and mesial areas, due to occlusion of the left posterior cerebral artery. AA had typical acquisition of language and reading skills. She also reported that before the stroke she could read without any difficulty, and that she used to be a passionate reader of weekly magazines and (occasionally) of novels. At admission to the rehabilitation unit, 10 days after the event, the neurological examination revealed mild hyposthenia of the right limbs and right hemianopia, which was acknowledged but not completely compensated by the patient (Figure 2.1).

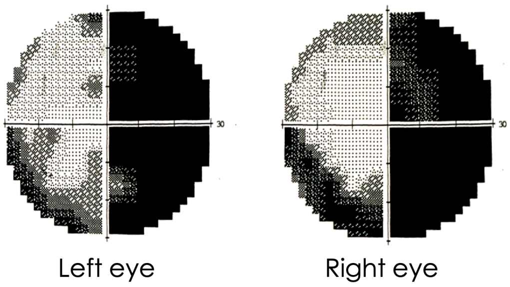

Figure 2.1 | Humphrey's visual field perimetry of patient AA.

The neuropsychological evaluation detected severe reading difficulties. Patient AA's overt reading abilities were tested by means of the Italian version of the Aachen Aphasia Test (AAT, Huber, Poeck & Willmes, 1984; Luzzatti et al., 1996). Written language tasks revealed a moderate impairment (33/90). In particular, reading aloud was severely impaired (1/30): she was unable to read aloud any of the stimuli (letter-by-letter reading strategy), while composing words and phrases from blocks was moderately impaired (11/30), and writing words and phrases to dictation was only mildly impaired (21/30). Her reading abilities were further assessed by means of a letter naming task: AA could identify and name only 11 out of the 21 uppercase letters of the Italian alphabet (52%). Despite her considerable reading difficulties, she did not show any major deficit either in speech production (AAT spontaneous speech was rated 4/5 for communicative behavior, 5/5 for articulation and prosody, 5/5 for the emergence of formulaic language, 4/5 for lexical/semantic structure, 5/5 for phonemic structure and 5/5 for syntactic structure), or in repetition (149/150) and oral comprehension (48/60), while her written comprehension was severely impaired (0/60). Besides her reading impairments, AA showed moderate-to-severe naming deficits on visual presentation: she scored 55/120 on the AAT naming subtest and 15/48 (raw score) on the naming subtest of the Catricalà et al. (2013) semantic battery, while her naming to description (Novelli et al., 1986) was within the normal range (raw score = 36/38). Lexical retrieval was further explored by asking the patient to name 25 real objects, after both visual and tactile (left hand while blindfolded) stimulation. She named 12/25 stimuli (48%) in the visual modality and 22/25 (88%) stimuli after tactile exploration (χ^2 (1) = 9.191, $p = 0.002$).

AA's reading deficit is therefore definable as pure alexia (associated with letter-by-letter reading strategy and only minor handwriting deficits). As far as the naming deficit is concerned, it predominantly involved the visual modality. The selectivity of the impairment makes the naming deficit compatible with optic aphasia[2] (Lhermitte & Beauvois, 1973; Luzzatti et al., 1998).

Materials and methods

A computerized tachistoscopic lexical decision task was administered, to address whether patient AA showed any sign of implicit reading and, if this was the case, which categories of stimuli she could most easily identify as words. The patient provided written informed consent to the participation in the study. The study was run according to the guidelines of the Helsinki declaration and was approved by the local ethical committee. Stimuli were 40 4-letter words (nouns) and 40 4-letter legal pseudowords. Word stimuli were 20 high-frequency (>100 absolute frequency; Bertinetto et al., 2005) and 20 low-frequency (<50 absolute frequency) items; half of the words were “high-” and half were “low-imageability” items (see Appendix, Table A.2.1). Imageability scores were obtained by means of the averaging of the ratings on a 7-point Likert scale of 21 volunteers. Spearman’s rank correlation between frequency and imageability is -0.08, $p = 0.63$. Thus, frequency and imageability were largely orthogonal. Stimuli were presented on the screen for 500 ms, the best reported exposition time for eliciting implicit reading by discouraging the use of a letter-by-letter reading strategy (Coslett & Saffran, 1994). Stimuli occupied 10.64° of the visual field horizontally and 3.58° vertically and they were flashed with their right boundary 1.68° left from the patient’s midline. Left visual field presentation was adopted to avoid targeting AA’s blind right half of the visual field. Each trial was initiated by the experimenter, after checking patient’s central fixation. AA reported not being able to overtly identify any of the target items. Despite her inability to recognize stimuli explicitly, she was encouraged to provide a response to all stimuli. She was required to respond by using the index (= word) and middle (= pseudoword) fingers of her left hand. Accuracy data were analyzed through logistic regressions by means of the R software. Two sets of analyses were conducted: one on both words and pseudowords and one on words only, in order to address

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[2] The nature of this disorder is still debated, as it has been considered a possible mild form of visual agnosia (see, for instance, Hillis & Caramazza, 1995; Riddoch & Humphreys, 1987).

the effects of word frequency and imageability. In both analyses, factors were used as independent variables, hence dummy coding was adopted.

In the model on both words and pseudowords, words were attributed the value 0 and pseudowords the value 1. Given that significance of the intercept indicates whether it is significantly different from 0 and that 0 in the logit scale corresponds to 50%, the significance of the intercept term in this model indicates whether words were processed significantly better or worse than chance level. The significance of the lexicality effect indicates whether there is a difference in accuracy between words and pseudowords. In the model on words only, low- and high-frequency words were attributed the values 0 and 1, respectively. Similarly, low and high-imageability words were attributed the values 0 and 1, respectively. Hence, the significance of the intercept term indicates whether performance for low-frequency-low-imageability words was significantly different from chance level (50% accurate). Simple effects indicate whether there is a significant effect of frequency and/or imageability on performance. The significance of the frequency-by-imageability interaction effect indicates whether the joint effect of these variables toward accuracy is more than additive.

Lesion-based disconnectome study

The lesion was detected through inspection of the T1-weighted structural MRI of AA's brain. The mask of the lesion was traced on the MRI image oriented in native space by means of the MRIcron software (https:// www.nitrc.org/projects/mricron) and subsequently validated by a neurologist with long-lasting experience in lesion mapping (Professor Claudio Luzzatti). The structural MRI and the lesion mask both oriented in native space were then used as an input for the Normalization function of the BCBToolkit (Foulon et al., 2018) to be normalized to the standard Montreal Neurological Institute (MNI) space. The Normalization function of the BCBToolkit allows to calculate and apply the computed spatial deformations to the whole brain except the lesion mask, so as to avoid deformation of the lesioned tissue (Brett et al., 2001; see also Dalla Barba et al., 2018). Lesioned gray matter areas on the normalized lesion were subsequently identified by means of the Harvard Oxford template.

A disconnectome map (BCBToolkit) was then calculated. This method employs diffusion-weighted images of healthy controls (Rojkova et al., 2016) -in this case 10- to track the fibers running through the lesion. The normalized lesion in the standard MNI152 space is registered to each control native space and used as a seed for a tractography (estimated as in Thiebaut de Schotten et al., 2011) conducted by means of the Trackvis software (Wang et al., 2007). Each tractographic map from each control subject is then converted into a visitation map, binarized, and back-transformed to the MNI space. As a final step, a percentage overlap map is produced by averaging, for each voxel of the MNI space, the normalized binarized visitation maps of the healthy subjects. Therefore, each voxel in the final disconnectome map indicates the probability (from 0 to 1) of being disconnected from the lesion site (Thiebaut de Schotten et al., 2015). This approach has been adopted to provide a measure of the impact of stroke on the whole brain (Salvalaggio et al., 2020). The involved white matter tracts were identified by means of the Natbrainlab (https://www.natbrainlab.co.uk/atlas-maps) template, after thresholding the disconnectome map at 50%. For the three branches of Superior Longitudinal Fasciculus (not present in the Natbrainlab template), masks from Rojkova et al. (2016) (freely available at http://toolkit.bcblab.com/) were adopted. The disconnectome maps were finally plotted on a standard brain by means of the FSLeyes software (https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSLeyes).

Results

Behavioral results

As far as the regression model for both words and pseudowords is concerned, the intercept was not significant ($z = 1.256$, $p = 0.209$). This indicates that performance for words was overall not significantly different from chance level (Table 2.1). The effect of lexicality was significant ($z = -2.433$, $p = 0.015$), indicating worse performance for pseudowords (32% accurate) than for words (60% accurate). The regression model for words revealed a non-significant intercept ($z = 0.628$, $p = 0.530$), indicating that performance was not significantly different from chance level for low-frequency-low-imageability words. Both the main effects of frequency ($z = -0.449$, $p = 0.654$) and imageability ($z = -0.888$, $p = 0.374$) turned out to be non-significant. This indicates that performance was not significantly better than the chance level in both the high-frequency-low-imageability (50% accurate) and the low-frequency-high-imageability conditions (40% accurate). On the contrary, the frequency-by-imageability interaction was significant (z = 1.965, p = 0.049), suggesting that AA's performance in lexical decision was only accurate for high-frequency-high-imageability stimuli (90% accurate).

Table 2.1 | overview of the accuracy data of the tachistoscopic lexical decision task. HF = high frequency; LF = low frequency; HI = high imageability; LI = low imageability.

	Overall	Pseudowords	Words	HF	LF	HI	LI	HF-HI	HF-LI	LF-HI	LF-LI
N	80	40	40	20	20	20	20	***10***	10	10	10
Accurate responses	37	13	24	14	10	13	11	***9***	5	4	6
%accurate	.46	.32	.60	.70	.50	.65	.55	***.90***	.50	.40	.60

Lesion-based structural disconnectome

MRI confirmed the involvement of the left occipital lobe and temporal infero-mesial cortex, together with the splenial fibers (Figure 2.2). In particular, the lesion occupied the occipital pole, the lingual gyrus, the intracalcarine cortex, the inferior portion of the lateral occipital cortex, the fusiform gyrus, the parahippocampal gyrus, the posterior cingulum, and the precuneus.

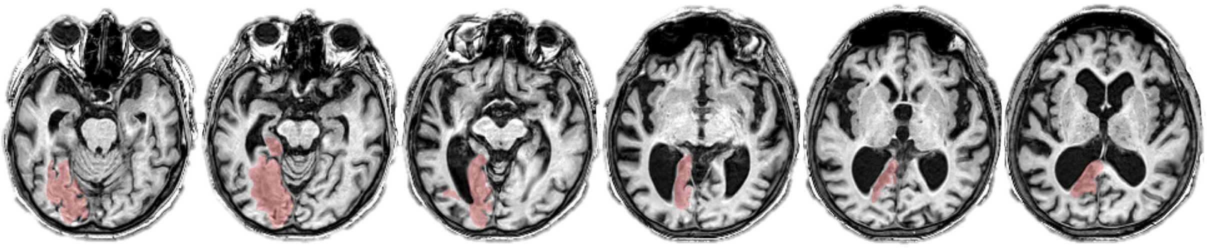

Figure 2.2 | Structural (T1-weighted) MRI showing the left occipital lesion extending to the interhemispheric splenial pathways (highlighted in red).

The disconnection profile primarily involved the splenial fibers. It also involved the cingulum and the IFOF bilaterally (although mainly in the LH). Also, other white-matter tracts within the LH were involved, such as the left optic radiations, the anterior commissure, the fornix, the cortico-ponto-cerebellar projections, the uncinate fasciculus, both the long and posterior segments of the AF, the ILF, as well as of all three branches of the SLF (Figure 2.3). The disconnectome map also overlapped with portions of the internal capsule and the left cortico-spinal tract, which are unlikely to be affected by the lesion, given their dorso-ventral direction. For this reason, they will not be discussed further.

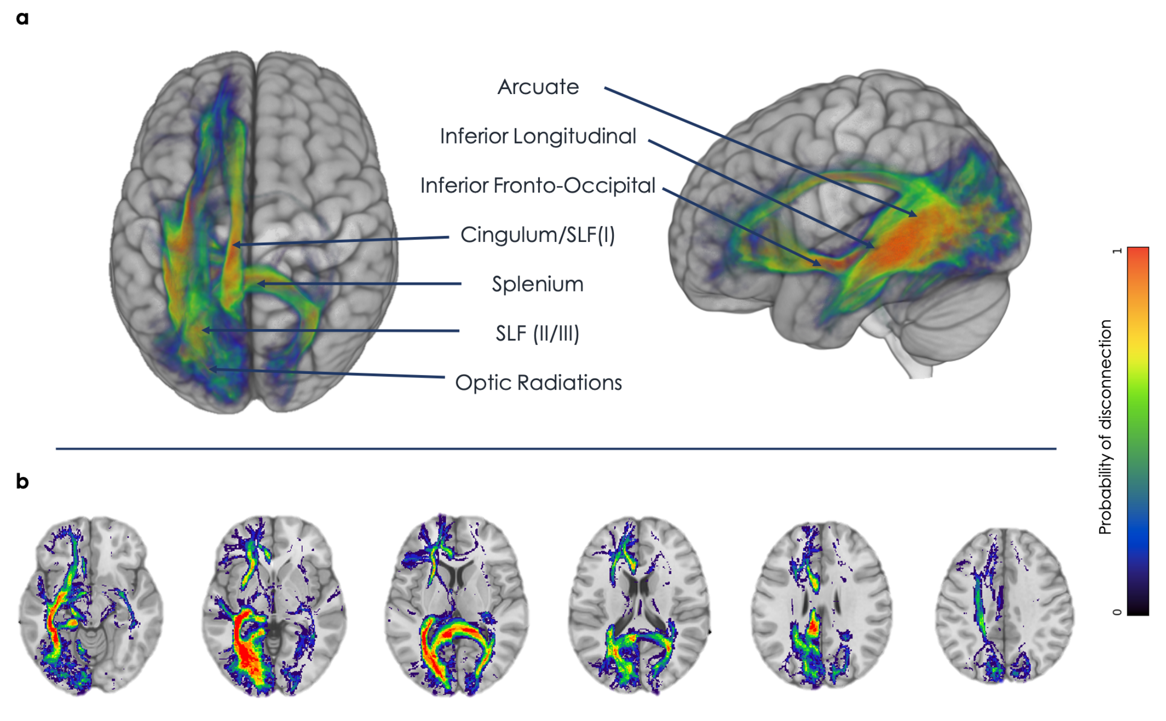

Figure 2.3 | Structural disconnectome pattern for patient AA: (a) 3D and (b) 2D axial rendering in the standard MNI space of AA's disconnectome map (i.e. the probability-from 0 to 1- for each voxel of being disconnected from the lesion site). Two-dimensional images are reported according to the neurological convention (left is left).

Discussion

The behavioral, lesional, and structural disconnectome patterns of AA, an 81-year-old patient who showed pure alexia due to the occlusion of the left posterior cerebral artery was analyzed. As in previous descriptions of patients with pure alexia (see, for instance, Coslett & Saffran, 1994; Lambon Ralph, Hesketh & Sage, 2004; Roberts, Lambon Ralph & Woollams, 2010; Saffran & Coslett, 1998; Shan et al., 2010), patient AA showed a dissociation between a severe impairment in overt reading and some signs of orthographic residual abilities in a covert reading task (implicit reading). Implicit reading in patient AA was revealed by accuracy in a tachistoscopic lexical decision task in which concreteness and word frequency were modulated.

The overall performance of AA for words was not significantly different from chance level. However, for high-frequency concrete words, accuracy was at 90%. Implicit reading in pure alexia has been interpreted as due to partial sparing and activation of the LH visual word form system (Lambon Ralph, Hesketh & Sage, 2004; Roberts, Lambon Ralph & Woollams, 2010), in line with an *absolute* view of LH dominance over the RH for reading (see for instance Dejerine, 1892; Ellis, 2004; Ellis et al., 1988). An alternative framework complying with a *relative* account of LH dominance for reading assumes that the RH might not be completely word-blind, and it suggests implicit reading in pure alexia to be a sign of RH reading (Coslett & Saffran, 1994; Saffran & Coslett, 1998, see also Larsen et al., 2004). From a cognitive point of view, the LH framework is the most conservative one, as it does not require the existence of an RH homologue of the visual word-form system.

However, for this hypothesis to hold, not only some neural centers of the LH visual word-form system must be spared, connected (through the ILF; Epelbaum et al., 2008), and active. Also, connectivity between these centers and (pre)frontal areas (in which the decision-related part of the task is implemented) must be spared by the lesion. Remarkably, this was not the case for patient AA. In fact, patient AA showed a lesion involving the left primary visual cortex, the fusiform gyrus, and the splenium. At the same time, AA's lesion suggested a disconnection pattern involving left optic radiations, the splenium, and among other white-matter tracts, the long and the posterior segments of the AF, the ILF, the IFOF and all three branches of the SLF. Due to the lack of functional imaging data, I cannot provide a conclusive explanation of the neural underpinnings of implicit reading in patient AA. Nevertheless, structural and disconnectome data can be used to compare the LH and RH hypotheses in terms of their plausibility. Indeed, it may not be possible to state which hemisphere was actively performing the task of reading, but it is possible to identify the sources of probable reduction in the quality of information due to the lesion and consequent disconnection. Indeed, a brain structure directly or indirectly affected by the lesion is likely to process or transfer incoming orthographic information in an inaccurate way. The more these sources of degradation, the lower shall be the quality of the processed/transferred information. In order to identify these sources of information loss, it is useful to reconstruct the stream of information from primary visual cortices to decision-related (pre)frontal areas predicted by the two hypotheses.

Due to the left visual field presentation, visual information is first processed in the right occipital cortex. According to the LH hypothesis, information has to reach the LH visual word form system. To do so, at least in the case of patient AA, it should “survive” five major sources of degradation: it shall be transmitted via the disconnected splenium, be processed in the LH lesioned occipital region, and transferred via the disconnected ILF. It should be subsequently processed by the lesioned LH visual word-form system, and, eventually, flow to frontal and prefrontal decision-related areas via the disconnected AF, IFOF, and/or SLF.

Conversely, the RH account does not imply any lesion, or disconnection-related sources of information loss. Therefore, in light of the lesion and of disconnectome profile, it is comparatively more plausible than the LH one. Information could flow from the spared RH primary visual cortex to the spared RH homologue of the visual word-form system (see also Rauschecker et al., 2012; Chu & Meltzer, 2019), and be projected to decision-related frontal centers, either in the RH or in the LH after crossing the midline via a spared, more anterior, callosal tract.

This interpretation thus suggests that the RH is not word blind. Rather, it would contain lexical orthographic representations independent from those of the LH, as these latter -due to lesion and disconnection- could neither be accessed, nor used to formulate lexical decisions.

It is worthy to note that performance in patient AA was accurate only for high-frequency, concrete words. This provides support for the idea that in the RH only high-frequency, concrete words are sufficiently well represented to be effectively activated (Coltheart 1980; 2000; Saffran et al., 1980; see also Luzzatti, 2003). More in general, these data support the “two orthographic lexicons” framework and a *relative* dominance of the LH over the RH for reading.

Obviously, there are some inevitable caveats: first, the intrinsic limitations of a single case study; second, the use of a relatively limited set of trials per condition in order to preserve the patient’s compliance; a third caveat comes from the fact the lack of neurofunctional evidence in favor of the RH mediation of implicit reading in patient AA. In other words, this study can provide indirect support in favor of the RH hypothesis, i.e., by bringing evidence against the LH one. A fourth limitation is the fact that disconnectome data were not derived from patient’s structural connectivity data, but from “normative” data from healthy subjects. Further studies combining structural, disconnectome, and neurofunctional techniques are required to provide conclusive evidence toward the ultimate role of the RH in implicit reading in pure alexia, as well as to re-assess more in general the role of RH in reading.

In the next chapter, I will try to extend the exploration on whether the dominance of the LH over the RH for reading is *absolute* or *relative* to healthy young subjects. To do so, I will present data from a divided visual field lexical decision task in which both pre-lexical and lexical factors were simultaneously manipulated in a highly controlled experimental setting.

References

Bertinetto, P. M., Burani, C., Laudanna, A., Marconi, L., Ratti, D., Rolando, C., & Thornton, A. M. (2005). CoLFIS (Corpus e Lessico di Frequenza dell'Italiano Scritto). *http://www. istc. cnr.it/material/database*, 67-73.

Bouhali, F., de Schotten, M. T., Pinel, P., Poupon, C., Mangin, J. F., Dehaene, S., & Cohen, L. (2014). Anatomical connections of the visual word form area. *Journal of Neuroscience, 34*(46), 15402-15414.

Brett, M., Leff, A. P., Rorden, C., & Ashburner, J. (2001). Spatial normalization of brain images with focal lesions using cost function masking. *Neuroimage, 14*(2), 486–500.

Catani, M., & Thiebaut de Schotten, M. (2008). A diffusion tensor imaging tractography atlas for virtual in vivo dissections. *Cortex, 44*(8), 1105–1132.

Catricalà, E., Della Rosa, P. A., Ginex, V., Mussetti, Z., Plebani, V., & Cappa, S. F. (2013). An Italian battery for the assessment of semantic memory disorders. *Neurological Sciences, 34*(6), 985–993.

Cattinelli, I., Borghese, N. A., Gallucci, M., & Paulesu, E. (2013). Reading the reading brain: A new meta-analysis of functional imaging data on reading. *Journal of Neurolinguistics, 26*(1), 214–238.

Chu, R. K., & Meltzer, J. A. (2019). Interhemispheric connectivity during lateralized lexical decision. *Human Brain Mapping, 40*(3), 818–832.

Cohen, L., Dehaene, S., McCormick, S., Durant, S., & Zanker, J. M. (2016). Brain mechanisms of recovery from pure alexia: A single case study with multiple longitudinal scans. *Neuropsychologia, 91*(1), 36–49.

Cohen, L., Dehaene, S., Naccache, L., Lehéricy, S., Dehaene-Lambertz, G., Hénaff, M. A., & Michel, F. (2000). The visual word form area: Spatial and temporal characterization of an initial stage of reading in normal subjects and posterior split-brain patients. *Brain, 123*(2), 291–307.

Cohen, L., Martinaud, O., Lemer, C., Lehéricy, S., Samson, Y., Obadia, M., ... & Dehaene, S. (2003). Visual word recognition in the left and right hemispheres: anatomical and functional correlates of peripheral alexias. *Cerebral Cortex, 13*(12), 1313-1333.

Coltheart, M. (1980). Deep dyslexia: A right-hemisphere hypothesis. In M. Coltheart, K. Patterson, & J. C. Marshall (Eds.), *Deep Dyslexia* (pp. 326–380). Routledge and Kegan Paul.

Coltheart, M. (1998). Seven questions about pure alexia (letter-by-letter reading). *Cognitive Neuropsychology*, *15*(1–2), 1–6.

Coltheart, M. (2000). Deep dyslexia is right-hemisphere reading. *Brain and Language, 71*(2), 299–309.

Coslett, H. B., & Saffran, E. M. (1994). Mechanisms of implicit reading in alexia. In M. Farah & G. Ratcliff (Eds.), *The neuropsychology of high-level vision* (pp. 299–330). Lawrence Erlbaum Associates.

Coslett, H. B., & Monsul, N. (1994). Reading with the right hemisphere: Evidence from transcranial magnetic stimulation. *Brain and Language, 46*(2), 198–211.

Coslett, H. B., & Saffran, E. M. (1989). Evidence for preserved reading in pure alexia. *Brain, 112*(2), 327–359.

Dalla Barba, G., Brazzarola, M., Barbera, C., Marangoni, S., Causin, F., Bartolomeo, P., & Thiebaut de Schotten, M. (2018). Different patterns of confabulation in left visuo-spatial neglect. *Experimental Brain Research, 236*(7), 2037–2046.

Dejerine, J. (1892). Contribution à l'étude anatomopathologique et clinique des différents variétés de cécité verbale. *Mémoires de la Société de Biologie, 4*, 61–90.

Ellis, A. W. (2004). Length, formats, neighbours, hemispheres, and the processing of words presented laterally or at fixation. Brain and Language, 88(3), 355–366. Ellis, A. W., Young, A. W., & Anderson, C. (1988). Modes of word recognition in the left and right cerebral hemispheres. *Brain and Language, 35*(2), 254–273.

Ellis, H. D., & Shepherd, J. W. (1974). Recognition of abstract and concrete words presented in left and right visual fields. *Journal of Experimental Psychology, 103*(5), 1035.

Ellis, A. W., Young, A. W., & Anderson, C. (1988). Modes of word recognition in the left and right cerebral hemispheres. *Brain and Language, 35*(2), 254-273.

Epelbaum, S., Pinel, P., Gaillard, R., Delmaire, C., Perrin, M., Dupont, S., Dehaene, S., & Cohen, L. (2008). Pure alexia as a disconnection syndrome: New diffusion imaging evidence for an old concept. *Cortex, 44* (8), 962–974

Foulon, C., Cerliani, L., Kinkingnehun, S., Levy, R., Rosso, C., Urbanski, M., Volle, E., & Thiebaut de Schotten, M. (2018). Advanced lesion symptom mapping analyses and implementation as BCBtoolkit. *GigaScience, 7*(3), giy004.

Gold, B. T., Powell, D. K., Xuan, L., Jiang, Y., & Hardy, P. A. (2007). Speed of lexical decision correlates with diffusion anisotropy in left parietal and frontal white matter: Evidence from diffusion tensor imaging. *Neuropsychologia, 45*(11), 2439–2446.

Hansen, K., & Starrfelt, R. (2019). Pure Alexia: A combined first-person account and neuropsychological investigation. *Cognitive and Behavioral Neurology, 32*(4), 268–277.

Hillis, A. E., & Caramazza, A. (1995). Cognitive and neural mechanisms underlying visual and semantic processing: Implications from "optic aphasia". *Journal of Cognitive Neuroscience, 7*(4), 457–478.

Hines, D. (1977). Differences in tachistoscopic recognition between abstract and concrete words as a function of visual half-field and frequency. *Cortex, 13*(1), 66–73.

Huang, M., Baskin, D. S., & Fung, S. (2016). Glioblastoma presenting with pure alexia and palinopsia involving the left inferior occipital gyrus and visual word form area evaluated with functional magnetic resonance imaging and diffusion tensor imaging tractography. *World Neurosurgery, 89*(1), 725–e5.

Huber, W., Poeck, K., & Willmes, K. (1984). The Aachen aphasia test. In F. C. Rose (Ed.), Advances in neurology, vol. 42: *Progress in aphasiology* (pp. 291–303). Raven Press.

Lambon Ralph, M. A., Hesketh, A., & Sage, K. (2004). Implicit recognition in pure alexia: The Saffran effect—a tale of two systems or two procedures? *Cognitive Neuropsychology, 21*(2–4), 401–421.

Larsen, J., Baynes, K., & Swick, D. (2004). Right hemisphere reading mechanisms in a global alexic patient. *Neuropsychologia, 42*(11), 1459–1476.

Lhermitte, F., & Beauvois, M. F. (1973). A visual-speech disconnexion syndrome: Report of a case with optic aphasia, agnosic alexia and colour agnosia. *Brain, 96*(4), 695–714.

Luzzatti, C. (2003). Optic aphasia and pure alexia: Contribution of callosal disconnection syndromes to the study of lexical and semantic representation in the right hemisphere. In E. Zaidel & M. Iacoboni (Eds.), *The parallel brain: The cognitive neuroscience of the corpus callosum* (pp. 479–499). MIT Press.

Luzzatti, C., Rumiati, R., & Ghirardi, G. (1998). A functional model of visuo-verbal disconnection and the neuroanatomical constraints of optic aphasia. *Neurocase, 4*(1), 71–87.

Luzzatti, C., Willmes, K., & De Bleser, R. (1996). Aachener Aphasie Test: Versione italiana. Organizzazioni Speciali.

Mayall, K., & Humphreys, G. (1996). A connectionist model of alexia: Covert recognition and case mixing effects. *British Journal of Psychology, 87*(3), 355–402.

McCandliss, B. D., Cohen, L., & Dehaene, S. (2003). The visual word form area: Expertise for reading in the fusiform gyrus. *Trends in Cognitive Sciences, 7*(7), 293–299.

McKeeff, T. J., & Behrmann, M. (2004). Pure alexia and covert reading: Evidence from Stroop tasks. Cognitive *Neuropsychology, 21*(2–4), 443–458.

Novelli, G., Papagno, C., Capitani, E., & Laiacona, M. (1986). Tre test clinici di ricerca e produzione lessicale. Taratura su sogetti normali. *Archivio di Psicologia, Neurologia e Psichiatria, 47*(4), 477–506.

Rauschecker, A. M., Bowen, R. F., Parvizi, J., & Wandell, B. A. (2012). Position sensitivity in the visual word form area. *Proceedings of the National Academy of Sciences, 109*(24), E1568–E1577.

Riddoch, M. J., & Humphreys, G. W. (1987). Visual object processing in optic aphasia: A case of semantic access agnosia. *Cognitive Neuropsychology, 4* (2), 131–185.

Roberts, D. J., Lambon Ralph, M. A., & Woollams, A. M. (2010). When does less yield more? The impact of severity upon implicit recognition in pure alexia. *Neuropsychologia, 48*(9), 2437–2446.

Rodríguez-López, C., Molina, M. P. G., & Salio, A. M. (2018). Pure alexia: Two cases and a new neuroanatomical classification. *Journal of Neurology, 265*(2), 436–438.

Rojkova, K., Volle, E., Urbanski, M., Humbert, F., Dell'Acqua, F., & De Schotten, M. T. (2016). Atlasing the frontal lobe connections and their variability due to age and education: A spherical deconvolution tractography study. *Brain Structure & Function, 221*(3), 1751–1766.

Rosazza, C., Isella, V., Appollonio, I., & Shallice, T. (2018). When mild pure alexia may not be reducible to hemianopic alexia. *Cognitive Neuropsychology, 35*(8), 479–484.

Rutherford, B. J., & Mathesius, J. R. (2012). The brain's hemispheres and controlled search of the lexicon: Evidence from fixated words and pseudowords. *Brain and Cognition, 79*(3), 188–199.

Sabsevitz, D. S., Middlebrooks, E. H., Tatum, W., Grewal, S. S., Wharen, R., & Ritaccio, A. L. (2020). Examining the function of the visual word form area with stereo EEG electrical stimulation: A case report of pure Alexia. *Cortex, 129*(1), 112–118.

Saffran, E. M., Bogyo, L. C., Schwartz, M. F., & Marin, O. S. M. (1980). Does deep dyslexia reflect right-hemisphere reading? In Coltheart, M., Patterson, K., & Marshall, J.C. (Eds.), *Deep Dyslexia* (pp. 381-406) London: Routledge and Kegan Paul.

Saffran, E. M., & Coslett, H. B. (1998). Implicit vs. letter-by-letter reading in pure alexia: A tale of two systems. *Cognitive Neuropsychology, 15*(1-2), 141–165.

Salvalaggio, A., De Filippo De Grazia, M., Zorzi, M., Thiebaut de Schotten, M., & Corbetta, M. (2020). Post-stroke deficit prediction from lesion and indirect structural and functional disconnection. *Brain, 143*(7), 2173–2188.

Shan, C., Zhu, R., Xu, M., Luo, B., & Weng, X. (2010). Implicit reading in Chinese pure alexia. *s*(3), 147–156.

Starrfelt, R., & Shallice, T. (2014). What's in a name? The characterization of pure alexia. *Cognitive neuropsychology, 31*(5-6), 367-377.

Thiebaut de Schotten, M., Dell'Acqua, F., Forkel, S., Simmons, A., Vergani, F., Murphy, D. G., & Catani, M. (2011). A lateralized brain network for visuo-spatial attention. *Nature Neuroscience, 14*(10), 1245–1246.

Thiebaut de Schotten, M., Dell'Acqua, F., Ratiu, P., Leslie, A., Howells, H., Cabanis, E., Iba-Zizen, M. T., Plaisant, O., Simmons, A., Dronkers, N. F., Corkin, S., & Catani, M. (2015). From Phineas Gage and Monsieur Leborgne to HM: Revisiting disconnection syndromes. *Cerebral Cortex, 25*(12), 4812–4827.

Thiebaut de Schotten, M., Dell'Acqua, F., Valabregue, R., & Catani, M. (2012). Monkey to human comparative anatomy of the frontal lobe association tracts. *Cortex, 48*(1), 82–96.

Veldsman, M., Loetscher, T., Wood, A., & Brodtmann, A. (2017). Reading on the right when there's nothing left? Probabilistic tractography reveals hemispheric asymmetry in pure alexia. *Neurocase, 23*(3–4), 201–209.

Wang, R., Benner, T., Sorensen, A. G., & Wedeen, V. J. (2007, May). Diffusion toolkit: A software package for diffusion imaging data processing and tractography. *Proceedings of the International Society for Magnetic Resonance in Medicine*, 15, 3720.

Appendix

Table A.2.1 | Pseudoword and Word stimuli for experimental trials with frequency and imageability data.

Pseudowords		***Words***					
Stimulus	***Stimulus***	***Stimulus***	***Absolute Frequency (COLFIS)***	***Imageability***	***Stimulus***	***Absolute Frequency (COLFIS)***	***Imageability***
BANA	NELO	CANE	174	6.90	NAVE	126	6.90
BEDA	NIFO	CASO	1797	1.48	PACE	454	2.62
BEFO	NILA	CONO	14	6.81	PALA	8	6.81
DAGO	NOBO	CUBO	13	6.67	PANE	168	6.95
DELA	PEBO	DIGA	10	5.95	PENA	263	2.09
DEMA	PEGE	DOGE	4	3.29	PEPE	108	6.67
DOBA	PIFO	FAME	175	2.86	PUMA	2	6.43
FEPA	PUSO	FARO	27	6.81	RIMA	3	3.71
FIMO	RAPO	FEDE	238	3.95	RUPE	5	5.90
FOTA	REPO	FESA	2	4.52	SEDE	349	3.48
FUNA	RUFO	FOCA	4	6.81	SENO	107	6.71
GOPA	SELO	FOGA	15	2.24	SUGO	18	6.67
LEMA	SESA	LAGO	139	6.87	TANA	21	5.81
LOPO	SISO	LOTO	2	4.67	TECA	5	5.67
MOGO	SUVA	MANO	1104	6.95	TEMA	316	4.24
MUFA	TAME	MARE	625	6.90	TOMO	5	4.81
MUPE	VACE	MESE	712	3.09	VANO	18	4.33
NAFO	ZABA	MURO	202	6.86	VOCE	784	3.05
NALO	ZAPO	MUSA	10	3.29	ZELO	15	1.33
NEGE	ZOMO	NASO	125	6.81	ZONA	574	3.14

Chapter 3

One or two orthographic lexicons? A divided visual field lexical decision study in healthy right-handed participants.

In the previous chapter, a behavioral and disconnectome study of a patient with pure alexia was presented. Data revealed that, in spite of the inability to recognize words explicitly, the patient was able to identify high-frequency concrete words as lexical strings. The lesion and disconnectome profile suggested that the RH is more likely than the LH to mediate implicit reading in the patient. These results imply that the RH could contain an orthographic lexicon that is separate from the LH one, in which only representations for highly frequent and/or concrete items can be effectively activated. The present study aims at testing the existence of one vs. two orthographic lexicons (complying with an *absolute* and *relative* account of LH dominance for reading, respectively) in healthy young participants, by means of a highly controlled divided visual field reading paradigm. In the attempt of replicating the lexical-semantic effects observed in patient AA, experimental manipulation of word frequency and imageability were included. Also, pre-lexical experimental modulations were introduced, in order to test whether pre-lexical factors, rather than lexical-semantic factors determine hemispheric differences in reading.

Introduction

Divided visual field studies on reading take advantage of the crossed configuration of the visual system (whereby visual stimuli presented in the RVF target the primary visual cortex of the LH and vice-versa) to explore laterality effects in orthographic processing.

This set of techniques has been widely employed to study the functional lateralization of cognitive processes in patients who underwent surgical resection of the corpus callosum to avoid the generalization of drug-resistant epilepsy. Indeed, in this cohort of subjects, the lack of inter-hemispheric communication assures that lateralized stimuli are perceived and processed by one single hemisphere. These studies reported that, in line with classical neuropsychological data (Dejerine, 1892), LH is typically dominant over the RH for reading (see for instance Gazzaniga & Sperry, 1967). In order to generalize results obtained with split-brain patients and to exclude those results to be affected by functional reorganization due to chronic epilepsy, divided visual field paradigms have also been administered to healthy subjects. The validity of this methodology has been supported by the description of a consistent advantage for the processing of word stimuli projected in the RVF/LH over stimuli projected in the LVF/RH (Leiber, 1976; Babkoff & Ben-Uriah, 1983; Chiarello, Senehi & Soulier, 1986; Hernandez, Nieto & Barroso, 1992; Chiarello et al., 2005; Willemin et al., 2016; Hausmann et al., 2019; De Clercq & Brysbaert, 2020). However, given that the two hemispheres are not disconnected in healthy subjects, at least two different functional brain models could underly this effect.

Explaining the visual field effect in lateralized reading

A possible mechanism giving rise to the visual field effect in lateralized reading entails (direct) access -for stimuli targeting the LVF- to a set of RH orthographic representations which are either limited in number or less easily activated compared to that of the LH. Imperfect processing by the limited RH orthographic input lexicon (as opposed to the proficient visual word form system operating in the LH) would determine the lower performance for LVF/RH stimuli than for RVF/LH ones. This account has been fostered by neuropsychological evidence on the residual reading abilities of patients with deep dyslexia (Coltheart, 1980; 2000; Saffran et al., 1980) and on implicit reading in Pure Alexia (see for instance Coslett & Saffran, 1989, 1994; Saffran & Coslett, 1998; see also Chapter 2), and it assumes that there are *two orthographic lexicons* in the brain, one in each hemisphere (Saffran & Coslett, 1998; Coslett & Saffran 1994; Luzzatti, Rumiati & Ghirardi, 1998; Luzzatti, 2003), with that of the RH being able to activate only representations for highly frequent and/or concrete words. According to this view (which is in line with a *relative* account of LH dominance for reading), lexical-semantic factors (e.g.: word frequency and/or imageability/concreteness) should explain visual field/hemisphere difference in lateralized reading.

A different framework suggests that visual field differences in reading could depend on factors preceding lexical access, making the existence of a coarse RH orthographic lexicon an unnecessary assumption. A first line of research, assuming that initial letters of incoming stimuli are more salient than final letters (see for instance Rayner & Kaiser, 1975), suggested that the comparative LVF disadvantage in word recognition could depend on suboptimal perception of initial letters in the LVF for left-to-right reading languages (Kirsner & Schwartz, 1986). Nevertheless, evidence of a RVF advantage also for Hebrew, in which reading is performed through a right-to-left visual scanning procedure, has suggested that perceptual factors are not sufficient to account for the visual field effect in lateralized reading (Babkoff & Ben-Uriah, 1983; Faust et al., 1993). An alternative model similarly pointing to a pre-lexical explanation of the visual field effect (Ellis, Young & Anderson, 1988; Ellis, 2004) has focused on the cost of the preliminary processing operations that are necessary to access a *single* set of orthographic representations, located in the LH. This framework (that complies with an *absolute* model of LH dominance for reading and a *callosal relay* account) suggests that orthographic stimuli targeting the LVF must undergo (1) *stepwise*[1] word-letter-dependent abstraction of letter identities and (2) transfer to the LH either to access the lexicon (for words) -as the RH is meant to lack an orthographic lexicon-, or the grapheme-to-phoneme conversion system (for unknown words or pseudowords). Conversely, known word stimuli presented in a common horizontal format to the RVF would directly access the LH orthographic lexicon without the need of being converted into abstract letter identities one letter at a time. Therefore, word stimuli presented to the RVF would access the single LH lexicon directly in a fast, *parallel* way, whereas stimuli targeting the LVF would engage a *stepwise* reading system, prone to word-length-dependent latency and information loss (due to information transfer). According to the model, a *stepwise* reading system (implying step-by-step conversion of stimuli into abstract letter units) would be also available in the LH, but -being excessively time-consuming- it would only be used for processing pseudowords prior to grapheme-to-phoneme conversion and for reading words presented in an unconventional format (e.g.: in MiXeD

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[1] As clarified in Chapter 1, *stepwise* processing does not imply left-to right processing (Ellis, Young & Anderson, 1988; Ellis, 2004). According to the model, this process could occur in a "ends-in" manner. The crucial point is that -in this pathway- letters within a given orthographic string are processed one at a time.

CaSe or vertically). This model was based on the observation of a seemingly consistent word length-by-visual field effect, indicating that, while the RVF/LH is only mildly sensitive to stimuli length, the LVF/RH is associated with lower performance as word length increases (Young & Ellis 1985; and Brysbaert & d'Ydewalle 1990). In other words, the greater the amount of orthographic information to process, the larger the behavioral difference among hemispheres. Furthermore, Lavidor and Ellis (2002) reported a difference between hemispheres in the effect of Orthographic Neighborhood (N) size (i.e., the number of words with the same length differing from a target item for a single letter), which is meant to provide a measure of top-down influence from lexical knowledge to single-letter processing. Lavidor and Ellis observed that N size affects LVF and not RVF reading. According to the model by Ellis (2004), N size effects arise only when the single LH lexicon is accessed through a *stepwise* reading strategy, as a form of top-down facilitation effect from the lexicon to letter-level analysis of the stimulus (for a different account on how the length-by-visual field and N size-by-visual field interactions arise, see Whitney, 2001)[2]. Accordingly, a N size effect would be observable for stimuli projected to the LVF/RH due to the use of a *stepwise* procedure to access the *single* LH lexicon, while it would not be observed for stimuli targeting the RVF/LH, as in this case a *parallel* reading procedure is adopted.

One or two orthographic lexicons?

As mentioned in the first chapter, both frameworks have been used as functional brain models to explain the visual field effect in lateralized reading tasks (e.g., Day, 1977; Babkoff & Ben-Uriah, 1983; Chiarello, Senehi & Soulier, 1986; Waldie & Moseley, 2000, Ellis, Young & Anderson, 1988; Olk & Hartje, 2001; Whitney & Lavidor, 2005; De Clercq & Brysbaert, 2020). On the one hand, the lack of a shared functional brain model meant to explain the visual field effect in lateralized reading has led to the paradoxical existence of studies focusing on how the RH processes high-order semantic features of words such as the emotional valence of stimuli (see for instance De Clercq & Brysbaert, 2020), while still there is no consensus on whether the RH is word-blind or not. On the other hand, such lack of consistency poses a problem for studies advocating the use of divided visual field reading to measure hemispheric dominance language as a less-expensive alternative to neurofunctional

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[2] Although an N size effect involves feedback from the orthographic lexicon, for the purposes of this work N size will be considered as a pre-lexical factor, as its effect is meant to facilitate orthographic processing at the letter level (Ellis, 2004).

methods (e.g., Hunter & Brysbaert, 2008). Indeed, while according to the "single orthographic lexicon" model, pre-lexical factors impact the visual field effect, according to the "two orthographic lexicons" model, lexical-semantic variables modulate the visual field effect in lateralized reading. Not knowing the relative weight of pre-lexical and lexical-semantic factors in lateralized reading implies that laterality measurements could depend on pre-lexical and/or lexical psycholinguistic features of the stimuli to an unknown extent. For this reason, a comprehensive experimental approach capable of measuring the relative weight of different pre-lexical and lexical psycholinguistic variables on the visual field effect in lateralized reading is necessary. Among the 11 lateralized lexical decision studies in which hypotheses of word-blindness vs. non-word-blindness of the RH were formally compared published from 1976 to 2020 (Table 3.1), none involved the simultaneous exploration of the effects of word frequency, imageability, N size, and word length. Furthermore, some of these studies presented stimuli that were very close to the central midline, with relatively long presentation times, without overt instrumental control for eye movements, thus casting doubts on the reliability of their findings[3]. The present experiment was designed with the aim of testing the effect of different pre-lexical and lexical psycholinguistic variables on the visual field effect in lateralized reading. On the one hand, this empirical exploration allows the definition of the relative importance of pre-lexical and lexical-semantic factors in lateralized reading. On the other hand, it can provide insights on which brain model between the "single orthographic lexicon" one and the "two orthographic lexicons" one best explains the visual field effect.

The "two orthographic lexicons" hypothesis predicts different lexical-semantic (i.e., word frequency and/or imageability) effects for stimuli presented in the two visual fields/hemispheres. Conversely, the single (LH) orthographic lexicon view anticipates greater length and N-size effects in the LVF/RH than in the RVF/LH, whereas visual field differences for lexical-semantic variables are not expected. In this experiment, I simultaneously controlled for word frequency, word length, imageability, and N size in a lateralized lexical decision task. Participants' eye fixation position before each trial was monitored with an eye-tracking device.

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[3] The only exception could be the magnetoencephalographic (MEG) study by Chu & Meltzer (2019) in which, although not overtly mentioned in the paper, authors probably rejected eye movement artifacts to run analyses.

Table 3.1 | Overview of the lateralized lexical decision studies that formally compared hypotheses of word-blindness vs. non-word-blindness of the RH (Exp.= Experiment, N= sample size, Hand Pref. = Hand Preference, Stim. Mod. = Stimulation Modality, N size= orthographic neighborhood size, Freq = word Frequency, Concr./Imag = Concreteness/Imageability, VF x pre-lexical = interaction between Visual Field and pre-lexical factors, VF x lexical/sem = interaction between Visual Field and lexical/semantic factors; RHs =Right-Handers, Uni = Unilateral, Bi= Bilateral).

Experiment				*Divided visual field protocol*					*Pre-lexical factors*			*Lexical-semantic factors*			*Interaction effects*	
Authors	*Year*	*Exp*	*N*	*Stimuli Eccentricity*	*Stimuli Duration*	*Fixation control*	*Hand Pref.*	*Stim. Mod.*	*N size*	*Length*	*Other*	*Freq.*	*Concr./Imag.*	*Other*	*VF x pre-lexical*	***VF x lexical/sem.***
Leiber	1976	1	30	2°, 26'	100 ms	Indirect	Any	Uni	-	+		+	-		+	+
Day	1977	1	14	1.5°	100 ms	None	RHs	Uni	-	-		-	+			+
Babkoff & Ben-Uriah	1983	1	6	2.29°	200 ms	None	RHs	Uni	-	-		-	-			
		2	6	2.29°	200 ms	None	RHs	Uni	-	-		-	-			
Chiarello, Senehi & Soulier	1986	1	60	2°	25, 50, 100, 150ms	None	RHs	Uni	-	-	Exposure time	-	-		-	
		2	60	1, 2,3°	100 ms	None	RHs	Uni	-	-	Eccentricity	-	-		-	
		3	60	2°	100 ms	None	RHs	Uni	-	-	Horizontal Angle	-	-		-	
Measso & Zaidel	1990	1	64	2°	80ms	None	RHs	Uni	-	-		-	-			
Mohr, Pulvermüller & Zaidel	1994	1	22	1.23°	100 ms	Direct	RHs	Uni	-	-		+	-	Grammatical class		+
Iacoboni & Zaidel	1996	1	24	1.5°	120 ms	None	RHs	Uni/Bi	-	+		+	-		+	-
Waldie & Mosley	2000	1	38	3°	116 ms	None	Any	Uni	-	-		-	-			
Lavidor, Babkoff & Faust	2001	1	24	2.5°	150 ms	None	RHs	Uni	-	+	Orientation angle	-	-		+	
Perea, Acha & Fraga	2008	1	30	2.5°	150 ms	None	RHs	Uni	+	-		-	-		+	
		2	44	2.5°	150 ms	None	RHs	Uni	+	-	N Frequency and Type	-	-		+	
Chu & Meltzer	2019	1	19	1.5°	200 ms	MEG	RHs	Uni/Bi	-	-		-	-			

Materials and methods

Participants

Sixty neurologically healthy volunteers (30 males, 30 females; *mean* age = 23.07 years, *sd* = 2.79), with normal or corrected-to-normal vision, participated in the experiment. All were native Italian university students (*mean* education level = 14.70 years, *sd* = 2.07) and right-handed, according to the Edinburgh Handedness Inventory (Oldfield, 1971; *mean*= 89.72, *sd*= 13.05).

Stimuli

Experimental stimuli consisted of 160 words and 160 pronounceable pseudowords, all presented in upper case. Pronounceable pseudowords were preferred over unpronounceable non-words (e.g. string of consonants) to assure that lexical decision was based on lexical access rather than on phonotactic (and graphotactic) regularity, a pre-lexical factor which has no relevance with respect to the experimental questions and the models of orthographic processing being compared. Word stimuli (see Appendix, Table A.3.1) were 4-letters (80) and 5-letters (80) disyllabic nouns taken from the "Corpus e Lessico di Frequenza dell'Italiano Scritto" (CoLFIS) database (Bertinetto et al., 2005). The stimuli were selected in order to exclude –when possible- noun-verb homographs, to avoid any lexical ambiguity as well as unwanted biases in stimuli imageability due to grammatical class. The structure of the 4-letter words was consonant-vowel-consonant-vowel (CVCV) and consonant-vowel-consonant-consonant-vowel (CVCCV) for the 5-letter words. For the 5-letter words, double consonants (e.g. BIRRA, beer, CASSA, case) and the orthographic bigrams (or trigrams) GN, GL, SC(I/E), which in Italian correspond to the single phonemes /ɲ/, /ʎ/ and /ʃ/, respectively, were excluded. For both word length conditions (4 and 5 letters)[4], 40 stimuli were high-frequency words (absolute frequency above 100), while 40 were low-frequency words (absolute frequency below 50). In addition, stimuli were divided into high and low imageability (median splitting) according to the mean ratings of 21 previously recruited volunteers on a 7-points Likert scale.

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[4] I adopted the contrast between 4 and 5 letters in order to use only two-syllable stimuli. Adopting longer strings would have implied using stimuli with a different number of syllables, that would have resulted in greater phonological load, likely favoring LH processing over the RH. Instead, by using such manipulation of stimuli length, I aimed at loading orthographic processing without having an impact on phonemic processing.

The 160 pseudoword stimuli[5] (see Appendix, Table A.3.2) were randomly generated using the same CV structure of 4-letter (CVCV) and 5-letter (CVCCV) word stimuli and individually checked in order to avoid illegal items. For the 5-letter pseudowords the same consonant clusters as for 5-letter words were employed. The N size was also computed for both words and pseudowords (http://ip146172.psy.unipd.it/claudio/vicini2.php) according to the number of words that can be obtained by changing a single letter of the target item. In particular, for each stimulus, two measures of N size were computed: one for the complete letter string and one for the initial letter (Nfirst). The latter variable was employed to regress-out any possible effect due to poor recognition of the first letter in the presented items (see for instance Kirsner & Schwartz, 1986). Descriptive statistics for the experimental stimuli are reported in the Appendix, Table A.3.3.

Task and procedure

Each subject was administered with a lateralized lexical decision task programmed in E-Prime (version 2.0, Psychology Software Tools Inc.) and administered by means of a Lenovo ThinkCentre PC. During each trial, subjects were first presented with a central fixation cross, after which, a word or a pseudoword occupying about 5.72° (on average) horizontally and 1.23° vertically, briefly appeared either left or right from the center of the screen[6]. Subjects were asked to indicate with a mouse key press whether the previous stimulus had been either a word or a "non-word" (pseudoword). After each trial, a slide depicting grayscale random dots appeared for 1 second. According to the proposal put forward by Bourne (2006), I employed an eye-tracking device (EyeLink 1000 – SR Research, sampling rate = 1000 Hz) to control for eye movements. In particular, I adopted an eye-contingent procedure similar to that employed by Jordan, Patching and Thomas (2003): during each trial, eye movements were monitored while the central fixation cross was presented. As soon as each subjects' dwell time, in a squared window of 1° around the central position, reached the threshold of 250 ms, a stimulus (either word or pseudoword) appeared left or right from the fixation cross. Stimuli appeared for 128 ms with an eccentricity of 3.5° from the internal

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[5] During data analysis, I noticed that two pseudowords were actual, although extremely infrequent, lexical strings (CEBO, MUGO). For this reason, they were excluded from analyses. As a result, the final database included 158 pseudoword stimuli.

[6] Contrary to Hausmann et al. (2019), who presented two lateralized stimuli in each trial to implicitly control for eye movements, I presented just one stimulus during each trial and I explicitly controlled for eye movements. The choice of adopting a unilateral presentation was also guided by data suggesting that the lexicality of the unattended lateralized stimulus in bilateral presentations has an impact on performance (see for instance Iacoboni & Zaidel, 1996).

boundary of the stimulus to central fixation. This “safe” eccentricity parameter was chosen according to the conservative threshold suggested by Bourne’s revision of previous literature (2006). If during a given trial the fixation time of the central cross did not reach the threshold of 250 ms in a time window of 10 s, that trial was considered as invalid.

In one half of the trials the participants responded with their right hand, while in the other half they responded with their left hand (the order of such blocks was counterbalanced across subjects). Subjects were positioned in order to have their index and middle fingers on the left and right mouse keys. For each subject, regardless of the responding hand, each of the two fingers was associated to either response (e.g. index finger = “WORD”, middle finger “NON-WORD”). The association between fingers and response was counterbalanced across participants. Such double counterbalancing (responding hand and fingers) was performed in order to minimize any possible effect of stimulus-response compatibility.

After being instructed on the experimental procedure, subjects provided written informed consent. Each volunteer then comfortably sat in front of a computer screen (27”), with her/his chin placed on a chin rest, which was positioned in order to keep a distance of 70 cm between the screen and participants’ eyes. The experimenter then positioned the eye tracker (desktop mount) in order to find the best configuration from which each participant’s dominant eye could be tracked. Then, each volunteer underwent a brief training session during which two blocks of trials were presented. Before each trial block, the experimenter told the participants with which hand they had to respond and calibrated the eye-tracking system according to a 5-point calibration procedure. For the training session, 32 stimuli (16 words and 16 pseudowords) different from those presented during the proper experimental session were employed. During the training blocks (but not during the experimental phase) participants received feedback of their performance. After the training session, two experimental blocks (160 stimuli each) were administered. For each participant, the order of the responding hand and the finger-response association was kept fixed among training and experimental trials. As for the training session, also during the experimental session two calibration procedures (one before each experimental block) were run. Such procedure allowed to reach an average tracking precision of 0.19° (*sd* = 0.06). The order of presentation of the stimuli was completely randomized within each subject. Each participant saw each stimulus only once to avoid any learning effect, possibly capable of smoothing hemispheric differences in behavioral performance.

The study was run according to the guidelines of the declaration of Helsinki (World Medical Association, 2001) and was approved by the local ethical committee.

Data analysis

All data points from all subjects (19200 records) were merged in a single database. I first discarded the trials in which no response was produced (with each trial's time limit being set at 3s), as well as trials in which reaction times (RTs) were below 250ms (159 trials and 190 trials, respectively). I also checked that no invalid trials, due to the absence of stable central fixation (748 trials), were included in the final dataset, which was composed of 18103 records.

As one of the goals was to describe the processing limits of orthographic information of the two hemispheres, both RTs and accuracy data were taken into account. For each subject, separately for each trial, accuracy of responses in dichotomous form (1 = correct, 0 = incorrect) and log-transformed RTs of accurate responses (i.e. RTs of errors were discarded) were employed as dependent variables in a series of Mixed-effects models. Subjects and stimuli were modeled as random intercepts[7] (Baayen, 2008).

Logarithmic transformation was adopted to obtain a better approximation to a Normal distribution than that of raw RTs (see Appendix, Figure A.3.1). In line with Baayen's (2008) suggestion, a log transformation was adopted to avoid that "just a few extreme outliers might dominate the outcome, partially or even completely obscuring the main trends characterizing the majority of datapoints". A logarithmic transformation to "normalize" RTs was preferred to a Generalized Mixed Model with Gamma reference distribution and identity link function (Lo & Andrews, 2015), as the latter would not have allowed me to adopt a model selection procedure (see below) due to algorithm convergence issues.

Accuracy data were analyzed by means of logistic regressions. All analyses were performed by means of the statistical software R and the lme4 package (Bates, Maechler, Bolker, & Walker, 2015). Dummy coding of dichotomous variables was done through the function `contrasts(variable)<- contr.sum(2)`, resulting in the weights 1 and -1 being attributed to factor levels in alphanumeric order (e.g., factor "Length", level "4 letters" = 1, level "5 letters"= -1; factor "Visual Field", level "LVF"= 1, level "RVF"= -1).

Given the explorative nature of this study, I did not know *a priori* which models best fitted data. Therefore, a backward model selection procedure (see Appendix, Table A.3.4) was run. The starting

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[7] No random slopes were included in the models as they would have made convergence impossible for all initial models adopted as starting points for model selection. Adding random slopes made algorithm convergence impossible also for the final models (i.e., the simplest ones) emerging from model selection.

point for the model selection procedure of each group of analyses was the most complex model including the variables of interest in which the convergence of the algorithm succeeded for both accuracy and RTs. At each step (starting from interaction effects and then moving to main effects), the effect whose regression parameter was closest to zero was removed. The likelihood associated with the model at each step was statistically compared with that of the previous step. The procedure was repeated until a given model proved to be associated with a significantly lower likelihood than the previous one (which was selected as the best model).

For reaction time data, outliers were removed by means of the model criticism procedure (Baayen, 2008). When necessary, for both accuracy and RTs data, χ^2 post-hoc pairwise comparisons were performed on significant interaction effects by means of the *testInteraction* function of the package Phia (De Rosario-Martinez, 2013) and corrected according to the Bonferroni method. This was done in order to keep Type I error under control in the most conservative possible way.

Prior to analyses directly focused on the main experimental questions, I tried to exclude that any visual field effect could only be due to poor perception of initial letters. To do so, I explored whether the perceptibility of the first letter had an impact on performance in the two visual fields. In particular, I used a measure of visual confusability of each stimulus' first letter with the remaining 25 letters of the alphabet. The confusability measure was taken from a letter visual-similarity matrix (Simpson et al., 2013), based on perceptual similarity ratings between couples of uppercase letters (which is the format used in this experiment). For each letter, a measure of average confusability with all other letters was computed. Then, within the database, I created a new variable in which, for all trials and subjects, I reported the confusability value for the first letter of the presented stimulus. This was done to have a measure of the visual confusability of the first letters of experimental stimuli. The resulting variable was used as an independent variable –together with the factor "visual field" and their interaction- in linear mixed models (as for all other analyses), with Accuracy and RTs as dependent variables.

Subsequently, in order to answer the main experimental questions, three different sets of analyses were set up. First, as a preliminary approach, I assessed the effect of any no-interest variable (i.e., variables that necessarily had to be modulated due to this experimental approach, albeit being unrelated to the main experimental enquiry: lexicality and responding hand) with a potential modulatory effect on the Visual Field effect ("Visual Field analyses"). In particular, the effect of responding hand was included in order to account for a possible effect of stimulus-response compatibility. This exploration was then deepened by a sensitivity analysis.

Second, “N size analyses” were conducted, in order to define the possible differential role of N size in the identification of words and pseudowords projected in the two Visual Fields.

Finally, I addressed the effects of Length, Frequency and Imageability on accuracy and RTs in the two Visual Fields (“Length, Frequency and Imageability analyses”), in response to words. This set of analyses was then deepened by a subsequent exploration of the distance from chance level in the two Visual Fields.

Results

Preliminary analyses excluded a major role for the first letter of the presented stimuli in performance. For RTs, both the main effect of first letter confusability *t*(490.645)= 0.197, *p* = 0.844 and its interaction with the visual field *t*(12642.659)= 1.006, *p* =0.315 were not significant. For Accuracy, while the main effect of first letter confusability was still not significant *z* = 0.325, *p* = 0.745, an apparent first letter confusability-by-visual field interaction *z* = -2.914, p = 0.003 was observed. However, in the attempt of exploring the meaning of this interaction, I repeated this analysis separately in the two visual fields and the impact of first letter confusability turned out to be not significant either in the LVF *z* = 0.188, *p* = 0.851 or in the RVF *z* =-1.795, *p* =0.072 (see Appendix, Figure A.3.2). Taken together, these data suggest that, in this experiment, the impact of word onset is minimally relevant.

Descriptive statistics for accuracy and RTs data are reported in Table 3.2. RTs refer to trials in which a correct response was given. Residuals of the three final models on log-transformed RTs (*Visual Field; N size; Length, Frequency and Imageability*) were normally distributed.

Table 3.2 | Descriptive statistics for accuracy and RTs in the experimental conditions explored by statistical models.

		Accuracy rate (mean ± sd)		**RTs (mean ± sd)**	
		Left Visual Field	*Right Visual Field*	*Left Visual Field*	*Right Visual Field*
4 Letters (words only)		0.66 ± 0.15	0.79 ± 0.14	799.40 ± 216.08	755.07 ± 187.65
5 Letters (words only)		0.52 ± 0.17	0.67 ± 0.16	871.62 ± 231.06	809.43 ± 199.54
High Frequency	*High Imageability*	0.66 ± 0.22	0.77 ± 0.19	808.50 ± 267.38	739.85 ± 194.55
	Low Imageability	0.66 ± 0.21	0.78 ± 0.22	812.81 ± 249.98	733.40 ± 212.75
Low Frequency	*High Imageability*	0.57 ± 0.24	0.73 ± 0.20	826.06 ± 235.80	812.08 ± 226.95
	Low Imageability	0.50 ± 0.19	0.65 ± 0.20	885.05 ± 260.03	858.56 ± 233.60
Total Words		0.59 ± 0.14	0.72 ± 0.14	829.16 ± 209.22	780.29 ± 188.83
Total Pseudowords		0.76 ± 0.12	0.76 ± 0.11	907.84 ± 265.66	911.05 ± 257.90

Visual Field analyses

The initial models included Visual Field, Responding Hand, Lexicality, the interaction between Visual Field and Lexicality, the interaction between Visual Field and Responding Hand, and Nfirst as a covariate. In general terms, the inclusion of a covariate in the model allows to disentangle the effects of interest from the effect of the covariate. This was done here in order to identify any modulation of the Visual Field effect while controlling for the relative discernibility of the first letter in stimuli recognition (Nfirst). All the variables that did not prove to have a significant effect on subjects' performance in these analyses were not taken into account for the subsequent ones.

With respect to accuracy (see Appendix, Table A.3.5, Figure 3.1a), the selected model included the significant main effects of Visual Field ($z = -9.733$, $p < 0.001$) and Lexicality ($z = 5.894$, $p < 0.001$), as well as the Visual Field-by-Lexicality interaction ($z = 9.674$, $p < 0.001$). Subsequent post-hoc comparisons (see Appendix, Table A.3.6) revealed a Visual Field effect (namely an advantage in accuracy for the RVF/LH over the LVF/RH) for lexical stimuli ($\chi^2(1) = 202.676$, $p < 0.001$), but not for pseudowords ($\chi^2(11) = 0.002$, $p = 1.000$). It is also worth noting that words presented to the LVF/RH were associated with significantly worse performance than pseudowords presented to either LVF/RH ($\chi^2(1) = 85.216$, $p < 0.001$), or RVF/LH ($\chi^2(1) = 85.714$, $p < 0.001$).

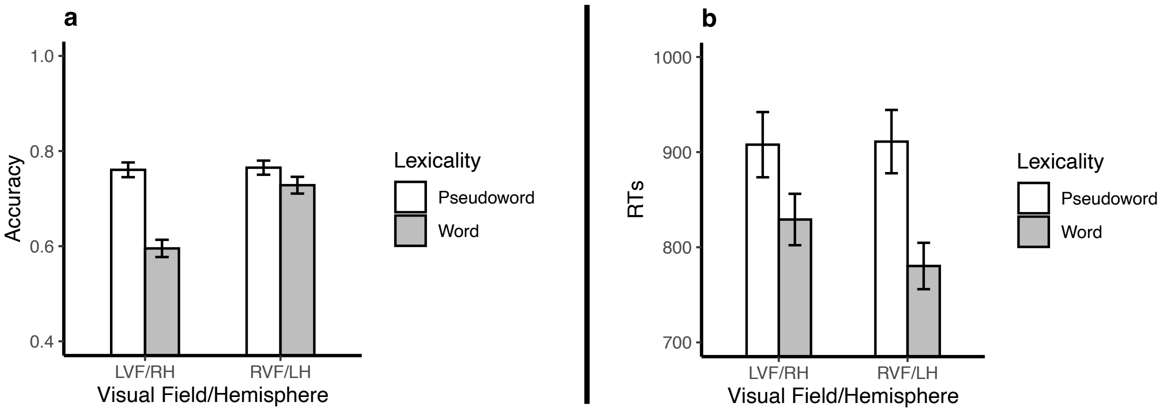

Figure 3.1 | Visual Field analyses: (a) Mean accuracy for words and pseudowords in the two visual fields. (b) Mean RTs for words and pseudowords in the two visual fields. Error bars indicate mean standard error.

Like for accuracy, the selected model for RT data (see Appendix, Table A.3.7, Figure 3.1b) included the main effects of Visual Field ($t(12443) = 5.094$, $p < 0.001$) and Lexicality ($t(307) = 11.669$, $p < 0.001$), as well as the Visual Field-by-Lexicality interaction ($t(12443)= -7.340$, $p < 0.001$). In particular (see Appendix, Table A.3.8), words initially projected to the LVF/RH were processed significantly slower than those targeting the RVF/LH ($\chi^2(1) = 72.214$, $p < 0.001$), whereas such difference was still non-significant for pseudowords ($\chi^2(1) = 2.741$, $p = 0.587$). In addition, words were processed significantly faster than pseudowords both in the LVF/RH ($\chi^2(1) = 47.195$, $p < 0.001$) and RVF/LH ($\chi^2(1) = 193.899$, $p< 0.001$).

In order to further explore these effects, a sensitivity analysis was conducted (see Appendix, Table A.3.9), in which *d* prime (*d'*) and response bias (criterion *c*) were computed for each subject, separately for each hemisphere, in line with Willemin et al. (2016). In the context of this experiment, the former index provides a measure of the ability to distinguish between words and pseudowords, while the latter indicates whether there is a consistent tendency to respond either "word", or "non-word". The RVF/LH was associated with a greater *d'* than the LVF/RH ($t(59) = -7.31$, $p < 0.001$), indicating better ability in discriminating among words and pseudowords. In both cases, the *d'* index was significantly different from zero (LVF/RH $t(59) = 14.86$, $p < 0.001$, RVF/LH $t(59) = 19.81$, $p < 0.001$). Furthermore, the difference between visual fields/hemispheres for the response bias was significant ($V = 1522$, $p < 0.001$), revealing for the LVF/RH a greater tendency to respond "non-word".

These analyses revealed the Visual Field effect to be specific for lexical stimuli. Pseudowords showed a trade-off between accuracy and RTs, which did not differ across visual fields/hemispheres. Sensitivity analyses indicate that for stimuli targeting the LVF/RH there is a greater bias than for stimuli targeting the RVF/LH in favor of a “non-word” response, which may at least partly account for the lack of Visual Field effect for pseudowords. Overall sensitivity proved to be greater in the RVF/LH than in the LVF/RH, and, in any case, well above zero (see Appendix, Figure A.3.3).

N size analyses

The initial models included the main effects of Visual Field, N size, Lexicality, and their interaction. The selected model for accuracy (see Appendix, Table A.3.10) included the significant main effect of Visual Field ($z = -9.734, p < 0.001$), the significant main effect of Lexicality ($z = 5.623, p < 0.001$), the significant Visual Field-by-Lexicality interaction ($z = 9.660, p < 0.001$) and the significant N size-by-Lexicality interaction ($z = -3.004, p = 0.003$), although the main effect of N size was not significant ($z = 0.522$, $p = 0.602$). As Figure 3.2 shows, a greater N size leads to answer “word” to both word and pseudoword stimuli. Crucially, this pattern did not differ between the two hemifields. The Visual Field-by-Lexicality interaction mirrors what observed in the previous analysis.

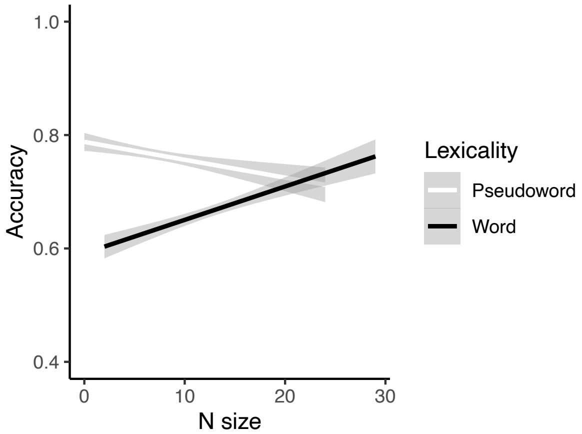

Figure 3.2 | Neighborhood (N) size analyses: predicted accuracy for words and pseudowords.

Considering RTs (see Appendix, Table A.3.11), the selected model included the significant main effects of Visual Field ($t(12440) = 5.039, p < 0.001$) and Lexicality ($t(312) = 10.091, p < 0.001$), the non-significant main effect of N size ($t(303) = -0.760$, $p = 0.448$), and the significant interactions among N size and Visual Field ($t(12412) = 2.212, p = 0.027$), Visual Field and Lexicality ($t(12446) = -5.482, p < 0.001$) and N size and Lexicality ($t(303) = 2.176, p = 0.030$). These data suggest that in both visual fields/hemispheres N size facilitates performance for lexical stimuli (Figure 3.3a), while it seems to have a detrimental effect in case of pseudoword stimuli. However, as shown in Figure 3.3b, the overall effect of N size on the speed of response is greater in the RVF/LH than in the LVF/RH.

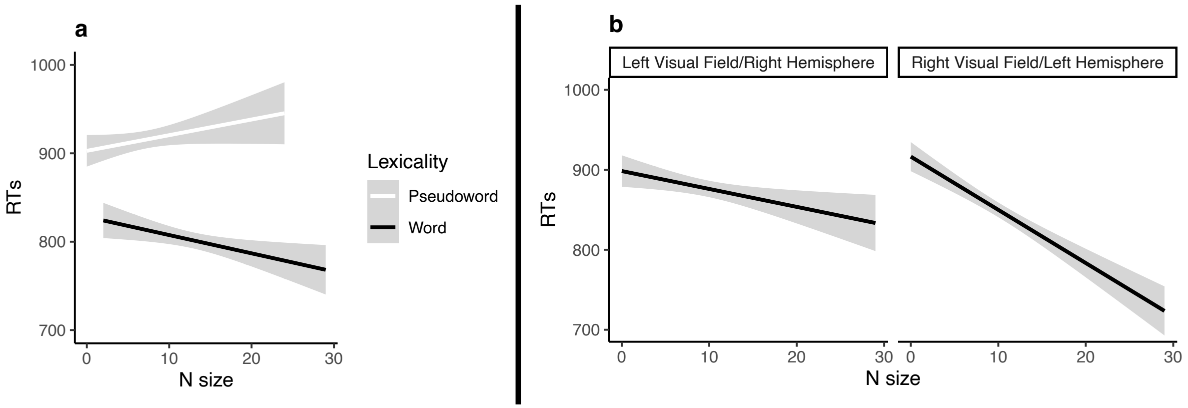

Figure 3.3 | Neighborhood (N) size analyses: (a) RTs for word and pseudoword stimuli; (b) RTs in the two visual fields/hemispheres for both words and pseudowords (collapsed in a single regression line).

Altogether, the results of these analyses suggest that greater N size leads to respond “word” when judging stimuli projected to either visual field/hemisphere, even though the overall effect of N size on RTs is comparatively stronger in the RVF/LH.

Length, Frequency and Imageability analyses

For this set of analyses (which involved only lexical stimuli), the initial models included the full combination of simple and interaction effects of Visual Field, word Length, word Frequency and Imageability.

Considering accuracy (see Appendix, Table A.3.12), the selected model included the significant main effects of Visual Field (z = -14.426, p < 0.001), word Frequency (z = 5.002, p < 0.001) and word Length (z = 6.117, p < 0.001), indicating better processing for the RVF/LH than the LVF/RH, an advantage for frequent over infrequent words across visual fields/hemispheres, as well as a more accurate performance for 4-Letters- than 5-Letters-words, which, crucially, did not differ between the RVF/LH and the LVF/RH. The selected model also included the factor Imageability, which revealed a significant interaction with word Frequency (z = -2.080, p = 0.037), although its main effect was not significant (z = 1.590, p = 0.112). Subsequent pairwise comparisons (see Appendix, Table A.3.13) revealed a marked frequency effect for stimuli associated with lowest imageability rates ($\chi^2(1)$ =

21.766, $p < 0.001$), whereas for stimuli associated with high imageability rates, this difference was not significant (χ^2 (1) = 0.299, $p = 0.500$). It is noteworthy that this effect did not differ between visual fields/hemispheres.

The selected model for RTs (see Appendix, Table A.3.14) included the significant main effects of Visual Field ($t(5778) = 9.432$, $p < 0.001$), word Frequency ($t(155) = -7.230$, $p < 0.001$), word Length ($t(154) = -5.669$, $p < 0.001$), with performance patterns mirroring those observed in the accuracy analysis. A Visual Field-by-Frequency interaction[8] ($t(5775) = 2.222$, $p = 0.026$) was also observed (Figure 4). Post-hoc comparisons (see Appendix, Table A.3.15) indicate that low-frequency words initially projected to the LVF/RH were associated with longer reaction times than either high-frequency words projected to the LVF/RH ($\chi^2(1) = 23.236$, $p < 0.001$), or low-frequency words projected to the RVF/LH ($\chi^2(1) = 24.074$, $p < 0.001$). Figure 3.4 also suggests a different frequency effect in the two visual fields/hemispheres. I averaged RTs by Subjects separately for high- and low-frequency words and for the LVF/RH and RVF/LH, and I computed (for each subject) the difference between RTs for low-frequency and high-frequency items in each visual field/hemisphere. The frequency effect turned out to be bigger in the RVF/LH than in the LVF/RH ($W = 1395$, $p = 0.033$).

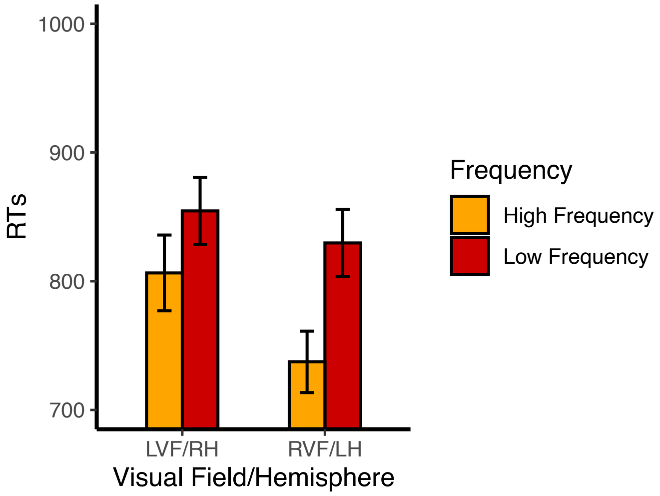

Figure 3.4 | Length, Frequency and Imageability analyses: Mean RTs for high- and low-frequency words projected in the two visual fields. Error bars indicate mean standard errors.

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[8] For the sake of the interpretability of this interaction effect, I assume a monotonic stimulus-response function underlying data (Garcia-Marques, Garcia-Marques & Brauer, 2014).

Remarkably, the effect of word Length proved not to differ in the two visual fields/hemispheres either for accuracy, or RTs. Conversely, a Visual Field-by-Frequency interaction was found in RTs, suggesting that low-frequency items may be particularly difficult to process by the LVF/RH. To further explore this effect on accuracy data despite the lack of formal interaction between visual field and frequency of the words, I evaluated whether the accuracy level reached absolute significance in each of the four classes of stimuli, high/low frequency, right/left hemifield. To do so, I employed chance-level (namely 50% correct) as a reference point in four one-sample Wilcoxon's tests. In light of the Visual Field-by-Frequency interaction found in RTs, the LVF/RH could have a chance-level-like performance in processing low-frequency words. While RVF/LH was associated with performances significantly differing from chance-level for both high frequency ($V = 1808$, $p < 0.001$) and low frequency words ($V = 1627.5$, $p < 0.001$), LVF/RH showed a performance that differs from chance-level for high frequency words ($V = 1676$, $p < 0.001$) but not for low-frequency words ($V = 1115.5$, $p = 0.082$, see Figure 3.5).It is worth noting that a chance-level-like performance for low-frequency words presented to the LVF/RH does not necessarily imply that RTs are meaningless. Indeed, this would be the case if subjects responded randomly without trying to activate some lexical representations. Conversely, a closer inspection of RTs when projecting stimuli to the LVF/RH shows that low-frequency words to which participants responded "non-word" were associated with RTs (*mean*= 905.55, *sd*= 428.17) indistinguishable from those of correctly discarded pseudowords (*mean*= 915.75, *sd*= 432.76, $\chi^2(1) = 0.02$, $p = 0.876$), while RTs associated with correctly-identified low-frequency words (*mean*= 860.82, *sd*= 373.66) were faster than both low-frequency words mistaken for pseudowords ($\chi^2(1) = 15.48$, $p < 0.001$) and correctly discarded pseudowords ($\chi^2(1) = 16.762$, $p < 0.001$). This suggests that for low-frequency words presented to the LVF/RH, lexical activation is low, as much as for pseudowords, and not sufficient to provide a reliable "word" decision (Grainger & Jacobs, 1996)[9]. This implies a long and unsuccessful search within the lexicon similar to that triggered by pseudowords, and an inconsistent response.

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[9] In the Multiple Read-Out Model (Grainger & Jacobs, 1996) word recognition occurs when appropriate whole-word orthographic representation reaches a critical level of activation (M criterion). A "word" response can be triggered when either the M criterion or the criterion of the overall (global) activity in the orthographic lexicon ($\sum$ criterion) are reached before the time limit (T) criterion. Reaction time is determined by the earliest moment in time that either the M criterion (i.e., a specific word has been identified), or the $\sum$ criterion are reached.

A negative lexical decision response is given when neither the M nor the $\sum$ criteria are reached before the T criterion.

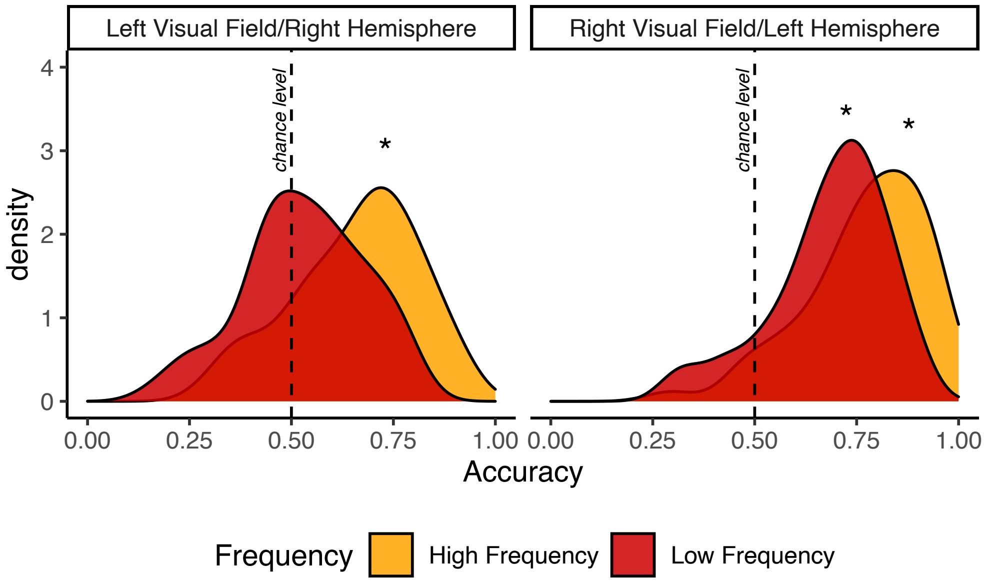

Figure 3.5 | Density plots for accuracy data in the two visual fields for high- and low-frequency words. Dashed lines indicate chance level (0.50) performance. Asterisks indicate a *p* value < .001 in the one-sample Wilcoxon's test.

Discussion

In spite of about 50 years of behavioral studies on hemispheric differences in reading on healthy subjects, still there is no complete consensus on where these differences arise from. On the one hand, it could be assumed that they originate from the different capability of two orthographic lexicons (one for each hemisphere); on the other hand, one may hypothesize the existence of a single lexical store, which is differently accessed by the two hemispheres. Much effort has been made in the attempt of characterizing hemispheric differences in reading, still leaving a crucial question unanswered: what functional brain mechanism gives rise to the visual field effect for lateralized reading in healthy subjects?

According to the "single-lexicon" view (Ellis, Young & Anderson, 1988; Ellis, 2004), the locus in which visual fields/hemispheres differences in reading arise should be in the early steps of pre-lexical stimuli encoding. Accordingly, the RH would adopt a *stepwise* processing strategy (sensitive to word Length and N size) to reach the single lexicon located in the LH, while the LH would adopt a fast, *parallel* strategy. Conversely, the "two-lexicons" framework (Coslett & Saffran, 1994; Saffran & Coslett, 1998; Luzzatti, Rumiati & Ghirardi, 1998; Luzzatti, 2003) predicts that hemispheric differences in reading should be due to the different availability of lexical contents in the two hemispheres, which should emerge as a different response to lexical and/or semantic factors (i.e., word frequency, imageability). In this experiment, all these factors were simultaneously manipulated, in order to evaluate the relative weight of pre-lexical and lexical factors on the visual field effect in lateralized reading. At the same time, stimuli eccentricity and stimuli presentation time were chosen (according to Bourne, 2006) in order to avoid stimuli to target both hemispheres and to avoid eye movements. For this latter purpose, eye-tracking was also adopted, to be certain that subjects were fixating the center of the screen prior to stimuli presentation.

In all analyses, a Visual Field effect emerged, suggesting a consistent advantage of the RVF/LH over the LVF/RH. Preliminary analyses on visual confusability suggested this effect not to be only due to poor perception of first letters (see also Whitney, 2001).

Contrary to the predictions of the “single- orthographic lexicon” framework, no significant Length-by-Visual Field interaction was detected in word processing. Indeed, the effect of number of letters (i.e.: lower accuracy and longer RTs for 5-letter than for 4-letter stimuli) was not different across visual fields. Also, while -according to the “single orthographic lexicon” framework- a N size effect was expected for stimuli projected in the LVF/RH and not in the RVF/LH, in this experiment an effect of N size -systematically leading to a “word” response regardless of the lexicality of the target stimulus- was found for both visual fields. The effect of N size on RTs was even more pronounced for stimuli projected in the RVF/LH than for stimuli presented in the LVF/RH. However, although the relationship between N size and RTs in this interaction resembles that observed for word stimuli, this effect did not formally interact with lexicality. Therefore, given that the meaning of this effect is essentially ambiguous, it will not be discussed further.

As far as lexical and semantic variables are concerned, imageability did not significantly interact with Visual Field. Conversely, a significant Visual Field-by-Frequency interaction was observed in RTs, with low-frequency words presented in the LVF/RH being associated with longer reaction times than either high-frequency words projected to the LVF/RH, or low-frequency words projected to the RVF/LH. These results are in line with the predictions of the “two orthographic lexicons model” (Coltheart 1980, 200; Saffran et al., 1980; Coslett & Saffran, 1994; Saffran & Coslett, 1998; Luzzatti, Rumiati & Ghirardi, 1998; Luzzatti, 2003). Remarkably, the shape of the Visual Field-by-Frequency interaction suggests that this effect is not simply due to a super-additivity of a domain-general “difficulty” factor. If this were the case (see for instance Brysbaert 1994), the effect of word frequency would have been bigger in the more difficult condition (LVF/RH) than in the easier condition (RVF/LH). As it happens, data from this experiment suggest the opposite: a compression of the frequency effect in the LVF/RH as compared with the RVF/LH. These data could be due to poorer discriminability of lexical representations in the RH than in the LH and are compatible with the idea of a different organization of lexical orthographic knowledge in the two hemispheres, with the lexicon of the RH being less capable of activating/retrieving orthographic lexical knowledge than the LH.

On the other hand, previous neuropsychological data have suggested that the RH cannot effectively activate lexical orthographic representations for low-frequency and/or abstract words, leading to the idea that the RH orthographic lexicon only contains representations for high-frequency and/or concrete words (Coltheart, 1980; 2000; Saffran et al., 1980; Saffran & Coslett, 1998; Ellis, Young & Anderson, 1988; Ellis, 2004). Apparently in line with these findings, accuracy in this task was not significantly better than chance level for low-frequency words presented in the LVF/RH.

Taken together, these results suggest that lexical factors have a comparatively more prominent role than pre-lexical factors in giving rise to the visual field effect in lateralized reading, and this supports the assumption of a "two orthographic lexicons" model. Accordingly, hemispheric differences in lateralized reading would emerge at the lexical level, due to the inability of the RH to effectively activate representations for low-frequency words. Of course, the distinction between high- and low-frequency words is arbitrary, and thus unlikely to occur with such defined boundaries in the brain. Rather, it is likely that words are represented in a continuous (i.e., non-discrete) way, according to their frequency. However, the rate of lexical activation given the same word frequency continuum could be higher in the LH than in the RH, due to more effective consolidation and/or retrieval of orthographic knowledge in the LH than the RH (this topic is discussed in Chapter 5). This would explain why a greater frequency effect in the LH than in the RH was observed.

Despite these data are seemingly incompatible with a "single orthographic lexicon" framework, a number of issues still remain open. A first issue involves the nature of the Frequency-by-Visual Field interaction. Indeed, I have assumed -according to the "two orthographic lexicons model"- that this effect originates from the orthographic lexicons located in the two cerebral hemispheres having different capabilities in terms of activation and/or retrieval of lexical representations. However, a Frequency-by-Visual Field interaction is also compatible with a "single orthographic lexicon" hypothesis, provided that input to the lexicon coming from the RH is more degraded than that coming from the LH. The purely behavioral nature of the data from this experiment does not allow us to exclude this possibility. However, degradation of the input to the LH lexicon from the RH should be due to greater pre-lexical processing costs for stimuli projected to the LVF than for those projected to the RVF, and this should be mirrored by a greater word Length effect in the RH than in the LH.

The lack of a Length-by-Visual Field interaction suggests that this is not the case. However, as this claim is based on a null result, I acknowledge that further evidence is required to fully support it. It is indeed possible that the lack of a significant Length-by-Visual Field interaction could be due to low statistical power of the present design. However, the present data are sufficient to suggest that any possible hemispheric difference in pre-lexical factors should be comparatively smaller in size than hemispheric differences in lexical factors.

Nevertheless, it may be crucial to exclude that the compression of the effect of word frequency in the RH depends on a “floor” effect in performance. This issue will be discussed in the next chapter.

A second issue involves the interpretation of the lack of a Visual Field effect for pseudowords.

On the one hand, this effect could be explained by the low tendency towards stimuli projected to the LVF/RH to be labeled as “words” (as in Vergilino Perez et al., 2012; Weems & Zaidel, 2005): while accurate performance for pseudowords in the RVF/LH could reflect correct stimulus classification, for LVF/RH, it could be due to a more general response bias leading to a “non-word” answer for most stimuli. On the other hand, this result could be due to the existence of a common mechanism underlying a “non-word” response shared by the two hemispheres. Although the similarity of performance for pseudowords in the two hemispheres for both accuracy and RTs suggests that this might be the case, further research is required to shed light on this point.

A third open question involves the fact that while a frequency effect in the LVF/RH was observed in both the sample of healthy subjects and in patient AA (described in Chapter 2), I failed to replicate the imageability effect observed in patient AA for stimuli projected in the LVF/RH in healthy subjects. It should not be excluded that the emergence of a sizeable imageability effect (at least for what concerns the list of stimuli I adopted) could happen only when a low amount of cognitive resources is available for the task. In other words, an imageability effect may be observable only in case of a brain lesion.

However, it is also possible that the facilitatory effect of imageability towards word detection could simply depend on age and/or on the years of formal education (see also Coltheart, 1980). As neither interpretation can be excluded, this point remains open for future enquiry.

Finally, it is worth noting that the volunteers recruited for this experiment were right-handers, and therefore likely characterized by a relatively homogeneous LH functional dominance pattern (Pujol et al., 1999). It may be interesting to explore to what extent the conclusions drawn from this experiment also apply to subjects who show greater variability in the functional language lateralization pattern (e.g.: left-handers). This topic will be addressed in the next chapter.

In conclusion, data from this experiment suggest that lexical factors, rather than pre-lexical factors, play a role in giving rise to the visual field effect in lateralized reading. These results provide insights for the design of future divided visual field studies of reading (i.e. the necessity of controlling lexical-semantic variables) and for the definition of a brain model accounting for the visual field effect in lateralized reading. Indeed, data from this experiment tip in favor of the "two orthographic lexicons" account, although further studies are required to provide conclusive evidence in this direction.

In the next chapter, an experimental study extending the present findings to left-handed healthy subjects will be presented, with the twofold aim of (1) excluding the compression of the Frequency effect in the RH to be only due to a "floor" effect in performance and (2) explore the effects of functional hemispheric dominance on the effects described in the present chapter.

References

Baayen, R. H. (2008). *Analyzing linguistic data: a practical introduction to statistics using R*. Cambridge, UK: Cambridge University Press.

Babkoff, H., & Ben-Uriah, Y. (1983). Lexical decision time as a function of visual field and stimulus probability. *Cortex, 19*(1), 13-30.

Bates, D., Maechler, M., Bolker, B., & Walker, S. (2015). lme4: Linear mixed-effects models using Eigen and S4. R package version 1.1-9 http://cran/. *R-project. org/package= lme4*.

Bertinetto, P. M., Burani, C., Laudanna, A., Marconi, L., Ratti, D., Rolando, C., & Thornton, A. M. (2005). CoLFIS (Corpus e Lessico di Frequenza dell'Italiano Scritto). *Available on http://www.istc.cnr.it/material/database.*

Bourne, V. J. (2006). The divided visual field paradigm: Methodological considerations. *Laterality, 11*(4), 373-393.

Brysbaert, M. (1994). Behavioral estimates of interhemispheric transmission time and the signal detection method: A reappraisal. *Perception & Psychophysics, 56*(4), 479-490.

Brysbaert, M., & d'Ydewalle, G. (1990). Tachistoscopic presentation of verbal stimuli for assessing cerebral dominance: reliability data and some practical recommendations. *Neuropsychologia, 28*(5), 443-455.

Chiarello, C., Senehi, J., & Soulier, M. (1986). Viewing conditions and hemisphere asymmetry for the lexical decision. *Neuropsychologia, 24*(4), 521-529.

Chiarello, C., Shears, C., Liu, S., & Kacinik, N. A. (2005). Influence of word class proportion on cerebral asymmetries for high-and low-imagery words. *Brain and Cognition, 57*(1), 35-38.

Chu, R. K., & Meltzer, J. A. (2019). Interhemispheric connectivity during lateralized lexical decision. *Human Brain Mapping, 40*(3), 818-832.

Coltheart, M. (1980). Deep dyslexia: a right-hemisphere hypothesis. In Coltheart, M., Patterson, K., & Marshall, J.C. (Eds.), *Deep Dyslexia*. London: Routledge and Kegan Paul.

Coltheart, M. (2000). Deep dyslexia is right-hemisphere reading. *Brain and Language, 71*(2), 299-309.

Coslett, H. B., & Saffran E. M. (1989). Evidence for preserved reading in 'pure alexia'. *Brain, 112*(2), 327-359.

Coslett, H. B., & Saffran, E. M. (1994). Mechanisms of implicit reading in alexia. In M. Farah & G. Ratcliff (Eds.), *The neuropsychology of high-level vision* (pp. 299–330). Lawrence Erlbaum Associates.

Day, J. (1977). Right-hemisphere language processing in normal right-handers. *Journal of Experimental Psychology: Human Perception and Performance, 3*(3), 518.

De Clercq, P., & Brysbaert, M. (2020). The influence of word valence on the right visual field advantage in the VHF paradigm: time to adjust the expectations. *Laterality,* 1-23.

De Rosario-Martinez, H. (2013). phia: Post-hoc interaction analysis. *R package version 0.1-3.*

Déjerine, J. (1892). Contribution à l'étude anatomopathologique et clinique des différents variétés de cécité verbale. *Mémoires de la Société de Biologie, 4*, 61-90.

Ellis, A. W. (2004). Length, formats, neighbours, hemispheres, and the processing of words presented laterally or at fixation. *Brain and Language, 88*(3), 355-366.

Ellis, A. W., Young, A. W., & Anderson, C. (1988). Modes of word recognition in the left and right cerebral hemispheres. *Brain and Language, 35*(2), 254-273.

Faust, M., Kravetz, S., & Babkoff, H. (1993). Hemispheric specialization or reading habits: Evidence from lexical decision research with Hebrew words and sentences. *Brain and Language, 44*(3), 254-263.

Garcia-Marques, L., Garcia-Marques, T., & Brauer, M. (2014). Buy three but get only two: The smallest effect in a 2× 2 ANOVA is always uninterpretable. *Psychonomic bulletin & review, 21*(6), 1415-1430.

Gazzaniga, M. S., & Sperry, R. W. (1967). Language after section of the cerebral commissures. *Brain, 90*(1), 131-148.

Grainger, J., & Jacobs, A. M. (1996). Orthographic processing in visual word recognition: A multiple read-out model. *Psychological review, 103*(3), 518.

Hausmann, M., Brysbaert, M., Van der Haegen, L., Lewald, J., Specht, K., Hirnstein, M., ... & Roch, M. (2019). Language lateralisation measured across linguistic and national boundaries. *Cortex, 111*, 134-147.

Hernandez, S., Nieto, A., & Barroso, J. (1992). Hemispheric specialization for word classes with visual presentations and lexical decision task. *Brain and Cognition, 20*(2), 399-408.

Hunter, Z. R., & Brysbaert, M. (2008). Visual half-field experiments are a good measure of cerebral language dominance if used properly: Evidence from fMRI. *Neuropsychologia, 46*(1), 316-325.

Iacoboni, M., & Zaidel, E. (1996). Hemispheric independence in word recognition: Evidence from unilateral and bilateral presentations. *Brain and language, 53*(1), 121-140.

Jordan, T. R., Patching, G. R., & Thomas, S. M. (2003). Assessing the role of hemispheric specialisation, serial-position processing, and retinal eccentricity in lateralised word recognition. *Cognitive Neuropsychology, 20*(1), 49-71..

Kirsner, K., & Schwartz, S. (1986). Words and hemifields: do the hemispheres enjoy equal opportunity? *Brain and Cognition, 5*(3), 354-361.

Lavidor, M., Babkoff, H., & Faust, M. (2001). Analysis of standard and non-standard visual word format in the two hemispheres. *Neuropsychologia, 39*(4), 430-439.

Lavidor, M., & Ellis, A. W. (2002) Orthographic neighborhood effects in the right but not in the left cerebral hemisphere. *Brain and Language, 80* (1), 63-76

Leiber, L. (1976). Lexical decisions in the right and left cerebral hemispheres. *Brain and Language, 3*(3), 443-450.

Lo, S., & Andrews, S. (2015). To transform or not to transform: Using generalized linear mixed models to analyse reaction time data. *Frontiers in Psychology, 6*, 1171.

Luzzatti, C. (2003). Optic aphasia and pure alexia: contribution of callosal disconnection syndromes to the study of lexical and semantic representation in the right hemisphere. In Zaidel, E., & Iacoboni, M. (Eds.), *The Parallel Brain: The Cognitive Neuroscience of the Corpus Callosum* (pp. 479-499). Cambridge, MA: MIT Press.

Luzzatti, C., Rumiati, R. I., & Ghirardi, G. (1998). A functional model of visuo-verbal disconnection and the neuroanatomical constraints of optic aphasia. *Neurocase, 4*(1), 71-87.

Measso, G., & Zaidel, E. (1990). Effect of response programming on hemispheric differences in lexical decision. *Neuropsychologia, 28*(7), 635-646.

Mohr, B., Pulvermüller, F., & Zaidel, E. (1994). Lexical decision after left, right and bilateral presentation of function words, content words and non-words: Evidence for interhemispheric interaction. *Neuropsychologia, 32*(1), 105-124.

Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia, 9*(1), 97-113.

Olk, B., & Hartje, W. (2001). The bilateral effect: Callosal inhibition or intrahemispheric competition?. *Brain and Cognition, 45*(3), 317-324.

Perea, M., Acha, J., & Fraga, I. (2008). Lexical competition is enhanced in the left hemisphere: Evidence from different types of orthographic neighbors. *Brain and Language, 105*(3), 199-210.

Pujol, J., Deus, J., Losilla, J. M., & Capdevila, A. (1999). Cerebral lateralization of language in normal left-handed people studied by functional MRI. *Neurology, 52*(5), 1038-1038.

Rayner, K., & Kaiser, J. S. (1975). Reading mutilated text. *Journal of Educational Psychology*, 67(2), 301.

Saffran, E. M., Bogyo, L. C., Schwartz, M. F., & Marin, O. S. M. (1980). Does deep dyslexia reflect right-hemisphere reading? In Coltheart, M., Patterson, K., & Marshall, J.C. (Eds.), *Deep Dyslexia* (pp. 381-406) London: Routledge and Kegan Paul.

Saffran, E. M., & Coslett, H. B. (1998). Implicit vs. letter-by-letter reading in pure alexia: A tale of two systems. *Cognitive Neuropsychology, 15*(1-2), 141-165.

Simpson, I. C., Mousikou, P., Montoya, J. M., & Defior, S. (2013). A letter visual-similarity matrix for Latin-based alphabets. *Behavior Research Methods, 45*(2), 431-439.

Vergilino Perez, D., Lemoine, C., Siéroff, E., Ergis, A. M., Bouhired, R., Rigault, E., & Doré-Mazars, K. (2012). The role of saccade preparation in lateralized word recognition: evidence for the attentional bias theory. *Neuropsychologia, 50*(12), 2796-2804.

Waldie, K. E., & Mosley, J. L. (2000). Hemispheric specialization for reading. *Brain and Language, 75*(1), 108-122.

Weems, S. A., & Zaidel, E. (2005). The effect of response mode on lateralized lexical decision performance. *Neuropsychologia, 43*(3), 386-395.

Whitney, C. (2001). How the brain encodes the order of letters in a printed word: The SERIOL model and selective literature review. *Psychonomic Bulletin & Review, 8*(2), 221-243.

Whitney, C., & Lavidor, M. (2005). Facilitative orthographic neighborhood effects: The SERIOL model account. *Cognitive Psychology, 51*(3), 179-213.

Willemin, J., Hausmann, M., Brysbaert, M., Dael, N., Chmetz, F., Fioravera, A., ... & Mohr, C. (2016). Stability of right visual field advantage in an international lateralized lexical decision task irrespective of participants' sex, handedness or bilingualism. *Laterality: Asymmetries of Body, Brain and Cognition, 21*(4-6), 502-524.

Young, A. W., & Ellis, A. W. (1985). Different methods of lexical access for words presented in the left and right visual hemifields. *Brain and Language, 24*(2), 326-358.

Appendix

Table A.3.1 | Word stimuli for experimental trials with length, frequency, imageability and N-size data.

Stimulus	Letters	Absolute Frequency (COLFIS)	Imageability	N size	Nfirst	Stimulus	Letters	Absolute Frequency (COLFIS)	Imageability	N size	Nfirst
BASE	4	666	3.95	14	4	BANCA	5	346	6.76	10	3
BICI	4	2	6.76	10	3	BANCO	5	126	6.62	7	1
CANE	4	174	6.90	24	10	BANDA	5	127	5.95	13	6
CASA	4	2735	6.86	21	5	BARCA	5	131	6.86	10	4
CASO	4	1797	1.48	22	7	BENDA	5	5	6.48	7	2
CERO	4	1	6.38	18	6	BOMBA	5	128	6.24	7	2
CETO	4	22	2.09	10	4	BORDO	5	235	5.43	8	4
CODA	4	121	6.67	16	5	BORSA	5	192	6.76	7	2
CONO	4	14	6.81	20	9	BOSCO	5	118	6.81	9	4
COSA	4	2813	2.29	21	6	BRUCO	5	1	6.71	5	0
CUBO	4	13	6.67	10	1	CALCE	5	12	4.67	12	2
DIGA	4	10	5.95	11	6	CALCO	5	3	3.76	12	3
DOGE	4	4	3.29	9	0	CAMPO	5	806	6.52	5	1
FAMA	4	113	2.43	15	7	CARNE	5	194	6.62	11	3
FAME	4	175	2.86	15	6	CARTA	5	431	6.71	13	4
FARO	4	27	6.81	20	5	CESTA	5	8	6.48	21	10
FASE	4	284	1.67	15	4	CESTO	5	12	6.52	20	9
FATO	4	2	1.48	17	6	CIFRA	5	135	4.86	2	0
FEDE	4	238	3.95	9	6	COLPA	5	295	1.71	10	1
FESA	4	2	4.52	9	6	COLPO	5	473	3.24	12	2
FINE	4	1655	2.52	19	6	CONCA	5	7	4.62	6	1
FOCA	4	4	6.81	8	4	CORPO	5	756	6.81	10	0
FOCE	4	10	4.52	8	2	COSTO	5	231	3.00	17	3
FOGA	4	15	2.24	7	3	DISCO	5	149	6.86	6	3
FUGA	4	263	3.62	4	1	DOGMA	5	9	1.38	2	0
FUNE	4	5	6.62	9	3	FALCE	5	5	6.09	13	2
GUFO	4	5	6.76	4	1	FALDA	5	5	3.19	7	1
LAGO	4	139	6.87	14	7	FELPA	5	8	6.76	1	0
LOBO	4	11	6.14	8	1	FESTA	5	397	5.76	14	11
LODE	4	9	1.67	14	5	FONDO	5	764	4.24	8	3

LOGO	4	4	4.90	14	5
LOTO	4	2	4.67	16	7
LUCE	4	630	5.95	11	3
LUNA	4	210	6.86	13	3
MANO	4	1104	6.95	22	6
MARE	4	625	6.90	28	8
MESE	4	712	3.09	13	4
MODA	4	426	3.19	18	5
MODO	4	2026	1.29	15	5
MOTO	4	109	6.05	17	7
MULO	4	7	6.48	14	2
MURO	4	202	6.86	15	5
MUSA	4	10	3.29	13	3
NASO	4	125	6.81	14	7
NAVE	4	126	6.90	18	8
NEVE	4	184	6.86	9	3
NUBE	4	9	6.43	7	4
PACE	4	454	2.62	13	4
PALA	4	8	6.81	23	8
PANE	4	168	6.95	21	9
PECE	4	1	4.62	10	2
PENA	4	263	2.09	19	10
PEPE	4	108	6.67	13	2
PIPA	4	16	6.76	13	1
POMO	4	6	4.76	12	6
PORO	4	1	5.14	20	7
PUMA	4	2	6.43	11	5
RANA	4	15	6.76	23	9
RAPA	4	1	6.24	15	3
RATA	4	12	2.24	19	6
RETE	4	418	6.57	11	3
RIMA	4	3	3.71	19	5
RUPE	4	5	5.90	7	2
SEDE	4	349	3.48	18	6
SENO	4	107	6.71	15	5
SITO	4	20	4.62	15	7
SOLE	4	582	6.67	17	9
SUGO	4	18	6.67	8	3
TANA	4	21	5.81	19	9
TECA	4	5	5.67	13	5
TEMA	4	316	4.24	12	2
TIPO	4	747	2.19	11	3
FONTE	5	137	4.57	12	4
GAMBO	5	6	6.19	8	3
GARBO	5	20	1.71	4	1
GARZA	5	5	6.33	6	0
GENTE	5	1058	6.05	9	6
GERME	5	7	3.48	5	3
GESTA	5	15	1.95	17	11
GESTO	5	226	4.24	15	9
GUSTO	5	238	1.95	5	2
LIMBO	5	11	2.24	3	1
MADRE	5	1026	6.48	5	1
MALTO	5	2	3.28	6	1
MANZO	5	5	6.09	11	4
MARZO	5	312	2.33	6	0
METRO	5	132	5.90	10	4
MILZA	5	4	4.19	2	0
MONDO	5	2220	6.48	12	3
MORBO	5	16	2.38	3	0
PADRE	5	1270	6.52	4	1
PALMO	5	23	6.76	8	2
PANCA	5	13	6.81	11	3
PARCO	5	169	6.62	12	2
PERLA	5	11	6.48	8	3
PERNO	5	8	4.43	6	1
PINZA	5	7	6.71	5	0
PISTA	5	241	6.19	10	4
PONTE	5	165	6.62	12	4
PURGA	5	5	3.57	4	1
RAMPA	5	5	6.05	9	5
RITMO	5	195	2.95	3	0
RONDA	5	7	2.90	13	7
ROSPO	5	10	6.62	5	1
RUSPA	5	6	6.62	3	0
SALMO	5	3	2.71	11	2
SENSO	5	858	2.29	10	4
SERPE	5	2	6.24	9	0
SISMA	5	6	4.33	3	1
SORSO	5	10	4.05	7	4
TARLO	5	7	3.33	7	4
TASCA	5	118	6.43	11	6
TASTO	5	12	6.52	12	5
TEMPO	5	3116	2.57	2	0

TOMO	4	5	4.81	20	6	TESTA	5	969	6.71	22	11
VANO	4	18	4.33	17	6	TESTO	5	245	6.00	20	9
VINO	4	232	6.81	20	11	TORSO	5	4	5.19	11	4
VISO	4	269	6.76	13	3	TURNO	5	233	2.33	8	0
VITA	4	2808	3.00	19	9	VENTO	5	308	4.62	14	7
VOCE	4	784	3.05	5	2	VERZA	5	2	6.09	6	1
ZELO	4	15	1.33	8	6	VETRO	5	145	6.38	7	4
ZONA	4	574	3.14	13	7	ZINCO	5	9	2.43	2	2

Table A.3.2 | Pseudoword stimuli for experimental trials with length and N size data. Items identified with a ° were not included in data analyses.

Stimulus	Letters	N size	Nfirst	Stimulus	Letters	N size	Nfirst
BANA	4	24	10	BEGRA	5	3	1
BATO	4	13	7	BERSA	5	11	3
BECA	4	15	6	BESMA	5	2	0
BEDA	4	16	7	BIRTA	5	5	1
BEFO	4	3	0	BOCLO	5	2	0
BICA	4	12	6	BOGRA	5	3	0
BIDA	4	10	6	BUNFA	5	1	0
BOMO	4	15	7	CASPO	5	5	0
BOTO	4	16	8	CELCO	5	5	0
BOZA	4	8	0	CENCO	5	9	2
CEBO°	4	10	3	CINCA	5	9	3
COFO	4	7	0	CIRMA	5	2	1
COPO	4	12	3	DANTA	5	9	6
DABA	4	12	3	DEMBO	5	2	1
DAGO	4	13	8	DENTO	5	13	8
DELA	4	14	7	DORCO	5	4	1
DEMA	4	11	3	FADRO	5	4	1
DIPO	4	11	4	FALMA	5	10	3
DISA	4	16	6	FARVA	5	8	2
DOBA	4	9	1	FENFA	5	0	0
DUTA	4	11	4	FERVA	5	5	1
FEPA	4	2	1	FONTO	5	9	4

FEPO	4	2	0
FIMO	4	12	3
FIRO	4	18	7
FOTA	4	13	6
FUNA	4	13	4
GEFO	4	2	0
GESO	4	6	4
GIMO	4	7	3
GOFA	4	4	0
GOPA	4	4	0
LAPA	4	12	4
LEMA	4	10	3
LOPO	4	13	3
MEBO	4	10	3
MOCO	4	14	5
MOGO	4	14	5
MUFA	4	5	0
MUGO°	4	11	4
MUPE	4	5	3
NAFO	4	3	0
NALO	4	10	4
NEGE	4	6	1
NELO	4	17	7
NIFO	4	11	4
NILA	4	13	8
NOBO	4	8	2
NOCA	4	17	5
NOPA	4	9	0
PAFE	4	7	0
PAVA	4	20	9
PEBO	4	7	3
PEGE	4	9	1
PIFO	4	8	4
PIMA	4	16	6
PUSO	4	10	4
RAPO	4	17	4
RELO	4	12	7
REPO	4	5	0
ROFA	4	9	0
RUCA	4	13	6
RUFO	4	4	1
SELO	4	17	7
FORVA	5	6	2
GARSO	5	5	1
GENDA	5	8	3
GERPO	5	1	0
GESCA	5	5	4
GILCA	5	3	1
GINDA	5	5	1
GIRTA	5	1	1
GORNA	5	7	3
LERVO	5	4	3
LIDRE	5	2	0
LILPO	5	0	0
LIRVO	5	0	0
LOSTO	5	7	4
LUSTA	5	4	2
MERPE	5	2	0
MIRLA	5	8	2
MORNO	5	9	4
NALPO	5	1	0
NARCA	5	7	5
NARTA	5	8	5
NASTO	5	6	6
NEGLA	5	3	0
NERMA	5	4	2
NIGLA	5	3	1
NILPO	5	0	0
NIRCE	5	1	1
NIRNO	5	0	0
NUMBE	5	0	0
NURBO	5	4	3
PALZA	5	7	3
PELCO	5	3	0
PESPA	5	4	2
PILCO	5	3	0
PISPA	5	3	1
POLCO	5	8	2
POLZA	5	6	1
POSCO	5	11	5
RIRTO	5	3	1
RURZA	5	0	0
SARLO	5	10	5
SIRTO	5	7	1

SESA	4	17	7	SORLO	5	4	1
SIPO	4	9	4	SUMPA	5	3	0
SISO	4	9	3	SURTO	5	6	1
SUVA	4	3	0	TOPRA	5	3	2
TALO	4	13	4	TURPA	5	4	0
TAME	4	17	7	TURZO	5	5	0
TOBO	4	13	2	VABRO	5	1	1
TUDE	4	6	2	VALMO	5	8	3
VACE	4	13	5	VILMO	5	1	1
VEPA	4	7	1	VIRTO	5	5	1
VUDA	4	8	3	VUCLA	5	0	0
VUTO	4	6	3	VURCA	5	2	1
ZABA	4	8	3	ZALTA	5	4	3
ZAPO	4	5	4	ZARPO	5	1	1
ZECA	4	11	6	ZESTO	5	10	10
ZOMO	4	10	7	ZIRPA	5	0	0

Table A.3.3 | Descriptive statistics for the experimental material.

				Frequency (mean ± sd)	Imageability (mean ± sd)	N size (mean ± sd)	N first (mean ± sd)
Words	4 Letters	High Frequency	High Imageability	418.40 ± 602.74	6.73 ± 0.27	17.60 ± 4.84	5.95 ± 2.66
			Low Imageability	873.15 ± 858.51	2.81 ± 0.83	15.50 ± 4.82	5.20 ± 2.28
		Low Frequency	High Imageability	9.33 ± 6.95	6.57 ± 0.26	13.89 ± 5.75	4.11 ± 2.65
			Low Imageability	8.73 ± 6.95	3.89 ±1.46	14.45 ± 4.48	4.91 ± 2.14
	5 Letters	High Frequency	High Imageability	483.91 ± 529.92	6.52 ± 0.27	11.09 ± 4.35	3.65 ± 2.62
			Low Imageability	487.36 ± 707.78	3.65 ± 1.39	10.18 ± 4.46	3.17 ± 3.26
		Low Frequency	High Imageability	7.68 ± 5.09	6.45 ± 0.26	9.84 ± 5.11	2.63 ± 2.95
			Low Imageability	8.09 ± 4.65	3.32 ± 1.06	7.81 ± 4.27	2.38 ± 2.62
Pseudowords	4 Letters	-	-	-	-	10.47 ± 4.67	3.767± 2.60
	5 Letters	-	-	-	-	4.46 ± 3.321	1.72 ± 1.99

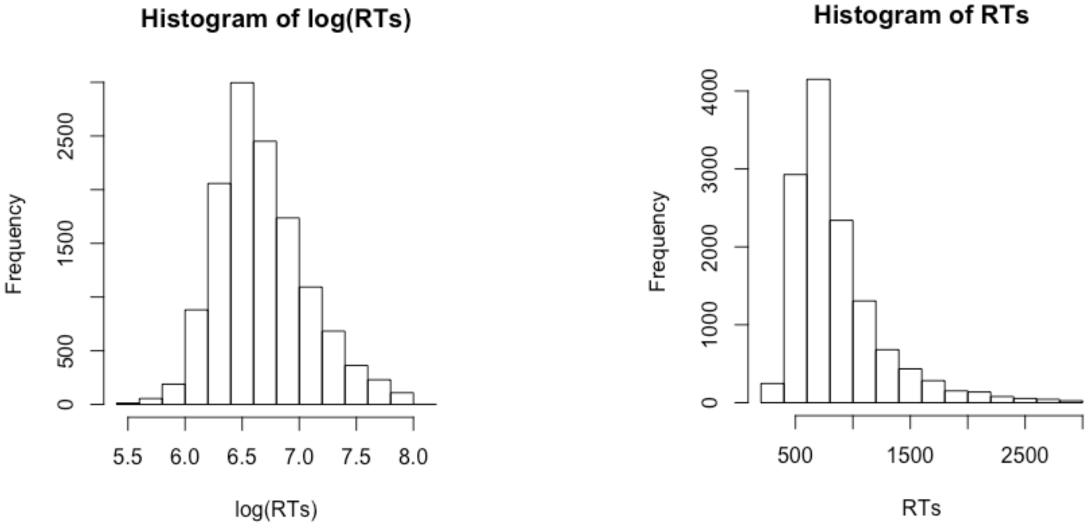

Figure A.3.1 | Histograms for raw and log-transformed RTs

Table A.3.4 | Overview of the model selection procedures in the three sets of analyses for both accuracy and RTs data. Selected models are reported in bold. Asterisks indicate interaction effects with simple effects. Colons indicate interaction effects without simple effects. Selected models are reported in bold.

Analysis	*Dep. Var.*		*Model*	*χ2*	*df*	*p(χ2)*
Visual Field Analysis	Accuracy	1	ACC ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field*(Lexicality+Responding Hand)+Nfirst	-	-	-
		2	ACC ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field*(Lexicality)+Nfirst+Responding Hand	1.074	1	0.300
		3	ACC ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field*(Lexicality)+Responding Hand	2.867	1	0.090
		4	***ACC ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field*Lexicality***	2.319	1	0.128
		5	ACC ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field+Lexicality	93.059	1	< 0.001
	RTs	1	log(RT) ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field*(Lexicality+Responding Hand)+Nfirst	-	-	-
		2	log(RT) ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field*(Lexicality)+Responding Hand+Nfirst	0.018	1	0.892
		3	log(RT) ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field*(Lexicality)+Responding Hand	2.305	1	0.129
		4	**log(RT) ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field*Lexicality**	2.833	1	0.092
		5	log(RT) ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field+Lexicality	44.372	1	< 0.001
N size	Accuracy	1	ACC ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field* Nsize*Lexicality	-	-	-
		2	ACC ~ 1+(1 | Subject)+(1 | Stimuli)+(Visual Field*(Nsize+Lexicality))+ Nsize:Lexicality	1.169	1	0.280
		3	***ACC ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field*Lexicality+ Nsize+ Nsize:Lexicality***	2.528	1	0.112
		4	ACC ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field+Lexicality+ Nsize+ Visual Field:Nsize	73.532	1	< 0.001
	RTs	1	log(RT) ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field* Nsize*Lexicality	-	-	-
		2	***log(RT) ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field*(Nsize+Lexicality)+ Nsize:Lexicality***	0.203	1	0.652
		3	*log(RT) ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field*(Nsize+Lexicality)*	5.291	1	0.021
	Accuracy	1	ACC ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field*(Length*Frequency*Imageability)	-	-	-

Length, Frequency, Imageability		2	ACC ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field+(Length*Frequency*Imageability)+Visual Field:Length+Visual Field:Frequency+Visual Field:Imageability+Visual Field:Length:Frequency+Visual Field:Length:Imageability+Visual Field:Frequency:Imageability	0.269	1	0.604
		3	ACC ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field+(Length+Frequency+Imageability)+Length:Frequency+Length:Imageability+Frequency:Imageability+Visual Field:Length+Visual Field:Frequency+Visual Field:Imageability+Visual Field:Length:Frequency+Visual Field:Length:Imageability+Visual Field:Frequency:Imageability	0.001	1	0.978
		4	ACC ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field+(Length+Frequency+Imageability)+Length:Frequency+Length:Imageability+Frequency:Imageability+Visual Field:Length+Visual Field:Frequency+Visual Field:Imageability+Visual Field:Length:Frequency+Visual Field:Length:Imageability	0.502	1	0.479
		5	ACC ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field+(Length+Frequency+Imageability)+Length:Frequency+Length:Imageability+Frequency:Imageability+Visual Field:Length+Visual Field:Frequency+Visual Field:Imageability+Visual Field:Length:Imageability	0.704	1	0.401
		6	ACC ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field+(Length+Frequency+Imageability)+Length:Frequency+Length:Imageability+Frequency:Imageability+Visual Field:Length+Visual Field:Frequency+Visual Field:Imageability	2.569	1	0.109
		7	ACC ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field+(Length+Frequency+Imageability)+Length:Imageability+Frequency:Imageability+Visual Field:Length+Visual Field:Frequency+Visual Field:Imageability	0.169	1	0.681
		8	ACC ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field+(Length+Frequency+Imageability)+Length:Imageability+Frequency:Imageability+Visual Field:Length+Visual Field:Imageability	0.246	1	0.620
		9	ACC ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field+(Length+Frequency+Imageability)+Length:Imageability+Frequency:Imageability+Visual Field:Length	0.252	1	0.616
		10	ACC ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field+(Length+Frequency+Imageability)+Length:Imageability+Frequency:Imageability	0.295	1	0.587
		11	***ACC ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field+(Length+Frequency+Imageability)+Frequency:Imageability***	1.746	1	0.186
		12	ACC ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field+Length+Frequency+Imageability	4.267	1	0.039
	RTs	1	log(RT) ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field*(Length*Frequency*Imageability)	-	-	-
		2	log(RT) ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field+(Length*Frequency*Imageability)+Visual Field:Length+Visual Field:Frequency+Visual Field:Imageability+Visual Field:Length:Frequency+Visual Field:Length:Imageability+Visual Field:Frequency:Imageability	1.076	1	0.299
		3	log(RT) ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field+(Length*Frequency*Imageability)+Visual Field:Length+Visual Field:Frequency+Visual Field:Imageability+Visual Field:Length:Frequency+Visual Field:Length:Imageability	1.496	1	0.221
		4	log(RT) ~ 1+(1 | Subject)+(1 | Stimuli)+Visual Field+Length+Frequency+Imageability+Length:Frequency+Length:Imageability+Frequency:Imageability+Visual Field:Length+Visual Field:Frequency+Visual Field:Imageability+Visual Field:Length:Frequency+Visual Field:Length:Imageability	0.264	1	0.607

5	log(RT) ~ 1+(1|Subject)+(1|Stimuli)+Visual Field+Length+Frequency+Imageability+Length:Frequency+Length:Imageability+Frequency:Imageability+Visual Field:Length+Visual Field:Frequency+Visual Field:Imageability+Visual Field:Length:Imageability	1.233	1	0.267
6	log(RT) ~ 1+(1|Subject)+(1|Stimuli)+Visual Field+Length+Frequency+Imageability+Length:Frequency+Length:Imageability+Frequency:Imageability+Visual Field:Length+Visual Field:Frequency+Visual Field:Imageability	1.661	1	0.197
7	log(RT) ~ 1+(1|Subject)+(1|Stimuli)+Visual Field+Length+Frequency+Imageability+Length:Frequency+Length:Imageability+Frequency:Imageability+Visual Field:Length+Visual Field:Frequency	0.003	1	0.957
8	log(RT) ~ 1+(1|Subject)+(1|Stimuli)+Visual Field+Length+Frequency+Imageability+Length:Frequency+Length:Imageability+Frequency:Imageability+Visual Field:Frequency	0.069	1	0.792
9	log(RT) ~ 1+(1|Subject)+(1|Stimuli)+Visual Field+Length+Frequency+Imageability+Length:Frequency+Frequency:Imageability+Visual Field:Frequency	0.247	1	0.619
10	log(RT) ~ 1+(1|Subject)+(1|Stimuli)+Visual Field+Length+Frequency+Imageability+Frequency:Imageability+Visual Field:Frequency	0.332	1	0.564
11	log(RT) ~ 1+(1|Subject)+(1|Stimuli)+Visual Field+Length+Frequency+Imageability+Visual Field:Frequency	3.037	1	0.081
12	***log(RT) ~ 1+(1|Subject)+(1|Stimuli)+Visual Field+Length+Frequency+Visual Field:Frequency***	3.574	1	0.059
13	log(RT) ~ 1+(1|Subject)+(1|Stimuli)+Visual Field+Frequency+Length	4.943	1	0.026

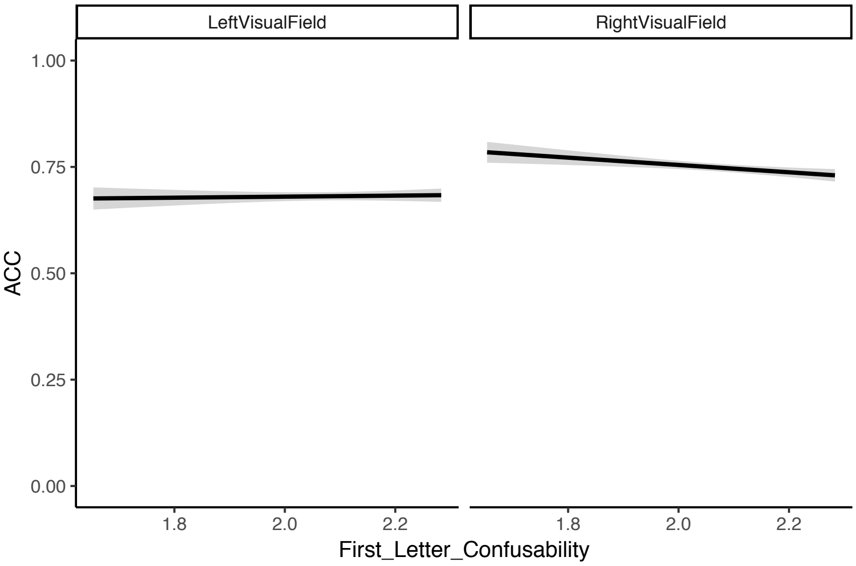

Figure A.3.2 | First letter confusability: predicted accuracy in the two visual fields.

Table A.3.5 | Visual Field analyses: summary of the selected model for accuracy.

Random Effects	***sd***						
Subject	0.432						
Stimuli	0.691						
Fixed Effects	***Estimate***	***Standard Error***	***z***	***p value***	χ^2	***df***	$p(\chi^2)$
Intercept	1.053	0.070	14.941	< 0.001			
Visual Field	-0.174	0.018	-9.733	< 0.001	109.097	1	< 0.001
Lexicality	0.252	0.043	5.894	< 0.001	36.880	1	< 0.001
Visual Field-by-Lexicality	0.173	0.018	9.674	< 0.001	93.577	1	< 0.001

Table A.3.6 | Visual Field analyses: summary of the Bonferroni-corrected pairwise comparisons for accuracy.

Post hoc (ACC)	***Value***	***df***	χ^2	***p***
(LVF Pseudoword) - (LVF Word)	0.701	1	85.216	< 0.001
(LVF Pseudoword) - (RVF Pseudoword)	0.499	1	0.002	1.000
(LVF Pseudoword) - (RVF Word)	0.539	1	2.795	0.567
(LVF Word) - (RVF Pseudoword)	0.298	1	85.714	< 0.001
(LVF Word) - (RVF Word)	0.332	1	202.676	< 0.001
(RVF Pseudoword) - (RVF Word)	0.539	1	2.872	0.541

Table A.3.7 | Visual Field analyses: summary of the selected model for RTs.

Random Effects	***sd***							
Subject	0.229							
Stimuli	0.077							
Residual	0.293							
Fixed Effects	***Estimate***	***Standard Error***	***df***	***t***	***p value***	***F***	***df***	***p(F)***
Intercept	6.660	0.030	61	221.435	< 0.001			
Visual Field	0.013	0.003	12443	5.094	< 0.001	21.022	1, 12445.2	< 0.001
Lexicality	0.060	0.005	307	11.669	< 0.001	141.872	1, 317.6	< 0.001
Visual Field-by-Lexicality	-0.019	0.003	12443	-7.340	< 0.001	53.875	1, 12448.2	< 0.001

Table A.3.8 | Visual Field analyses: summary of the Bonferroni-corrected pairwise comparisons for RTs.

Post hoc (RTs)	***Value***	***df***	***χ^2***	***p***
(LVF Pseudoword) - (LVF Word)	0.080	1	47.195	< 0.001
(LVF Pseudoword) - (RVF Pseudoword)	-0.012	1	2.741	0.587
(LVF Pseudoword) - (RVF Word)	0.146	1	165.480	< 0.001
(LVF Word) - (RVF Pseudoword)	-0.092	1	62.514	< 0.001
(LVF Word) - (RVF Word)	0.066	1	72.214	< 0.001
(RVF Pseudoword) - (RVF Word)	0.158	1	193.899	< 0.001

Table A.3.9 | Visual Field analyses: results of the sensitivity analysis in the two visual fields/hemispheres.

Left Visual Field		Stimulus		Right Visual Field		Stimulus	
		Word	Pseudoword			Word	Pseudoword
Response	Word	0.59	0.24	Response	Word	0.73	0.24
	Non-Word	0.41	0.76		Non-Word	0.27	0.76
		z(Hit)= 0.256	z(FA)= -0.774			z(Hit)= 0.653	z(FA)= -0.777
		d'= 1.030	c= 0.259			d'= 1.431	c= 0.062

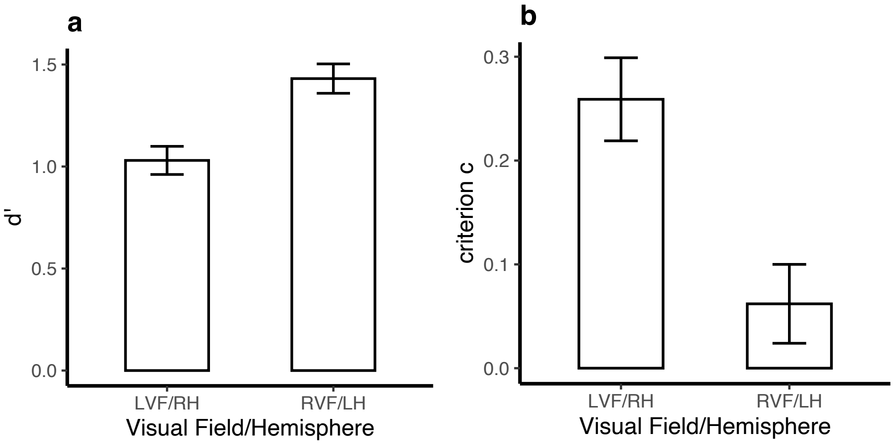

Figure A.3.3 | Sensitivity measures in the two visual fields/hemispheres: (a) *d prime*, (b) *criterion c*.

Table A.3.10 | N size analyses: summary of the selected model for accuracy.

Random Effects	***sd***						
Subject	0.432						
Stimuli	0.678						
Fixed Effects	***Estimate***	***Standard Error***	***z***	***p value***	***χ2***	***df***	***p(χ2)***
Intercept	0.991	0.073	13.597	< 0.001			
Visual Field	-0.174	0.018	-9.734	< 0.001	109.035	1	< 0.001
Lexicality	0.263	0.047	5.623	< 0.001	35.479	1	< 0.001
N size	0.025	0.047	0.522	0.602	0.889	1	0.346
Visual Field-by-Lexicality	0.173	0.018	9.660	< 0.001	93.315	1	< 0.001
N size-by-Lexicality	-0.142	0.047	-3.004	0.003	9.023	1	0.003

Table A.3.11 | N size analyses: summary of the selected model for RTs.

Random Effects	***sd***							
Subject	0.229							
Stimuli	0.077							
Residual	0.293							
Fixed Effects	***Estimate***	***Standard Error***	***df***	***t***	***p value***	***F***	***df***	***p(F)***
Intercept	6.665	0.030	62	220.987	< 0.001			
Visual Field	0.013	0.003	12440	5.039	< 0.001	21.266	1, 12439.9	< 0.001
N size	-0.004	0.006	303	-0.760	0.448	1.099	1, 314.7	0.295
Lexicality	0.057	0.006	312	10.091	< 0.001	104.667	1, 321.2	<0.001
N size-by-Visual Field	0.006	0.003	12412	2.212	0.027	4.893	1, 12417.1	0.027
Visual Field-by-Lexicality	-0.016	0.003	12446	-5.482	< 0.001	30.054	1, 12449.7	< 0.001
N size-by-Lexicality	0.012	0.006	303	2.176	0.030	4.735	1, 312.6	0.030

Table A.3.12 | Length, Frequency and Imageability analyses: summary of the selected model for accuracy.

Random Effects	***sd***
Subject	0.599
Stimuli	0.639

Fixed Effects	***Estimate***	***Standard Error***	***z***	***p(Z)***	χ^2	***df***	***p***(χ^2)
Intercept	0.834	0.096	8.673	< 0.001			
Visual Field	-0.360	0.025	-14.426	< 0.001	208.121	1	< 0.001
Length	0.346	0.056	6.117	< 0.001	37.417	1	< 0.001
Frequency	0.283	0.057	5.002	< 0.001	25.015	1	< 0.001
Imageability	0.090	0.057	1.590	0.112	2.652	1	0.103
Freqency-by-Imageability	-0.118	0.057	-2.080	0.037	4.328	1	0.037

Table A.3.13 | Length, Frequency and Imageability analysis: summary of the Bonferroni-corrected pairwise comparisons for accuracy.

Post hoc (ACC)	***Value***	***df***	χ^2	***p***
(High Frequency High Imageability) - (High Frequency Low Imageability)	0.474	1	0.368	1.000
(High Frequency High Imageability) - (Low Frequency High Imageability)	0.574	1	0.299	0.500
(High Frequency High Imageability) - (Low Frequency Low Imageability)	0.668	1	17.890	< 0.001
(High Frequency Low Imageability) - (Low Frequency High Imageability)	0.560	1	5.078	0.145
(High Frequency Low Imageability) - (Low Frequency Low Imageability)	0.692	1	21.766	< 0.001
(Low Frequency High Imageability) - (Low Frequency Low Imageability)	0.599	1	5.492	0.115

Table A.3.14 | Length, Frequency and Imageability analyses: summary of the selected model for RTs.

Random Effects	***sd***
Subject	0.215
Stimuli	0.074
Residual	0.283

Fixed Effects	***Estimate***	***Standard Error***	***df***	***t***	***p(t)***	***F***	***df***	***p(F)***
Intercept	6.610	0.029	64	230.739	< 0.001			
Visual Field	0.036	0.004	5778	9.432	< 0.001	93.538	1, 5779.4	< 0.001
Frequency	-0.050	0.007	155	-7.230	< 0.001	54.441	1, 156.5	< 0.001
Length	-0.039	0.007	154	-5.669	< 0.001	32.129	1, 157.0	< 0.001
Visual Field-by-Frequency	0.008	0.004	5775	2.222	0.026	4.936	1, 5777.3	0.026

Table A.3.15 | Length, Frequency, Imageability analyses: summary of the Bonferroni-corrected pairwise comparisons for RTs.

Post hoc (RTs)	***Value***	***df***	χ^2	***p***
(LVF High Frequency) - (LVF Low Frequency)	-0.084	1	23.236	< 0.001
(LVF High Frequency) - (RVF High Frequency)	0.088	1	74.896	< 0.001
(LVF High Frequency) - (RVF Low Frequency)	-0.029	1	2.960	0.512
(LVF Low Frequency) - (RVF High Frequency)	0.172	1	100.532	< 0.001
(LVF Low Frequency) - (RVF Low Frequency)	0.055	1	24.074	< 0.001
(RVF High Frequency) - (RVF Low Frequency)	-0.117	1	49.708	< 0.001

Chapter 4

Pre-lexical and lexical effects on lateralized reading in left- and right-handers.

In the last chapter, I observed that that lexical, rather than pre-lexical, factors play a primary role in giving rise to the commonly reported visual field effect in lateralized reading. On the one hand, these results suggest that controlling lexical-semantic variables is necessary to obtain reliable behavioral measurements of reading lateralization. On the other hand, data from this experiment tip in favor of the "two orthographic lexicons" account of LH dominance for reading as the most likely functional brain model giving rise to the visual field effect. However, these claims are based on the observed compression[1] of the word frequency effect in the LVF/RH compared to the RVF/LH. It is crucial to exclude that these results only depend on a "floor" effect in performance. In addition, it might be important to explore the extent to which the effects described in the previous experiment could be modulated by different patterns of hemispheric dominance. To accomplish these goals, in the present experiment I compared the sample of 60 right-handers (see Chapter 3) with a sample of 60 left-handers in the same eye-tracking-controlled lateralized lexical decision task.

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[1] Here and henceforth, with the term "compression", I refer to a reduction in the magnitude of the effect.

Introduction

In the last two chapters, I provided evidence that implicit reading can occur in Pure Alexia for frequent and concrete words even after a lesion impairing the LH visual word form system and disconnecting it from the rest of the LH. Furthermore, I showed that the visual field effect in lateralized reading, typically observed in healthy subjects, is most likely due to a different sensitivity of the two cerebral hemispheres to lexical-semantic factors. These results, that appear to be in line with previous neuropsychological (e.g.: Coltheart 1980, 2000; Saffran et al., 1980) and divided visual field behavioral studies (Bradshaw & Gates, 1978; Ellis & Shepherd, 1974; Hines, 1976; Hines, 1977)[2], provide support for a *relative* account of LH dominance over the RH for reading, according to the assumption of "two orthographic lexicons" in the brain, with processing of that of the RH being limited to frequent and/or concrete words (Coltheart 1980, 2000; Saffran et al., 1980; Coslett & Saffran, 1994; Saffran & Coslett, 1998; Luzzatti, Rumiati & Ghirardi, 1998; Luzzatti, 2003).

Nevertheless, in order to support this conclusion, it may be crucial to exclude that the behavioral pattern observed in Chapter 3 (namely a compression of the word frequency effect in the LVF/RH compared to the RVF/LH) is only due to a "floor" effect in performance (i.e., the compression of the frequency effect is a consequence of particularly poor performance in the LVF/RH for infrequent items)[3]. One way to accomplish this could be to modify the experimental paradigm, in order to increase performance in the LVF/RH, either by reducing stimuli eccentricity, or by increasing stimuli presentation time. However, such manipulations would have the side effect of reducing the likelihood of targeting two separate hemispheres, as well as augmenting the risk of observing target-driven eye-movements (see Bourne, 2006), therefore adding noise to the laterality measurements and hampering the comparison with the

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[2] Interestingly, relatively recent literature has suggested that the frequency effect could be constant between hemispheres (Coney, 2005). However, despite the lack of a formal Visual Field-by-Frequency interaction, Coney's data could suggest a greater range of the frequency effect for RTs in the RVF compared to the LVF, as well as a seemingly steeper decrease in RTs as a function of frequency in the RVF than in the LVF.

[3] In general terms, a "floor" effect in performance should result in amplified RTs. However, in a lexical decision task such as the one adopted in Chapter 2, an internal time limit is meant to exist in the response window (the time criterion "T", according to the Multiple Read-Out Model; Grainger & Jacobs, 1996). In principle, this could cause RTs theoretically tending to infinite to actually tend to the time limit. As a consequence, differences in RTs that should tend to infinite could actually tend to zero. The simultaneous presence of overall bad performance and of an internal time limit could therefore explain the "compression" of the frequency effect in the LVF/RH in right-handed subjects.

previous experiment. An alternative way to do so involves studying subjects that are expected to show a comparatively smaller sensitivity than right-handed subjects towards the manipulation of the hemifield of stimuli presentation in lateralized reading. In this regard, left-handed subjects represent a feasible option. Indeed, they have been consistently associated -as much as right-handers- with a RVF/LH advantage over the LVF/RH in lateralized reading (see for instance Waldie & Moseley, 2000; Willemin et al., 2016). Hence, if such LH advantage is underlaid by a poorer/weaker orthographic lexicon in the RH than in the LH, the same compression of the word frequency effect observed in right-handers should also be present in left-handers. On the other hand, the visual field asymmetry of left-handed subjects proved to be smaller than that of right-handers across studies, although this pattern rarely reaches significance within each study (Kim, 1994)[4].

Assuming that lateralization of reading processes depends on the functional lateralization of spoken language (Plaut & Behrmann, 2011; Behrmann & Plaut, 2015), a smaller visual field effect in left-handers than right-handers is expected due to the fact that, compared to right-handers, left-handed subject show a less-pronounced LH dominance for spoken language. Indeed, it was shown that while among right-handers 96% show a LH dominance for spoken language, 4% show a bilateral pattern, and 0% show a RH dominance, among left-handers 76% show a LH dominance for spoken language, 14% show a bilateral pattern and 10% show a RH dominance (Pujol et al., 1999; see also Branch, Milner & Rasmussen, 1964).

The present experiment aimed at exploring whether the compression of the frequency effect in the LVF/RH observed in right-handers could be observed also in left-handers, whose performance is expected to show less of a “floor” effect in performance than right-handers for stimuli projected to the LVF/RH, due to less sensitivity towards the manipulation of visual field in lateralized reading. For this purpose, a sample of 60 left-handed volunteers was tested with the same experimental paradigm described in the previous chapter, in order to compare performance with that of right-handers. In order to assess the generalizability of the findings of the previous experiment to left-handers, also in this experiment *Visual Field*, *N size*, and *Length, Frequency and Imageability* analyses were conducted.

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[4] The lack of significance of this pattern could be due to poor balancing between groups (see Waldie & Moseley, 2000; Willemin et al., 2016), or overall small sample size (Chiarello, Dronkers, Hardyck, 1984) of previous studies.

Materials and methods

Participants

For the present study, I compared the previously described sample of right-handers (see Chapter 3, N=60, 30 males, *mean* age= 23.07, *sd*= 2.79, *mean* education= 14.70, *sd*= 2.07) with a sample of 60 subjects (30 males, *mean* age= 22.03, *sd*= 3.27, *mean* education= 14.28, *sd*= 1.75) who defined themselves as left-handers. The group of right-handers had a *mean* handedness of 89.72, *sd*= 13.05, while the group of left-handers had a *mean* handedness= -50, *sd*= 28.12, which was measured according to the laterality index computed on the Edinburgh Handedness Inventory (Oldfield, 1971). Overall, one hundred and twenty individuals with normal or corrected-to-normal vision were included in this study. None of them reported any history of neurological or psychiatric disease. The study was run according to the guidelines of the declaration of Helsinki (World Medical Association, 2001) and was approved by the ethical committee. All subjects provided written informed consent for the participation to the study.

Stimuli and procedure

Stimuli and procedure were identical to those presented in Chapter 3. The task was an eye-tracking-controlled lateralized lexical decision task, in which stimuli were briefly flashed unilaterally either left or right from central fixation. In half of the trials, the participants responded with their right hand (160 trials), while in the other half (160 trials) they responded with their left hand (the order of such blocks was counterbalanced across subjects). Participants provided responses with their index and middle fingers via mouse keypresses. For each subject, regardless of the responding hand, each of the two fingers was associated to either response (e.g. index finger = "WORD", middle finger "NON-WORD"). The association between fingers and response was counterbalanced across participants.

Subjects' eyes were tracked with a *mean* accuracy of 0.19°, *sd*= 0.06° for right-handers and 0.22° ± 0.07° for left-handers.

Data Analysis

Data points from right-handed (19200 records) and left-handed (19200 records) participants were merged in one single dataset. First, I discarded trials in which no response had been recorded (159 in right-handers and 110 in left-handers) and those in which response had been faster than 250ms (190 trials in right-handers and 123 trials in left-handers). Trials in which no stable fixation had been recorded were also discarded (748 in right-handers and 1026 in left-handers). The final dataset included 36044 records, 18103 for right-handers and 17941 for left-handers.

Prior to the execution of analyses on accuracy and RTs, a preliminary cluster analysis was run, in order to probe the possible existence of different laterality subgroups within the samples of right-handed and, most importantly, left-handed subjects (Pujol et al., 1999, Branch, Milner & Rasmussen, 1964). This was done in order to ascertain that each hand preference group could be enough internally consistent in terms of functional lateralization to be considered as a homogeneous sample.

Separately for left- and right-handers, I computed -for each subject- a laterality coefficient (LC) on performance accuracy in the two visual fields/hemispheres (Marshall, Caplan & Holmes, 1975)[5].

$$LC = \frac{RVF_{acc} - LVF_{acc}}{RVF_{err} + LVF_{err}}$$

The *Mclust* function of the R package 'mclust' (Scrucca et al., 2016) was applied on LC data to identify (within each sample) any subsample of subjects showing a coherent lateralization pattern (see for instance Mazoyer et al., 2014).

As for the analyses described in Chapter 3, for each subject, and separately for each trial, the accuracy of responses in dichotomous form (1 = correct, 0 = incorrect) and log-transformed RTs of accurate responses (i.e., RTs of errors were discarded) were employed as dependent variables in a series of Mixed-effects models. As in the previous experiment, subjects and

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[5] Given that overall performance in all subjects was better than 50%, the reported equation was used. Please see Marshall, Caplan & Holmes (1975) for the computation of the LC for overall accuracy below 50%.

stimuli were modeled as random intercepts (Baayen, 2008)[6] and logarithmic transformation was adopted to obtain an approximation of a Normal distribution for RTs (see Appendix, Figure A.4,1). Dummy coding for dichotomous variables was done as in Chapter 3.

Accuracy data were analyzed by means of logistic regressions. All analyses were performed by means of the statistical software R and the lme4 package (Bates, Maechler, Bolker, & Walker, 2015). For reaction time data, outliers were removed by means of the model criticism procedure (Baayen, 2008). When necessary, for both accuracy and RTs data, χ^2 post-hoc pairwise comparisons were performed on significant interaction effects by means of the *testInteraction* function of the package Phia (De Rosario-Martinez, 2013) and corrected according to the Bonferroni method.

Three different sets of analyses were performed. The "*Visual Field Analyses"* (in which both words and pseudowords were included) explored whether performance for stimuli presented to the two visual fields (LVF/RH, RVF/LH) differed among hand preference groups (left-handers vs. right-handers). The same set of analyses also explored whether the lexical nature of the stimuli (words vs. pseudowords) could affect such interaction. Also, the effect or the response modality (left vs. right responding hand) was added in the model as a main effect, and as an interaction effect with Visual Field and Group. This latter choice was made in order to exclude that any possible interaction of the Visual Field effect with the Group variable could be due to the motor effector (left vs. right hand) with which responses were given.

The "*N size*" analyses were run in order to explore whether the Group factor could modulate the relationship between Visual Field, Lexicality and N size. Therefore, simple and interaction effects of these variables were included in these analyses.

The *"Length, Frequency and Imageability Analyses"* investigated the effects of Group (left-handers vs. right-handers), Visual Field (LVF/RH, RVF/LH), Length (4 letters vs. 5 letters), Frequency (high frequency vs. low frequency) and Imageability (high vs. low imageability) on accuracy and RTs of word recognition (pseudowords were excluded). In analogy with the "*Length, Frequency and Imageability*" analyses presented in the previous chapter, these analyses were performed in order to explore whether performance differences among hemispheres are due to lexical-semantic (i.e. word Frequency and/or Imageability),

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[6] This random structure was chosen over a maximal structure in order to assure comparability of these analyses with those of the previous chapter and to assure algorithm convergence.

rather than pre-lexical (i.e. word Length), while describing any possible differences among hand preference groups.

These analyses were complemented by a "*Chance level Analysis*", in which distance from chance level performance (50% correct) for accuracy was evaluated in both groups across visual fields for high- and low-frequency words, by means of a series of one-sample Wilcoxon tests.

Results

For both groups, the *Mclust* function yielded one single cluster as the best clustering solution, indicating relative homogeneity of the laterality patterns within the two groups (Table 4.1).

Table 4.1 | Summary of the best clustering solution for the groups of left-handed and right-handed subjects as identified by the *Mclust* function (BIC= Bayesian Information Criterion).

Sample	*Number of components*	*Log-likelihood*	*N*	*BIC*
Left-handers	1	9.992	60	11.796
Right-handers	1	10.419	60	12.650

Visual Field analyses

For what concerns accuracy (Figure 4.1, Appendix Table A.4.1), the main effects of Visual Field (z = -10.926, p < 0.001) and Lexicality (z = 4.639, p < 0.001) indicate better performance in the RVF/LH than in the LVF/RH and better performance for pseudowords than for words, respectively. The main effect of Group was not significant (z = 0.429, p = 0.668). Significant interaction effects emerged between Visual Field and Lexicality (z = 10.161, p < 0.001), Visual Field and Group (z = 2.907, p = 0.004), and Lexicality and Group (z = -4.510, p < 001). A significant three-way interaction also emerged between Visual Field, Lexicality and Group (z = -3.647, p < 0.001). Post-hoc comparisons (see Appendix, Table A.4.2) revealed an advantage of the RVF/LH over the LVF/RH for lexical stimuli in both groups (right-handers: $\chi^2(1)$= 206.362, p < 0.001; left-handers: $\chi^2(1)$= 55.064, p < 0.001). Conversely, no Visual Field effect was observed for pseudowords in either group (right handers: $\chi^2(1)= 0.001$, $p = 1.000$; left-handers: $\chi^2(1)= 0.538$, $p = 1.000$). Crucially, while no significant group differences emerged for pseudowords in either visual field and for words in the RVF/LH (all p values = 1), left-handers were significantly more accurate than right-handers for words presented to the LVF/RH ($\chi^2(1)= 10.571$, $p = 0.032$).

Responding Hand showed a substantial trend towards significance indicating overall better performance for responses given with the right hand ($z = -1.950$, $p = 0.051$) in both hand preference groups. However, this effect did not significantly interact either with Visual Field ($z= -0.687$, $p =0.492$), Group ($z= 0.033$, $p = 0.974$), or with their interaction ($Z= 0.854$, $p = 0.393$).

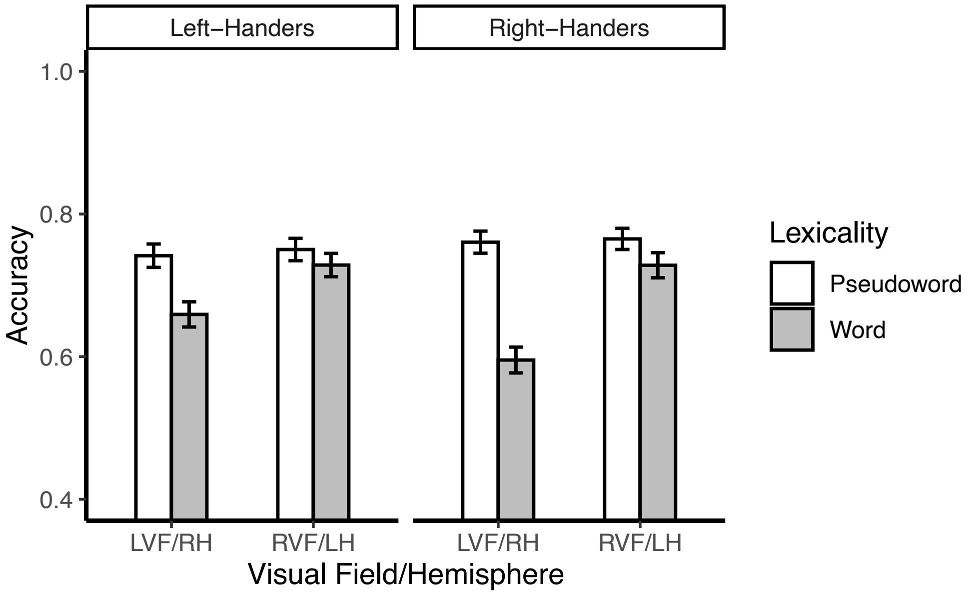

Figure 4.1 | Visual field Analyses. Visual Field-by-Lexicality-by-Group interaction for accuracy data. Error bars indicate mean standard errors.

As far as RTs are concerned (Figure 4.2, Appendix Table A.4.3), I found a significant main effects of Visual Field ($t(24902.7)=6.443$, $p < 0.001$) and Lexicality ($t(311.4)= 14.375$, $p < 0.001$), and a significant Visual Field-by-Lexicality interaction ($t(24904.5)= -9.032$, $p < 0.001$). The main effect of Group was not significant ($t(117.6)= -1.492$, $p = 0.138$), as well as its interaction with Visual Field ($t(24876.2)= -1.175$, $p = 0.240$), while Group interacted significantly with Lexicality ($t(24820.7)= 3.865$, $p < 0.001$) and with the Visual Field-by-

Lexicality interaction (*t*(24876.7)= 2.420, *p* = 0.016). Post-hoc analyses (see Appendix, Table A.4.4) revealed visual field effects for words in both right-handers ($\chi2(1)$= 84.437, $p < 0.001$) and left-handers ($\chi2(1)$= 34.585, $p < 0.001$), while no significant visual field effects emerged for pseudowords (all *p* values = 1.000). Differently from accuracy data, the Group difference in RTs for words presented in the LVF ($\chi2(1)$= 4.455, uncorrected *p* = 0.035) did not survive correction for multiple comparisons (Bonferroni-corrected *p* = 0.974).

Responding Hand showed a significant main effect indicating that, overall, responses given with the right hand were faster than those given with the left hand (*t*(24879.6)= 4.831, $p < 0.001$). However, this effect did not significantly interact either with Visual Field (*t*(24874.3)= -0.450, *p*= 0.653), Group (*t*(24887.3)= 1.443, *p*= 0.152), or their interaction (*t*(24883.8)= -0.648, *p*= 0.517).

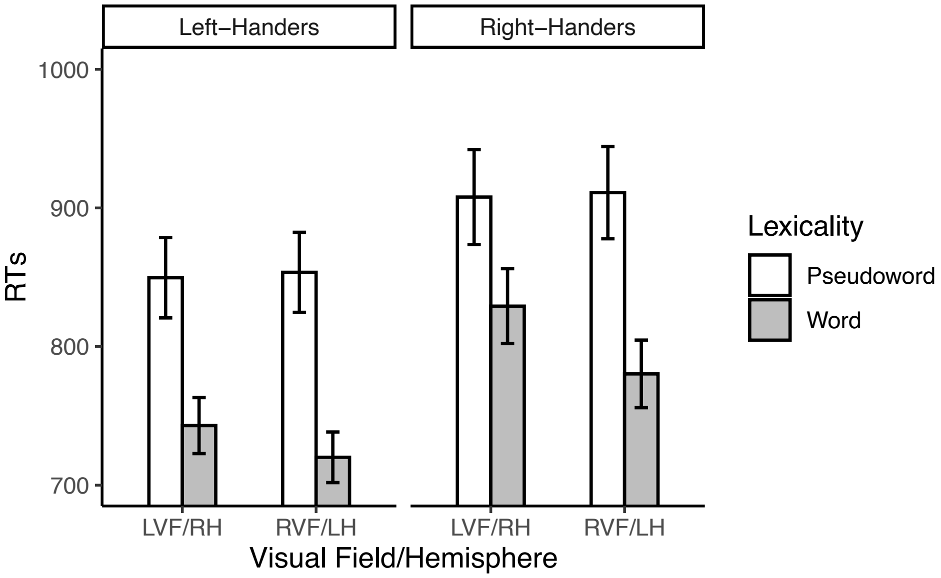

Figure 4.2 | Visual field Analyses. Visual Field-by-Lexicality-by-Group interaction for RTs. Error bars indicate mean standard errors.

N size analyses

With these analyses, the effects of Group, Visual Field, Lexicality and N size and their interactions were explored.

In analyses on accuracy data (see Appendix, Table A.4.5), significant main effects of Visual Field (*z*= -9.573, $p < 0.001$) and Lexicality (*z*= 4.599, $p < 0.001$) were detected, as well as their interaction (*z*= 8.123, $p < 0.001$). As in previous analyses, Group significantly interacted with Visual Field (*z*= 2.478, *p* = 0.013), Lexicality (*z*= -3.822, *p* < 0.001) and their interaction (*z*= -3.642, *p* < 0.001). The Lexicality-by-N size interaction was significant (*z*= -3.136, *p* = 0.002), suggesting that greater N size leads to answer "word" to both word and pseudoword stimuli (Figure 4.3a).

The Visual Field-by-N size interaction turned out to be significant (*z*= -2.795, *p* = 0.005), apparently indicating an overall greater effect of N size in the LVF/RH than in the RVF/LH, with this effect being negative in the LVF/RH and positive in the RVF/LH (Figure 4.3b). All other effects were not significant (*p* values > 0.3).

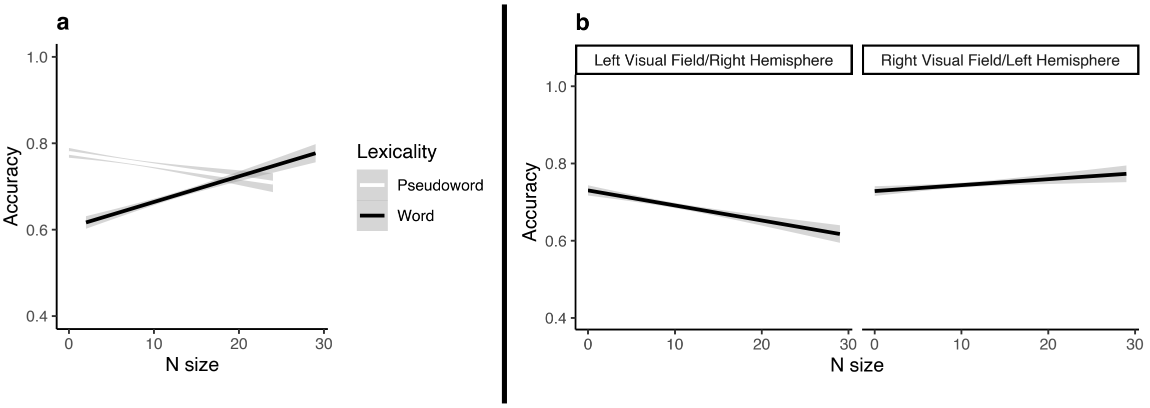

Figure 4.3 | Neighborhood (N) size analyses: (a) Accuracy for word and pseudoword stimuli; (b) Accuracy in the two visual fields/hemispheres for both words and pseudowords (collapsed in a single regression line).

As far as RTs are concerned (see Appendix, Table A.4.6), significant main effects of Visual Field (*t*(24906.6)= 6.015, *p* < 0.001) and Lexicality (*t*(313.4)= 12.577, *p* < 0.001) were detected, as well as their interaction (*t*(24909.1)= -6.798, *p* < 0.001). Group significantly interacted with Lexicality (*t*(24814.3)= 3.442, *p* < 0.001) and with the interaction between Visual Field and Lexicality (*t*(24861.4)= 2.051, *p*= 0.040). N size significantly interacted with Lexicality (*t*(308.8)= 2.220, *p*= 0.027), indicating a facilitating effect on performance for lexical stimuli and detrimental effect in case of pseudoword stimuli (Figure 4.4a), and with Visual Field (*t*(24881.9)= 2.744, *p*= 0.006), indicating an overall greater effect of N size in the RVF/LH than in the LVF/RH (Figure 4.4b). All other effects were not significant (*p* values > 0.100).

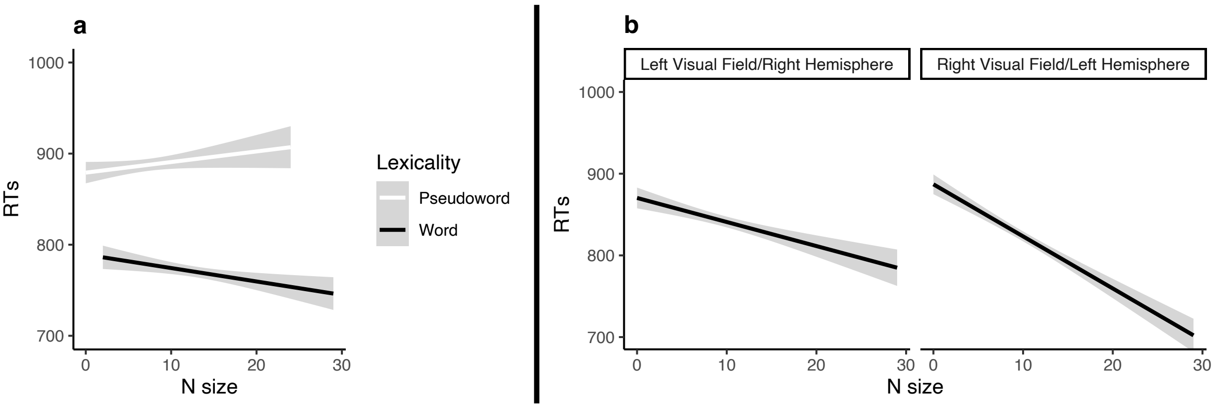

Figure 4.4 | Neighborhood (N) size analyses: (a) RTs for word and pseudoword stimuli; (b) RTs in the two visual fields/hemispheres for both words and pseudowords (collapsed in a single regression line).

Length, Frequency and Imageability Analyses

In this set of analyses, I explored the effects of Group, Visual Field, word Frequency, Imageability and word Length, together with their interactions.

With respect to accuracy (see Appendix, Table A.4.7), the significant main effects of Visual Field (z= -15.339, $p < 0.001$), Length (z= 6.517, $p < 0.001$) and Frequency (z= 5.058, $p < 0.001$) emerged, indicating better performance for the RVF/LH than for the LVF/RH, for 4-letter words than for 5-letter words and for high-frequency words than for low-frequency words, respectively. Also the Visual Field-by-Group interaction was significant ($z = 4.753$, $p < 0.001$; see Appendix, Table A.4.8), indicating better performance for left-handers than right-handers in the LVF/RH ($\chi^2(1)$= 7.876, $p = 0.030$) and not in the RVF/LH ($\chi^2(1)$= 0.001, $p = 1.000$). All other effects were not significant (p values > 0.057).

For what concerns RTs (see Appendix, Table A.4.9), significant main effects emerged for Visual Field (t(11756.3)= 11.673, $p < 0.001$), Length (t(150.8)= -5.949, $p < 0.001$), and Frequency (t(150.6)= -7.211, $p < 0.001$), with performance patterns resembling those emerging for accuracy data, as well as for Imageability (t(150.6)= -2.577, $p = 0.011$), indicating shorter RTs for high-imageability words than for low-imageability words. A significant effect of Group (t(117.1)= -2.100, $p = 0.038$) emerged, indicating faster performance for left-handers than right-handers. The Visual Field-by-Group interaction effect was significant (t(11738.9)= -3.196, p= 0.001). However, as in the *Visual Field Analyses*, the difference in RTs between left- and right-handers for stimuli projected to the LVF was not significant after Bonferroni correction (χ2(1)=

6.184, *p* = 0.077, see Appendix, Table A.4.10). A significant Frequency-by-imageability interaction was detected (*t*(150.5)= 2.108, *p* = 0.037, see Appendix, Table A.4.11), indicating the emergence of an Imageability effect for low-frequency words (χ^2(1)= 8.916, *p* = 0.017) and not for high-frequency words (χ^2(1)=0.002, *p* = 1.000).

The Visual Field-by-Frequency interaction (Figure 4.5) was also significant (*t*(11751.7)= 2.588, p= 0.010). Post-hoc analyses (see Appendix, Table 4.12) revealed RTs for low-frequency words projected to the LVF/RH to be significantly slower than high-frequency words projected to the LVF/RH (χ^2(1) =28.154, *p* < 0.001), as well as low-frequency words projected to the RVF/LH (χ^2(1) = 38.823, *p* < 0.001). As in Chapter 3, in order to further explore the meaning of this effect, I computed (for each subject) the difference between RTs for low-frequency and high-frequency items in each visual field/hemisphere. As expected, the frequency effect turned out to be bigger in the RVF/LH than in the LVF/RH (*W* = 2726, *p* = 0.018).

All other effects were not significant (all *p* values > 0.080).

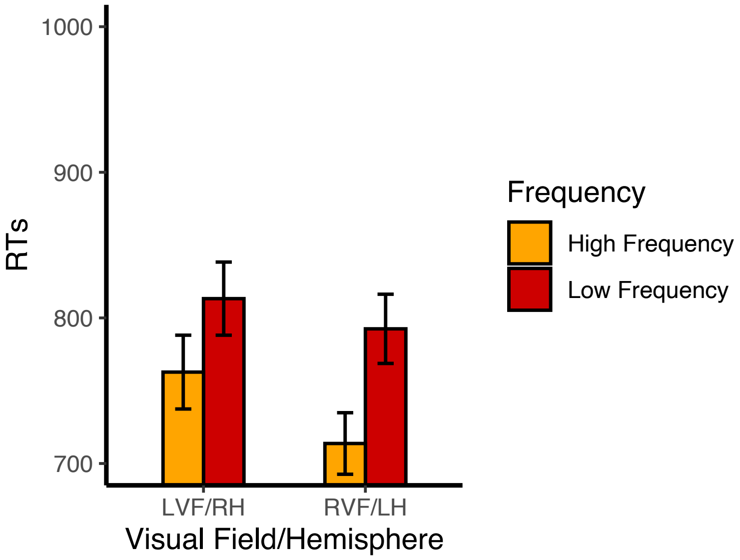

Figure 4.5 | Length and Frequency Analyses. Visual Field-by-Frequency interaction for RTs. Error bars indicate mean standard errors.

Chance Level Analysis

For what concerns right-handed subjects, accuracy was significantly different from chance level in the RVF/LH for both high- ($V = 1808$, $p < 0.001$) and low-frequency words ($V = 1627.5$, $p < 0.001$) and in the LVF/RH for high-frequency words ($V = 1676$, $p < 0.001$). Conversely, performance in the LVF/RH for low-frequency words turned out to be not significantly different from chance level ($V = 1115.5$, $p = 0.082$).

Left-handers showed a different pattern (Table 4.2, Figure 4.6): they achieved a significantly accurate performance on stimuli projected to both visual fields/hemispheres for high- as well as low-frequency words (all p values < 0.001).

Table 4.2 | Results of the Chance Level Analysis.

			Mean accuracy ± sd	***V***	***p***
Right-handers	LVF/RH	High Frequency	0.658 ± 0.154	1676	< 0.001
		Low Frequency	0.531 ± 0.149	1115.5	0.082
	RVF/LH	High Frequency	0.773 ± 0.147	1808	< 0.001
		Low Frequency	0.683 ± 0.143	1627.5	< 0.001
Left-handers	LVF/RH	High Frequency	0.710 ± 0.144	1730.5	< 0.001
		Low Frequency	0.608 ± 0.145	1368	< 0.001
	RVF/LH	High Frequency	0.772 ± 0.137	1756	< 0.001
		Low Frequency	0.684 ± 0.138	1758	< 0.001

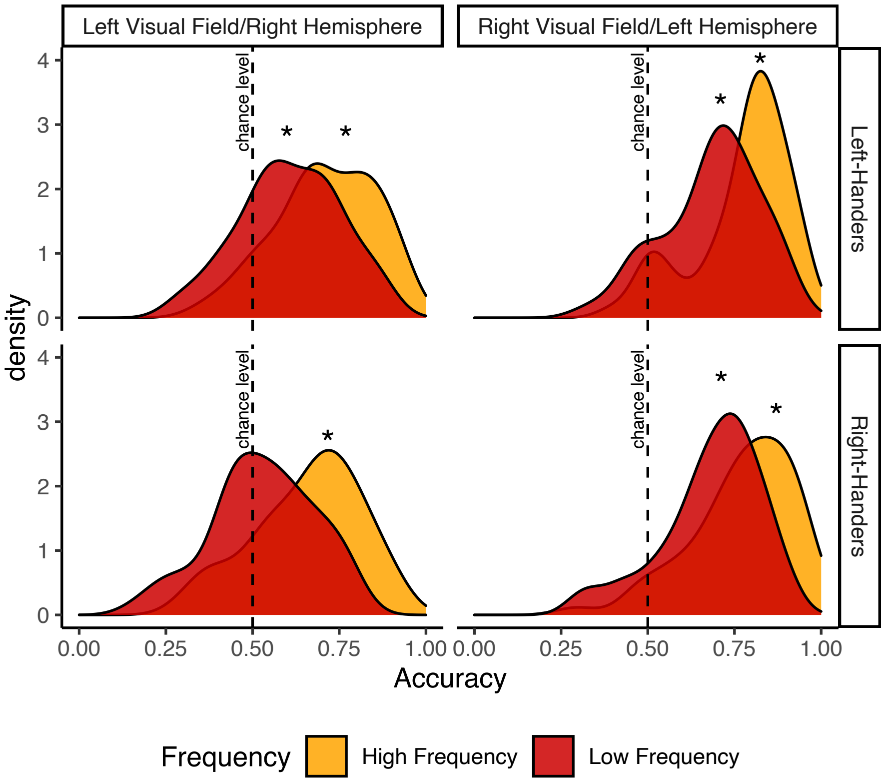

Figure 4.6 | Chance Level Analysis. Accuracy density plots for high- and low-frequency words in the two visual fields in the two groups. Dashed lines indicate chance level performance (50%). Asterisks indicate a significant difference from chance ($p < 0.001$) according to the one-sample Wilcoxon test.

Discussion

In the current study, I adopted an eye-tracking-controlled lateralized lexical decision task to compare the performance of left- and right-handed subjects in processing orthographic information projected in the left and right visual fields. This experiment was conducted with the twofold aim of (1) exploring whether the compression of the frequency effect in the LVF/RH described in Chapter 3 for right-handers could only be due to a "floor" effect in performance, and (2) probing the effects of functional hemispheric dominance on pre-lexical and lexical effects in lateralized reading.

The choice of exploring the performance of left-handed subjects and comparing it with that of right-handers was guided by the presence -as much as in right-handers- of a RVF/LH advantage in lateralized reading in left-handers (Waldie & Moseley, 2000; Willemin et al., 2016). Therefore, if the visual field effect in lateralized reading is due to weak lexical orthographic representations in the RH, the same compression of the word frequency effect observed in right-handers should be observable in left-handers. On the other hand, due to greater variability in the functional hemispheric dominance (Pujol et al., 1999, see also Branch, Milner & Rasmussen, 1964), a smaller magnitude of the visual field effect is expected in left-handers compared to right-handers (Kim, 1994). Hence, at a sample level, the performance of left-handed subjects should be less affected by the visual field manipulation than that of right-handers, and any compression of the frequency effect in the LVF/RH should less likely be attributable to "floor" effects in performance than in right-handers.

At a preliminary level, I observed that each of the two hand-preference groups was enough internally consistent in terms of behavioral functional laterality patterns to be considered as a homogeneous sample (cfr. Mazoyer et al., 2014), and therefore a comparison between the two groups was meaningful.

The three sets of analyses on accuracy and RTs data (namely the "*Visual Field*", "*N size*" and "*Length, Frequency and Imageability*" analyses) revealed that Group did not have a prominent effect on the relationship between Visual Field and the other manipulated psycholinguistic variables.

Remarkably, left-handers showed -as much as right-handers- a RVF advantage in performance, and they showed the same compression of the frequency effect in the LVF/RH observed in left-handers (no significant interaction with the Group factor), while performing significantly better than right-handers in the LVF/RH for words. In addition, they were associated with better-than-chance performance for low-frequency stimuli projected in the LVF/RH, while right-handers were not.

The conclusions that could be derived from these data are simple: the compression of the frequency effect observed for stimuli projected in the LVF/RH is associated with RVF advantage and it does not depend on a "floor" effect on performance in the LVF/RH. Indeed, left-handers showed the same compression effect observed in right-handers, while performing better than right-handers in the LVF/RH and better chance level in the LVF/RH for low-frequency words.

Taken together, these data provide further support for the idea that lexical/semantic, rather than pre-lexical factors, have a primary role in determining the visual field effect in lateralized reading, and support the assumption of a *relative* LH dominance over the RH for reading due to the existence of two orthographic lexicons in the brain, with that of the RH being limited to frequent units (Coltheart, 1908; 2000; Saffran et al., 1980; Saffran & Coslett, 1998; Coslett & Saffran, 1994; Luzzatti, Rumiati & Ghirardi, 1998; Luzzatti, 2003). What remains to be explored is the mechanism that determines the weakness of the RH lexicon for infrequent words. Indeed, it is biologically implausible that a "gating mechanism" exists in the RH that prevents low-frequency words to be encoded in (and subsequently retrieved from) the RH orthographic lexicon. This topic will be extensively addressed in the next Chapter.

Another point that will require further empirical exploration is the nature of the relationship between N size and Lexicality in the two visual fields. Similar to what we observed in the previous chapter, we described interaction effects between Lexicality and N size, suggesting that greater N size leads to respond "word" to both word and pseudoword targets. This effect did not interact with Visual Field. However, significant interaction effects also emerged between N size and Visual Field, with apparently different directions between accuracy and RTs. Accuracy data suggested an overall negative effect of N size on performance for stimuli projected to the LVF/RH, and a small positive effect of N size for stimuli projected to the LVF/RH. RTs, instead, suggested an overall greater facilitating effect of N size in the RVF/LH than in the LVF/RH. The lack of an interaction with Lexicality makes these effects impossible to interpret, because the relationship between N size and performance is opposite between words and pseudowords. Further data will be thus required to define the meaningfulness of these N size-by-Visual Field interaction effects.

Finally, a further point that deserves attention in future studies is the functional meaning of "chance level performance" for low-frequency words presented in the LVF/RH. Indeed, an easy and somewhat tempting interpretation would be one suggesting that such pattern simply represents the limit of the RH in its capability of processing orthographic information, thus directly paralleling interpretations derived from neuropsychological data (see for instance Coltheart, 1980; 2000; Saffran et al., 1980; Saffran & Coslett, 1998). According to this interpretation, data from this experiment suggest that left-handed subjects could have a comparatively "less-limited" RH orthographic lexicon than right-handers. However, for this conclusion to be drawn, direct dependence of performance for low-frequency words in the LVF/RH from the specific features of the experimental paradigm will need to be excluded by future studies.

References

Baayen, R. H. (2008). *Analyzing linguistic data: a practical introduction to statistics using R*. Cambridge, UK: Cambridge University Press.

Bates, D., Maechler, M., Bolker, B., & Walker, S. (2015). lme4: Linear mixed-effects models using Eigen and S4. R package version 1.1-9 http://cran/. *R-project. org/package= lme4*.

Behrmann, M., & Plaut, D. C. (2015). A vision of graded hemispheric specialization. *Annals of the New York Academy of Sciences, 1359*(1), 30-46.

Branch, C., Milner, B., & Rasmussen, T. (1964). Intracarotid sodium amytal for the lateralization of cerebral speech dominance: observations in 123 patients. *Journal of Neurosurgery*, *21*(5), 399-405.

Bradshaw, J. L., & Gates, E. A. (1978). Visual field differences in verbal tasks: effects of task familiarity and sex of subject. *Brain and Language, 5*(2), 166-187.

Chiarello, C., Dronkers, N. F., & Hardyck, C. (1984). Choosing sides: On the variability of language lateralization in normal subjects. *Neuropsychologia, 22*(3), 363-373.

Coltheart, M. (1980). Deep dyslexia: a right-hemisphere hypothesis. In Coltheart, M., Patterson, K., & Marshall, J.C. (Eds.), *Deep Dyslexia*. London: Routledge and Kegan Paul.

Coltheart, M. (2000). Deep dyslexia is right-hemisphere reading. *Brain and Language, 71*(2), 299-309.

Coney, J. (2005). Word frequency and the lateralization of lexical processes. *Neuropsychologia, 43*(1), 142-148.

Coslett, H. B., & Saffran, E. M. (1994). Mechanisms of implicit reading in alexia. In M. Farah & G. Ratcliff (Eds.), *The neuropsychology of high-level vision* (pp. 299–330). Lawrence Erlbaum Associates.

De Rosario-Martinez, H. (2013). phia: Post-hoc interaction analysis. *R package version 0.1-3*.

Ellis, H. D., & Shepherd, J. W. (1974). Recognition of abstract and concrete words presented in left and right visual fields. *Journal of Experimental Psychology, 103*(5), 1035-1036.

Grainger, J., & Jacobs, A. M. (1996). Orthographic processing in visual word recognition: A multiple read-out model. *Psychological review, 103*(3), 518.

Hines, D. (1976). Recognition of verbs, abstract nouns and concrete nouns from the left and right visual half-fields. *Neuropsychologia, 14*(2), 211-216.

Hines, D. (1977). Differences in tachistoscopic recognition between abstract and concrete words as a function of visual half-field and frequency. *Cortex, 13*(1), 66-73.

Kim, H. (1994). Distributions of hemispheric asymmetry in left-handers and right-handers: Data from perceptal asymmetry studies. *Neuropsychology, 8*(2), 148.

Luzzatti, C. (2003). Optic aphasia and pure alexia: contribution of callosal disconnection syndromes to the study of lexical and semantic representation in the right hemisphere. In Zaidel, E., & Iacoboni, M. (Eds.), *The Parallel Brain: The Cognitive Neuroscience of the Corpus Callosum* (pp. 479-499). Cambridge, MA: MIT Press.

Luzzatti, C., Rumiati, R. I., & Ghirardi, G. (1998). A functional model of visuo-verbal disconnection and the neuroanatomical constraints of optic aphasia. *Neurocase, 4*(1), 71-87.

Marshall, J. C., Caplan, D., & Holmes, J. M. (1975). The measure of laterality. *Neuropsychologia, 13*(3), 315-321.

Mazoyer, B., Zago, L., Jobard, G., Crivello, F., Joliot, M., Perchey, G., ... & Tzourio-Mazoyer, N. (2014). Gaussian mixture modeling of hemispheric lateralization for language in a large sample of healthy individuals balanced for handedness. *PloS one, 9*(6), e101165.

Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia, 9*(1), 97-113.

Plaut, D. C., & Behrmann, M. (2011). Complementary neural representations for faces and words: A computational exploration. *Cognitive Neuropsychology, 28*(3-4), 251-275.

Pujol, J., Deus, J., Losilla, J. M., & Capdevila, A. (1999). Cerebral lateralization of language in normal left-handed people studied by functional MRI. *Neurology, 52*(5), 1038-1038.

Saffran, E. M., Bogyo, L. C., Schwartz, M. F., & Marin, O. S. M. (1980). Does deep dyslexia reflect right-hemisphere reading? In Coltheart, M., Patterson, K., & Marshall, J.C. (Eds.), *Deep Dyslexia* (pp. 381-406) London: Routledge and Kegan Paul.

Saffran, E. M., & Coslett, H. B. (1998). Implicit vs. letter-by-letter reading in pure alexia: A tale of two systems. *Cognitive Neuropsychology, 15*(1-2), 141-165.

Scrucca, L., Fop, M., Murphy, T. B., & Raftery, A. E. (2016). mclust 5: clustering, classification and density estimation using Gaussian finite mixture models. *The R journal, 8*(1), 289.

Waldie, K. E., & Mosley, J. L. (2000). Hemispheric specialization for reading. *Brain and Language, 75*(1), 108-122.

Willemin, J., Hausmann, M., Brysbaert, M., Dael, N., Chmetz, F., Fioravera, A., ... & Mohr, C. (2016). Stability of right visual field advantage in an international lateralized lexical decision task irrespective of participants' sex, handedness or bilingualism. *Laterality: Asymmetries of Body, Brain and Cognition, 21*(4-6), 502-524

Appendix

Figure A.4.1 | Histograms for raw and log-transformed RTs

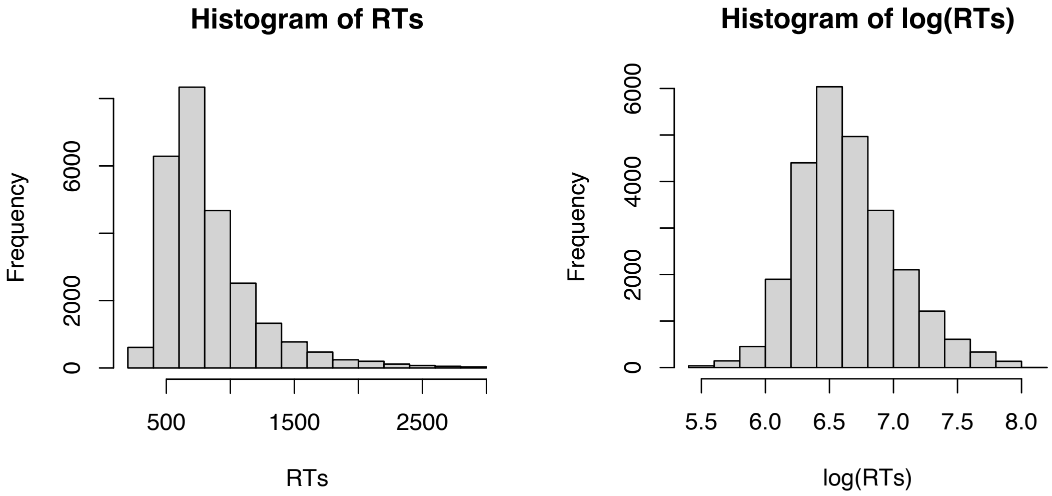

Table A.4.1 | Visual Field analyses: summary of the accuracy model.

Random Effects	***sd***
Subject	0.4693
Stimuli	0.6917

Fixed Effects	***Estimate***	***Standard Error***	***z***	***p value***	χ^2	***df***	***p(χ^2)***
Intercept	1.072	0.059	18.070	< 0.001			
Visual Field	-0.138	0.013	-10.926	< 0.001	134.000	1	< 0.001
Group	0.019	0.045	0.429	0.668	0.341	1	0.559
Lexicality	0.190	0.041	4.639	< 0.001	22.852	1	< 0.001
Responding Hand	-0.025	0.013	-1.950	0.051	3.943	1	0.047
Visual Field-by-Group	0.037	0.013	2.907	0.004	9.762	1	0.002
Visual Field-by-Lexicality	0.129	0.013	10.161	< 0.001	103.402	1	< 0.001
Visual Field-by-Responding Hand	-0.009	0.013	-0.687	0.492	0.480	1	0.489
Group-by-Lexicality	-0.057	0.013	-4.510	< 0.001	21.498	1	< 0.001

Group-by-Responding Hand	0.000	0.013	0.033	0.974	0.004	1	0.948
Visual Field-by-Group-by-Lexicality	-0.046	0.013	-3.647	< 0.001	13.298	1	< 0.001
Visual Field-by-Group-by-Responding Hand	0.011	0.013	0.854	0.393	0.729	1	0.393

Table A.4.2 | Visual Field analyses: summary of the Bonferroni-corrected pairwise comparisons for accuracy (LHs = left-handers; RHs = right-handers).

Post hoc (ACC)	***Value***	***df***	χ^2	***p***
(LVF Pseudoword LHs) - (LVF Pseudoword RHs)	0.477	1	0.863	1
(LVF Pseudoword LHs) - (LVF Word LHs)	0.606	1	21.784	< 0.001
(LVF Pseudoword LHs) - (LVF Word RHs)	0.679	1	35.564	< 0.001
(LVF Pseudoword LHs) - (RVF Pseudoword LHs)	0.491	1	0.538	1
(LVF Pseudoword LHs) - (RVF Pseudoword RHs)	0.476	1	0.887	1
(LVF Pseudoword LHs) - (RVF Word LHs)	0.516	1	0.459	1
(LVF Pseudoword LHs) - (RVF Word RHs)	0.512	1	0.152	1
(LVF Pseudoword RHs) - (LVF Word LHs)	0.628	1	17.238	< 0.001
(LVF Pseudoword RHs) - (LVF Word RHs)	0.699	1	83.656	< 0.001
(LVF Pseudoword RHs) - (RVF Pseudoword LHs)	0.514	1	0.302	1
(LVF Pseudoword RHs) - (RVF Pseudoword RHs)	0.500	1	0.001	1
(LVF Pseudoword RHs) - (RVF Word LHs)	0.539	1	1.516	1
(LVF Pseudoword RHs) - (RVF Word RHs)	0.536	1	2.330	1
(LVF Word LHs) - (LVF Word RHs)	0.579	1	10.571	0.032
(LVF Word LHs) - (RVF Pseudoword LHs)	0.385	1	25.707	< 0.001
(LVF Word LHs) - (RVF Pseudoword RHs)	0.372	1	17.329	< 0.001
(LVF Word LHs) - (RVF Word LHs)	0.409	1	55.064	< 0.001
(LVF Word LHs) - (RVF Word RHs)	0.406	1	14.868	0.003
(LVF Word RHs) - (RVF Pseudoword LHs)	0.313	1	39.192	< 0.001
(LVF Word RHs) - (RVF Pseudoword RHs)	0.301	1	83.984	< 0.001
(LVF Word RHs) - (RVF Word LHs)	0.335	1	48.427	< 0.001
(LVF Word RHs) - (RVF Word RHs)	0.332	1	206.362	< 0.001
(RVF Pseudoword LHs) - (RVF Pseudoword RHs)	0.486	1	0.317	1
(RVF Pseudoword LHs) - (RVF Word LHs)	0.525	1	1.173	1
(RVF Pseudoword LHs) - (RVF Word RHs)	0.522	1	0.474	1
(RVF Pseudoword RHs) - (RVF Word LHs)	0.539	1	1.542	1
(RVF Pseudoword RHs) - (RVF Word RHs)	0.536	1	2.374	1
(RVF Word LHs) - (RVF Word RHs)	0.497	1	0.019	1

Table A.4.3 | Visual Field analyses: summary of the RTs model.

Random Effects	***sd***							
Subject	0.2229							
Stimuli	0.07435							
Residual	0.27734							
Fixed Effects	***Estimate***	***Standard Error***	***df***	***t***	***p value***	***F***	***df***	***p(F)***
Intercept	6.628	0.021	127.6	317.906	< 0.001			
Visual Field	0.011	0.002	24902.7	6.443	< 0.001	41.514	1, 24902.7	< 0.001
Group	-0.030	0.020	117.6	-1.492	0.138	2.225	1, 117.6	0.138
Lexicality	0.065	0.005	311.4	14.375	< 0.001	206.633	1, 311.4	< 0.001
Responding Hand	0.009	0.002	24879.6	4.831	< 0.001	23.340	1, 24879.6	< 0.001
Visual Field-by-Group	-0.002	0.002	24876.2	-1.175	0.240	1.380	1, 24876.2	0.240
Visual Field-by-Lexicality	-0.016	0.002	24904.5	-9.032	< 0.001	81.570	1, 24904.5	< 0.001
Visual Field-by-Responding Hand	-0.001	0.002	24874.3	-0.450	0.653	0.203	1, 24874.3	0.653
Group-by-Lexicality	0.007	0.002	24820.7	3.865	< 0.001	14.941	1, 24820.7	< 0.001
Group-by-Responding Hand	0.003	0.002	24887.3	1.433	0.152	2.055	1, 24887.3	0.152
Visual Field-by-Group-by-Lexicality	0.004	0.002	24876.7	2.420	0.016	5.859	1, 24876.7	0.016
Visual Field-by-Group-by-Responding Hand	-0.001	0.002	24883.8	-0.648	0.517	0.420	1, 24883.8	0.517

Table A.4.4 | Visual Field analyses: summary of the Bonferroni-corrected pairwise comparisons for RTs (LHs = left-handers; RHs = right-handers).

Post hoc (RTs)	***Value***	***df***	χ^2	***p***
(LVF Pseudoword LHs) - (LVF Pseudoword RHs)	-0.043	1	1.087	1
(LVF Pseudoword LHs) - (LVF Word LHs)	0.121	1	120.667	< 0.001
(LVF Pseudoword LHs) - (LVF Word RHs)	0.033	1	0.621	1
(LVF Pseudoword LHs) - (RVF Pseudoword LHs)	-0.005	1	0.525	1
(LVF Pseudoword LHs) - (RVF Pseudoword RHs)	-0.057	1	1.888	1
(LVF Pseudoword LHs) - (RVF Word LHs)	0.163	1	224.801	< 0.001
(LVF Pseudoword LHs) - (RVF Word RHs)	0.101	1	5.709	0.473
(LVF Pseudoword RHs) - (LVF Word LHs)	0.164	1	15.071	0.003
(LVF Pseudoword RHs) - (LVF Word RHs)	0.076	1	47.264	< 0.001
(LVF Pseudoword RHs) - (RVF Pseudoword LHs)	0.038	1	0.849	1
(LVF Pseudoword RHs) - (RVF Pseudoword RHs)	-0.014	1	3.999	1
(LVF Pseudoword RHs) - (RVF Word LHs)	0.206	1	23.868	< 0.001
(LVF Pseudoword RHs) - (RVF Word RHs)	0.144	1	175.968	< 0.001
(LVF Word LHs) - (LVF Word RHs)	-0.087	1	4.455	0.974
(LVF Word LHs) - (RVF Pseudoword LHs)	-0.126	1	131.057	< 0.001

(LVF Word LHs) - (RVF Pseudoword RHs)	-0.177	1	17.698	< 0.001
(LVF Word LHs) - (RVF Word LHs)	0.042	1	34.585	< 0.001
(LVF Word LHs) - (RVF Word RHs)	-0.020	1	0.234	1
(LVF Word RHs) - (RVF Pseudoword LHs)	-0.038	1	0.822	1
(LVF Word RHs) - (RVF Pseudoword RHs)	-0.090	1	65.893	< 0.001
(LVF Word RHs) - (RVF Word LHs)	0.130	1	9.802	0.049
(LVF Word RHs) - (RVF Word RHs)	0.067	1	84.437	< 0.001
(RVF Pseudoword LHs) - (RVF Pseudoword RHs)	-0.052	1	1.570	1
(RVF Pseudoword LHs) - (RVF Word LHs)	0.168	1	239.001	< 0.001
(RVF Pseudoword LHs) - (RVF Word RHs)	0.106	1	6.290	0.340
(RVF Pseudoword RHs) - (RVF Word LHs)	0.220	1	27.150	< 0.001
(RVF Pseudoword RHs) - (RVF Word RHs)	0.157	1	211.300	< 0.001
(RVF Word LHs) - (RVF Word RHs)	-0.062	1	2.262	1

Table A.4.5 | N size analyses: summary of the accuracy model.

Random Effects	***sd***
Subject	0.470
Stimuli	0.678

Fixed Effects	***Estimate***	***Standard Error***	***z***	***p value***	χ^2	***df***	***p***(χ^2)
Intercept	1.011	0.062	16.322	< 0.001			
Group	0.020	0.045	0.452	0.652	0.353	1	0.553
Visual Field	-0.133	0.014	-9.573	< 0.001	133.724	1	< 0.001
Lexicality	0.205	0.045	4.599	< 0.001	23.942	1	< 0.001
N size	0.038	0.045	0.835	0.404	1.355	1	0.244
Group-by-Visual Field	0.034	0.014	2.478	0.013	9.702	1	0.002
Group-by-Lexicality	-0.053	0.014	-3.822	< 0.001	15.671	1	< 0.001
Visual Field-by-Lexicality	0.113	0.014	8.123	< 0.001	65.348	1	< 0.001
Group-by-Nsize	0.010	0.014	0.692	0.489	0.426	1	0.514
Visual Field-by-N size	-0.040	0.014	-2.795	0.005	9.075	1	0.003
Lexicality-by-N size	-0.141	0.045	-3.136	0.002	9.729	1	0.002
Group-by-Visual Field-by-Lexicality	-0.051	0.014	-3.642	< 0.001	13.115	1	< 0.001
Group-by-Visual Field-by-Nsize	-0.011	0.014	-0.804	0.421	0.555	1	0.456
Group-by-Lexicality-by-N size	0.002	0.014	0.117	0.907	0.009	1	0.923
Visual Field-by-Lexicality-by-N size	0.015	0.014	1.034	0.301	1.073	1	0.300
Group-by-Visual Field-by-Lexicality-by-N size	-0.006	0.014	-0.408	0.683	0.167	1	0.683

Table A.4.6 | N size analyses: summary of the RTs model.

Random Effects	***sd***
Subject	0.223
Stimuli	0.074
Residual	0.277

Fixed Effects	***Estimate***	***Standard Error***	***df***	***t***	***p value***	***F***	***df***	***p(F)***
Intercept	6.633	0.021	130.2	316.329	< 0.001			
Group	-0.031	0.020	118.1	-1.519	0.132	2.306	1, 118.1	0.132
Visual Field	0.012	0.002	24907.6	6.015	< 0.001	36.176	1, 24907.6	< 0.001
Lexicality	0.063	0.005	313.4	12.577	< 0.001	158.176	1, 313.4	< 0.001
N size	-0.005	0.005	308.7	-0.898	0.370	0.806	1, 308.7	0.370
Group-by-Visual Field	-0.001	0.002	24860.8	-0.652	0.514	0.426	1, 24860.8	0.514
Group-by-Lexicality	0.007	0.002	24814.3	3.442	< 0.001	11.845	1, 24814.3	0.001
Visual Field-by-Lexicality	-0.014	0.002	24909.1	-6.798	< 0.001	46.216	1, 24909.1	0.000
Group-by-Nsize	0.000	0.002	24803.7	-0.175	0.861	0.031	1, 24803.7	0.861
Visual Field-by-N size	0.005	0.002	24881.9	2.744	0.006	7.529	1, 24881.9	0.006
Lexicality-by-N size	0.011	0.005	308.8	2.220	0.027	4.928	1, 308.8	0.027
Group-by-Visual Field-by-Lexicality	0.004	0.002	24861.4	2.051	0.040	4.206	1, 24861.4	0.040
Group-by-Visual Field-by-Nsize	-0.001	0.002	24845.5	-0.337	0.736	0.114	1, 24845.5	0.736
Group-by-Lexicality-by-N size	-0.001	0.002	24803.6	-0.337	0.736	0.114	1, 24803.6	0.736
Visual Field-by-Lexicality-by-N size	0.001	0.002	24882.2	0.623	0.533	0.388	1, 24882.2	0.533
Group-by-Visual Field-by-Lexicality-by-N size	0.001	0.002	24846.0	0.713	0.476	0.508	1, 24846	0.476

Table A.4.7 | Length, Frequency and Imageability analyses: summary of the accuracy model.

Random Effects	***sd***
Subject	0.606
Stimuli	0.647

Fixed Effects	***Estimate***	***Standard Error***	***z***	***p value***	χ^2	***df***	***p***(χ^2)
Intercept	0.923	0.078	11.855	< 0.001			
Visual Field	-0.277	0.018	-15.339	< 0.001	245.120	1	< 0.001
Length	0.356	0.055	6.517	< 0.001	41.764	1	< 0.001
Frequency	0.276	0.055	5.058	< 0.001	25.974	1	< 0.001
Imageability	0.086	0.055	1.568	0.117	2.574	1	0.109
Group	0.081	0.058	1.390	0.165	2.399	1	0.121
Visual Field -by- Length	-0.006	0.018	-0.355	0.722	0.086	1	0.769
Visual Field -by- Frequency	0.006	0.018	0.315	0.753	0.236	1	0.627
Length -by- Frequency	0.010	0.055	0.180	0.857	0.022	1	0.883
Visual Field -by- Imageability	0.001	0.018	0.072	0.943	0.036	1	0.851

Length -by- Imageability	0.072	0.055	1.324	0.186	1.923	1	0.166
Frequency -by- Imageability	-0.104	0.055	-1.907	0.057	3.511	1	0.061
Visual Field -by- Group	0.086	0.018	4.753	< 0.001	23.564	1	< 0.001
Length -by- Group	0.005	0.018	0.256	0.798	0.069	1	0.793
Frequency -by- Group	-0.011	0.018	-0.598	0.550	0.195	1	0.659
Imageability -by- Group	-0.007	0.018	-0.379	0.705	0.202	1	0.654
Visual Field -by- Length -by- Frequency	-0.026	0.018	-1.435	0.151	2.043	1	0.153
Visual Field -by- Length -by- Imageability	0.029	0.018	1.620	0.105	2.677	1	0.102
Visual Field -by- Frequency -by- Imageability	0.017	0.018	0.951	0.342	0.922	1	0.337
Length -by- Frequency -by- Imageability	-0.027	0.055	-0.503	0.615	0.237	1	0.627
Visual Field -by- Length -by- Group	0.013	0.018	0.702	0.483	0.439	1	0.507
Visual Field -by- Frequency -by- Group	-0.007	0.018	-0.392	0.695	0.082	1	0.775
Length -by- Frequency -by- Group	-0.016	0.018	-0.922	0.357	0.853	1	0.356
Visual Field -by- Imageability -by- Group	0.008	0.018	0.427	0.670	0.264	1	0.607
Length -by- Imageability -by- Group	0.003	0.018	0.171	0.864	0.039	1	0.844
Frequency -by- Imageability -by- Group	0.016	0.018	0.874	0.382	0.953	1	0.329
Visual Field -by- Length -by- Frequency -by- Imageability	0.000	0.018	-0.011	0.991	< 0.001	1	0.998
Visual Field -by- Length -by- Frequency -by- Group	-0.006	0.018	-0.335	0.738	0.101	1	0.751
Visual Field -by- Length -by- Imageability -by- Group	-0.012	0.018	-0.650	0.516	0.332	1	0.564
Visual Field -by- Frequency -by- Imageability -by- Group	-0.001	0.018	-0.075	0.940	0.001	1	0.979
Length -by- Frequency -by- Imageability -by- Group	-0.020	0.018	-1.138	0.255	1.475	1	0.225
Visual Field -by- Length -by- Frequency -by- Imageability -by-Group	-0.017	0.018	-0.925	0.355	0.855	1	0.355

Table A.4.8 | Length, Frequency and Imageability analyses: summary of the Bonferroni-corrected pairwise comparisons for accuracy.

Post hoc (ACC)	***Value***	***df***	χ^2	***p***
(LVF Left-Handers) - (LVF Right-Handers)	0.584	1	7.876	0.030
(LVF Left-Handers) - (RVF Left-Handers)	0.406	1	57.851	< 0.001
(LVF Left-Handers) - (RVF Right-Handers)	0.405	1	10.070	0.009
(LVF Right-Handers) - (RVF Left-Handers)	0.327	1	35.299	< 0.001
(LVF Right-Handers) - (RVF Right-Handers)	0.326	1	212.674	< 0.001
(RVF Left-Handers) - (RVF Right-Handers)	0.499	1	0.001	1

Table A.4.9 | Length, Frequency and Imageability analyses: summary of the RTs model.

Random Effects	***sd***
Subject	0.203
Stimuli	0.073
Residual	0.270

Fixed Effects	***Estimate***	***Standard Error***	***df***	***t***	***p value***	***F***	***df***	***p(F)***
Intercept	6.570	0.020	139.5	335.548	< 0.001			
Visual Field	0.030	0.003	11756.3	11.673	< 0.001	136.264	1, 11756.3	< 0.001
Length	-0.038	0.006	150.8	-5.949	< 0.001	35.392	1, 150.8	< 0.001
Frequency	-0.046	0.006	150.6	-7.211	< 0.001	52.003	1, 150.6	< 0.001
Imageability	-0.016	0.006	150.6	-2.577	0.011	6.643	1, 150.6	0.011
Group	-0.039	0.019	117.1	-2.100	0.038	4.412	1, 117.1	0.038
Visual Field -by- Length	-0.002	0.003	11753.2	-0.891	0.373	0.793	1, 11753.2	0.373
Visual Field -by- Frequency	0.007	0.003	11751.7	2.588	0.010	6.696	1, 11751.7	0.010
Length -by- Frequency	-0.010	0.006	150.6	-1.508	0.134	2.273	1, 150.6	0.134
Visual Field -by- Imageability	-0.003	0.003	11752.2	-1.144	0.253	1.308	1, 11752.2	0.253
Length -by- Imageability	-0.005	0.006	150.5	-0.786	0.433	0.618	1, 150.5	0.433
Frequency -by- Imageability	0.013	0.006	150.6	2.108	0.037	4.445	1, 150.6	0.037
Visual Field -by- Group	-0.008	0.003	11738.9	-3.196	0.001	10.213	1, 11738.9	0.001
Length -by- Group	0.001	0.003	11704.9	0.578	0.564	0.334	1, 11704.9	0.564
Frequency -by- Group	0.004	0.003	11703.5	1.570	0.116	2.466	1, 11703.5	0.116
Imageability -by- Group	-0.003	0.003	11702.3	-1.074	0.283	1.153	1, 11702.3	0.283
Visual Field -by- Length -by- Frequency	-0.003	0.003	11751.8	-1.198	0.231	1.436	1, 11751.8	0.231
Visual Field -by- Length -by- Imageability	-0.004	0.003	11752.7	-1.560	0.119	2.432	1, 11752.7	0.119
Visual Field -by- Frequency -by- Imageability	0.001	0.003	11752.9	0.353	0.724	0.125	1, 11752.9	0.724
Length -by- Frequency -by- Imageability	0.002	0.006	150.6	0.321	0.748	0.103	1, 150.6	0.748
Visual Field -by- Length -by- Group	-0.002	0.003	11735.2	-0.675	0.500	0.456	1, 11735.2	0.499
Visual Field -by- Frequency -by- Group	-0.001	0.003	11734.4	-0.563	0.573	0.317	1, 11734.4	0.573
Length -by- Frequency -by- Group	-0.001	0.003	11702.6	-0.561	0.575	0.315	1, 11702.6	0.575
Visual Field -by- Imageability -by- Group	0.000	0.003	11735.0	-0.035	0.972	0.001	1, 11735	0.972
Length -by- Imageability -by- Group	0.000	0.003	11702.1	-0.068	0.946	0.005	1, 11702.1	0.946
Frequency -by- Imageability -by- Group	0.000	0.003	11703.0	-0.054	0.957	0.003	1, 11703	0.957
Visual Field -by- Length -by- Frequency -by- Imageability	0.001	0.003	11751.9	0.375	0.707	0.141	1, 11751.9	0.707
Visual Field -by- Length -by- Frequency -by- Group	0.002	0.003	11734.7	0.698	0.485	0.487	1, 11734.7	0.485
Visual Field -by- Length -by- Imageability -by- Group	0.001	0.003	11735.0	0.290	0.772	0.084	1, 11735	0.772
Visual Field -by- Frequency -by- Imageability -by- Group	0.004	0.003	11735.1	1.714	0.087	2.938	1, 11735.1	0.087
Length -by- Frequency -by- Imageability -by- Group	-0.002	0.003	11703.1	-0.709	0.478	0.503	1, 11703.1	0.478
Visual Field -by- Length -by- Frequency -by- Imageability -by- Group	-0.003	0.003	11734.5	-1.099	0.272	1.208	1, 11734.5	0.272

Table A.4.10 | Length, Frequency and Imageability analyses: summary of the Bonferroni-corrected pairwise comparisons for RTs (Visual Field-by-Group interaction).

Post hoc (RTs)	***Value***	***df***	***χ^2***	***p***
(LVF Left-Handers) - (LVF Right-Handers)	-0.094	1	6.184	0.077
(LVF Left-Handers) - (RVF Left-Handers)	0.044	1	39.635	< 0.001
(LVF Left-Handers) - (RVF Right-Handers)	-0.018	1	0.216	1
(LVF Right-Handers) - (RVF Left-Handers)	0.138	1	13.357	0.002
(LVF Right-Handers) - (RVF Right-Handers)	0.076	1	113.530	< 0.001
(RVF Left-Handers) - (RVF Right-Handers)	-0.062	1	2.668	0.614

Table A.4.11 | Length, Frequency and Imageability analyses: summary of the Bonferroni-corrected pairwise comparisons for RTs (Frequency-by-Imageability interaction).

Post hoc (RTs)	***Value***	***df***	***χ^2***	***p***
(High Frequency High Imageability) – (High Frequency Low Imageability)	0.001	1	0.002	1
(High Frequency High Imageability) – (Low Frequency High Imageability)	-0.062	1	10.214	0.008
(High Frequency High Imageability) – (Low Frequency Low Imageability)	-0.121	1	41.225	< 0.001
(High Frequency Low Imageability) – (Low Frequency High Imageability)	-0.063	1	9.749	0.011
(High Frequency Low Imageability) – (Low Frequency Low Imageability)	-0.121	1	38.684	< 0.001
(Low Frequency High Imageability) – (Low Frequency Low Imageability)	-0.058	1	8.916	0.017

Table A.4.12 | Length, Frequency and Imageability analyses: summary of the Bonferroni-corrected pairwise comparisons for RTs (Visual Field-by-Frequency interaction).

Post hoc (RTs)	***Value***	***df***	***χ^2***	***p***
(LVF High Frequency) - (LVF Low Frequency)	-0.081	1	28.154	< 0.001
(LVF High Frequency) - (RVF High Frequency)	0.071	1	109.981	< 0.001
(LVF High Frequency) - (RVF Low Frequency)	-0.035	1	5.362	0.124
(LVF Low Frequency) - (RVF High Frequency)	0.152	1	101.017	< 0.001
(LVF Low Frequency) - (RVF Low Frequency)	0.046	1	38.823	< 0.001
(RVF High Frequency) - (RVF Low Frequency)	-0.106	1	50.460	< 0.001

Chapter 5

A computational analysis of the two orthographic lexicons.

Data presented in Chapters 2, 3 and 4 provided evidence in favor of a *relative* account of LH dominance over the RH for reading, according to the idea of "two orthographic lexicons" in the brain, with the RH being able to process accurately only highly frequent words. In the computational modelling study reported in this chapter, I simulated consolidation of lexical orthographic knowledge in the two hemispheres by means of the Naïve Discriminative Learning approach, assuming that learning is less efficient in the RH than in the LH. In particular, random noise attenuating the relationship between orthographic sub-lexical units (letters, bigrams) and lexical orthographic units (words) was introduced to simulate lexical consolidation in the RH. Simulated RTs from the "noiseless" learning model (mimicking lexical consolidation in the LH) and a noisy learning model (mimicking lexical consolidation in the RH) were then compared with human data, to explore the extent to which "noisy" learning in the RH can account for the effects of Visual Field, Frequency and the Visual Field-by-Frequency interaction (i.e., compression of the Frequency effect in the RH) described in human data.

Introduction

The experimental studies reported so far were conducted with the aim of exploring whether the nature of the ubiquitous LH-over-the-RH dominance for reading is *absolute* or *relative*, i.e., whether the RH is completely word-blind, or rather is more limited than the LH in its capability of processing orthographic information. According to the first perspective, one single orthographic lexicon would exist in the brain, and it would be located in the LH (Ellis, Young & Anderson, 1988; Ellis, 2004). According to the second perspective, there would be two orthographic lexicons in the brain -one located in each cerebral hemisphere (Coltheart, 1980; 2000; Saffran et al., 1980; Saffran & Coslett, 1998; Luzzatti, Rumiati & Ghirardi, 1998; Luzzatti, 2003). In the previous experimental studies, I have provided evidence that implicit reading phenomena can occur (at least for high-frequency and highly imageable words) even in case of a brain insult impairing the LH visual word form system and interrupting its afferent and efferent connections with the rest of the brain. I also provided evidence that the visual field effect typically described in lateralized reading in healthy subjects is most likely due to a different sensitivity of the two cerebral hemispheres to lexical-semantic factors, as testified by a compression of the word frequency effect in the RH that cannot be simply explained by a "floor" effect in performance.

This set of evidence is hardly compatible with a "single orthographic lexicon" account. Indeed, according to this framework, reading is impossible if the LH visual word form system is lesioned and isolated from the rest of the brain. In addition, according to this view, pre-lexical (rather than lexical/semantic) effects should explain the visual field effect in lateralized reading for healthy subjects. Data presented in the previous chapters support, instead, the existence of two orthographic lexicons in the brain and a *relative* view of LH dominance for reading.

A crucial feature of this account is the assumption that the RH orthographic lexicon is limited with respect to that of the LH, and in particular it would be limited to high-frequency and /or highly imageable words (Coltheart 1980, 2000; Saffran et al., 1980; Saffran & Coslett, 1998; Luzzatti, Rumiati & Ghirardi, 1998; Luzzatti, 2003). However, the studies advocating the existence of a poorer/weaker RH lexicon compared to the LH one do not make clear predictions of how the lexical "limitations" of the RH lexicon would come about.

In particular, for what concerns word frequency (no reliable effect of imageability was detected in studies presented in Chapters 3 and 4), it is implausible that the brain contains a "gating" mechanism that prevents word below a certain frequency threshold to be encoded in (and subsequently retrieved from) the orthographic lexicon of the RH. Indeed, for identifying frequent words while blocking access to infrequent words, a "lexicon before the lexicon" would be required. A more plausible -and less circular- explanation of this phenomenon involves the possibility that all words are encoded in a weaker way in the RH than in the LH. This view is in line with data presented in Chapters 3 and 4 of this work, indicating a compression of the word frequency effect in the LVF and suggesting poorer discriminability of lexical representations in the RH compared to the LH. In other words, the consolidation process of lexical orthographic representations could be more difficult and "noisier" in the RH than in the LH.

In this study, I adopted a computational approach to simulate the consolidation of orthographic knowledge (operationalized as the process of learning the association between sub-lexical cues and words) in the two cerebral hemispheres, assuming that this learning process could occur in a less efficient way in the RH than in the LH. To do so, I employed the Naïve Discriminative Reader model (Baayen et al., 2011; see also Milin et al., 2017). This computational framework was developed to simulate word processing through a two-layer symbolic network in which input units were letter pairs, and output units were lexical-semantic units (*lexomes*) represented by whole words. This method proved to simulate effectively word recognition, and in particular many properties (including a word frequency effect) of reaction times data obtained in a real lexical decision task (Baayen et al., 2011). A peculiarity of this method is the fact that associations between input and output units develop through discriminative learning[1]. This implies that the association weights of a cue to a given outcome depend not only on their frequency of co-occurrence, but also on how often that given cue co-occurs with all other outcomes (Milin et al., 2017). In other words, learning (and subsequent lexical retrieval) is considered to be effective when there is a consistent and distinctive relation between an orthographic cue and an outcome. This feature of the Naïve Discriminative Reader model makes it particularly feasible to simulate the consolidation of orthographic knowledge in the two cerebral hemispheres. Indeed, the observation of a compression of the frequency effect in

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[1] This model also assumes the independence for the association strengths to the different outputs, in line with the independence assumption in naïve Bayes classifiers, hence the name "Naïve Discriminative Reader" (Baayen et al., 2011).

the LVF/RH compared to the RVF/LH (Chapters 3 and 4) suggests that orthographic representations could be less discriminable in the lexicon of the RH than in the LH.

Naïve Discriminative Learning

Naïve Discriminative Learning involves the estimation of the stable state (Danks, 2003) of a learning process simulated according to a model of classical conditioning, i.e.: the Rescorla-Wagner model of learning (Rescorla & Wagner, 1972). Accordingly, the association between a cue and an outcome develops through different trials and follows this general law (V_i^{t+1} being the strength -or *weight*- of the association between the cue C_i and outcome O_j at the current trial or time-point t+1):

$$V_{ij}^{t+1} = V_{ij}^{t} + \Delta V_{ij}^{t}$$

In this formula, V_i^t represents the strength of the association between the cue and the outcome of the previous trial or time-point t, while ΔV_i^t represents the change in the association strength computed in the previous trial or time-point as follows (Baayen et al., 2011):

$$\Delta V_i^t = \begin{cases} 0 & if\ ABSENT\left(C_j, t\right) \\ \alpha_i \beta_1 \left(\lambda - \Sigma_{PRESENT(C_j,t)} V_j\right) & if\ ABSENT\left(C_j, t\right) \quad \& \quad PRESENT(O, t) \\ \alpha_i \beta_2 \left(0 - \Sigma_{PRESENT(C_j,t)} V_j\right) & if\ ABSENT\left(C_j, t\right) \quad \& \quad ABSENT(O, t) \end{cases}$$

The parameter α is the salience of a cue, whereas the parameter β represents the intensity (or "significance") of the outcome and the parameter λ represents the "maximum associability" between cues and outcomes. The parameters are set so that $\lambda = 1$, all αs equal and $\beta_1 = \beta_2$ (Baayen et al., 2011). If in a given learning event t a cue is absent among the list of active cues C_j, the change in its association strength with the outcome is zero. If that cue is present and the outcome is present as well, the change in the association strength is the product of α and $\beta_1$multiplied by the overall amount of "associability" between cue and outcome minus the sum of the association weights between the other cues active in that learning event and the outcome. If the cue is present but the outcome is not, the change in the association strength is the product of α and $\beta_1$multiplied zero minus the sum of the association weights between the other cues active in that learning event and the outcome. In other words, in this case, the association weight is negative.

In the original formulation of the Naïve Discriminative Reader model, input units were letter pairs, and output units were lexical-semantic units (Baayen et al., 2011, see also Milin et al., 2017). In this study, the same two-layer network (see Figure 5.1) was adopted to simulate the association between sub-lexical orthographic cues (letters and bigrams) and lexical orthographic outcomes (words).

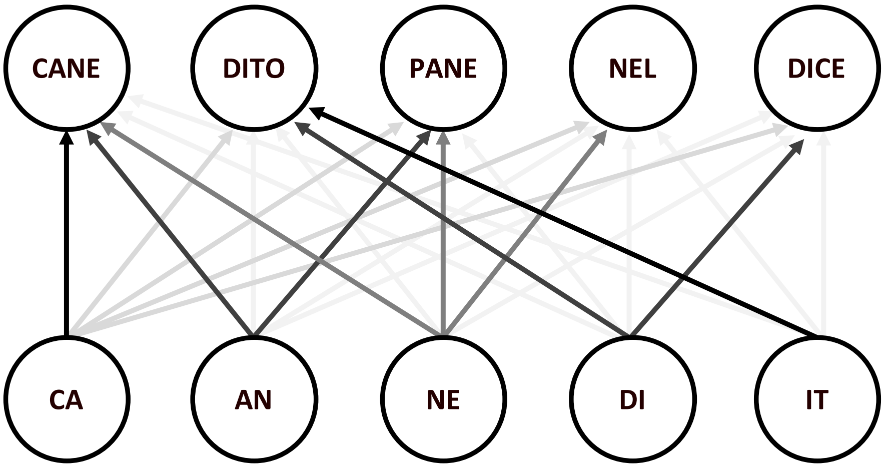

Figure 5.1 | Layout of the two-layer network adopted for the present study. The top row indicates output units; the bottom row indicates input units. Adapted from Milin et al. (2017).

This was done in a context of efficient, "noiseless" learning, to simulate consolidation of lexical orthographic representations in the LH. In order to simulate inefficient learning in the RH, a variable amount of noise was introduced in the weight matrix connecting cues and outcomes. These models were constructed with the ultimate aim of replicating the main effects of Visual Field and Frequency, as well as to simulate the compression of the frequency effect in the LVF/RH relative to the RVF/LH described in Chapters 3 and 4.

Materials and methods

Training

Word stimuli were taken from the Phonitalia corpus, containing 120,000 word entries (Goslin, Galluzzi & Romani, 2014)[2]. Given that word frequencies reported in the Phonitalia are derived from the same database used for the studies presented in Chapters 2, 3 and 4 of this thesis (the COLFIS database, Bertinetto et al., 2005), I wanted to exclude results to be somewhat circular and dependent on the specific corpus used. For this reason, word frequencies from the subtlex-it corpus (Crepaldi et al., 2013) were adopted for this study.

For each word (*outcome*), a set of cues was defined through the *orthoCoding* function of the R package *ndl* (Arppe et al., 2014), after setting `grams = c(1,2)`, in order to obtain cues constituted by single letters and bigrams. Therefore, for the outcome "casa", the set of cues was: c_a_s_a_#c_ca_as_sa_a#.

In order to train the two-layer (grapheme-to-word) network in the context of "noiseless" efficient learning in the LH, the *estimateWeights* function of the *ndl* package was used. This function requires a set of outcomes (in this case words), a set of corresponding cues (in this case letters and bigrams) and a vector of frequencies that define the frequency of each outcome (in this case corresponding to word frequencies according to the subtlex-it corpus). The output of this function is a matrix of weights for cue-outcome pairs representing the equilibrium state of learning of the Rescorla-Wagner model (Danks, 2003).

Noise

In order to simulate learning in the RH, different ranges of random uniform noise were introduced in a matrix of cue-outcome weights identical to that obtained for the LH lexicon. In particular, each cue-outcome weight was multiplied by a number ranging from 0 to 1, acting as a "scaling factor". The closer this number to 1, the lower the noise and the attenuation of the cue-outcome weight. I adopted a scaling factor instead of adding or subtracting a random number to the weight in order to avoid that noise could produce (by chance) paradoxically

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[2] The choice of using a corpus containing phonological representations of words was guided by the idea of leaving open the possibility of future developments of this computational model involving phonological components.

bigger weights in absolute value (i.e., by adding a positive random number to a positive weight or adding a negative number to a negative weight) than the noiseless condition, or even change the sign of the weights.

Noise range was treated as a free parameter, and 20 possible levels were considered. For each of them (see Table 5.1), a matrix with the same dimensions of that of the cue-outcome weights was produced, containing random scaling factors with a uniform distribution between a maximum and a minimum.

Table 5.1 | Noise ranges for the simulation of learning in the RH orthographic lexicon.

Model	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***
Range of scaling factors	0.96-1.00	0.91-0.95	0.86-0.90	0.81-0.85	0.76-0.80	0.71-0.75	0.66-0.70	0.61-0.65	0.56-0.60	0.51-0.55
Model	***11***	***12***	***13***	***14***	***15***	***16***	***17***	***18***	***19***	***20***
Range of scaling factors	0.46-0.50	0.41-0.45	0.36-0.40	0.31-0.35	0.26-0.30	0.21-0.25	0.16-0.20	0.11-0.15	0.06-0.10	0.01-0.05

Each weight in the cue-outcome weights matrix was multiplied by its corresponding scaling factor in the scaling factor matrix. Given that results were non-deterministic, for each noise range the position of the scaling factors in the scaling factor matrix was permuted 60 times. Hence, for each noise range, 60 noise-attenuated weights matrices were obtained (1200 simulations in total).

Testing

The word stimuli adopted in the behavioral experiments presented in Chapters 3 and 4 were used as targets. For each target, activations of lexical representations were encoded in a vector as the sum of the weights associated to the letters and bigrams that were present in the target word (as in Baayen et al., 2011). For instance, for the fictitious target “ora” (= “now”/ “hour”), the activation vector would be obtained by summing, for each target column, the rows corresponding to the cues “o”, “r”, “a”, “#o”, “or”, “ra”, “a#”. Each dimension in the resulting vector would indicate the degree of activation of each possible outcome in the lexicon given the sub-lexical information present in the target.

For each matrix of cue-outcome weights (noiseless for the LH simulation and noisy for the RH simulations), the *estimateActivations* function of the *ndl* package was used to extract, for each target, the activation vector. As in Baayen et al., 2011, for each activation vector obtained from each target, the probability of correctly identifying the target among its 20 most active competitors (Pid) was calculated as the ratio between the activation of the target and the sum of the activations of the target and its 20 most activated competitors, and simulated RTs were computed as *log(1/Pid)*. This was done for the noiseless model of the LH and for each of the 60(permutations)*20(noise ranges) models simulating the RH lexicon. For each noise range, results were averaged between different permutations. Therefore, for each target, a Pid value and a simulated RT were obtained for the simulation of LH reading. For RH simulations 20 Pid and 20 simulated RTs were obtained, one for each noise range.

As a first sanity check, in order to evaluate the face-validity of the simulations, simulated RTs were correlated with real RTs of right-handed subjects (Chapters 3 and 4) for stimuli projected in the RVF/LH, averaged by item. For all simulations, the frequency effect was computed as the difference between simulated RTs for low frequency and high-frequency items.

A mixed ANOVA with Visual Field/Hemisphere as a within-items factor and Frequency as a between-items factor was run on human RTs (after logarithmic transformation). In order to explore the extent to which simulations were effective in recreating the effects observed for human data, simulated RTs from the 20 noisy models entered, together with simulated RTs obtained from noiseless learning in the LH, in 20 mixed ANOVAs with Visual Field/Hemisphere as a within-items factor and Frequency as a between-items factor. Simulated RTs of the noisy model providing the best fit with human data were correlated with real RTs for stimuli projected in the LVF/RH. P values from post-hoc pairwise comparisons were corrected according to the Bonferroni method. Comparisons between human data and simulations were run on word targets in which simulated data were available. These analyses were run on the Jamovi software.

Results

Data from three low-frequency targets were not available, due to the absence of these stimuli in the training set (DOGE, GARBO, GARZA). As far as the "noiseless" LH model is concerned, a significant positive rank correlation with human data for stimuli projected to the RVF/LH was observed (Spearman's *rho*= 0.509, $p < 0.001$, Figure 5.2).

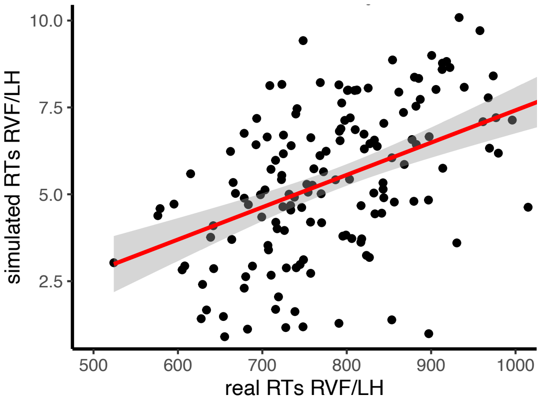

Figure 5.2 | Correlation between real (right-handed subjects) RTs in the RVF and simulated RTs in the "noiseless" model of LH lexicon.

In line with what described in Chapter 3, Real RTs averaged by item yielded a main effect of Visual Field ($F(1,155)= 29.94$, $p < 0.001$) indicating longer RTs for stimuli projected to the LVF/RH than for stimuli projected to the RVF/LH, a main effect of Frequency ($F(1,155)= 35.9$, $p < 0.001$) indicating faster responses for high-frequency than low-frequency words, and a Visual Field-by-Frequency interaction ($F(1,155)= 5.61$, $p = 0.019$). Post-hoc pairwise comparisons revealed that low-frequency words processed in the LVF/RH were associated with longer RTs than high-frequency words processed in the LVF/RH ($t(155)= -3.23$, $p = 0.004$) and low-frequency words were processed slower in the LVF/RH than in the RVF/LH, although significance did not survive correction for multiple comparisons ($t(76)= 2.220$, $p = 0.060$). As expected, from a descriptive point of view, the magnitude of the average Frequency effect turned out to be bigger in the RVF/LH (103.320ms) than in the LVF/RH (61.504ms).

The models simulating noisy learning in the RH revealed that, as noise increased (i.e.: the closer the range of scaling factors to 0), RTs increased exponentially (Figure 5.3a) and the size of the frequency effect decreased exponentially (Figure 5.3b).

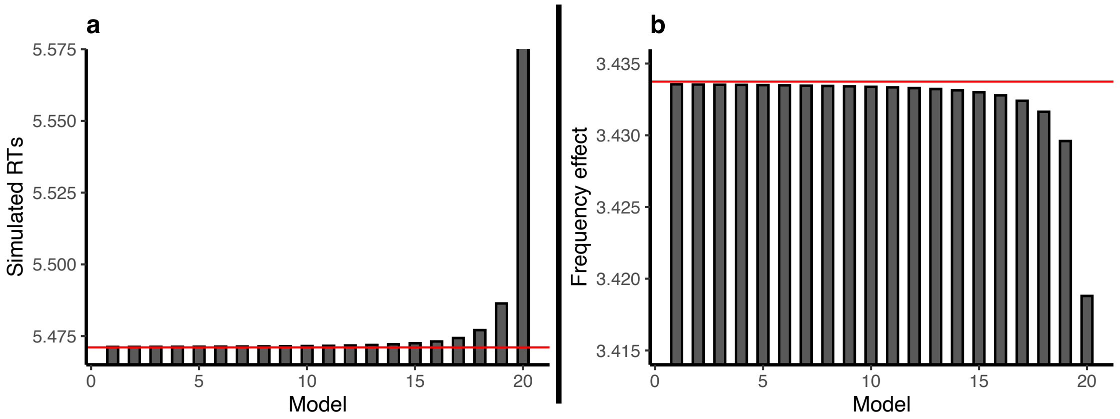

Figure 5.3 | Overview of simulated RTs in the RH models: (a) Mean RTs in the different RH models. The red line indicates the mean RTs of the noiseless LH simulation; (b) Frequency effect in the different RH models. The red line indicates the frequency effect of the noiseless LH simulation.

Among the 20 noisy models simulating orthographic consolidation in the RH (Figure 5.4), only model 20 (that with scaling factors comprised between 0.01 and 0.05) was able to replicate human data yielding the significant main effects of Visual Field/Hemisphere (*F*(1,155) = 771.290, *p* < 0.001) indicating longer RTs of the RH model than for the LH model, and Frequency (*F*(1,155) = 240, *p* < 0.001) indicating longer RTs for low-frequency than high-frequency words, as well as a substantial trend towards significance for the Visual Field-by-Frequency interaction (*F*(1,155) = 3.890, *p* = 0.050).

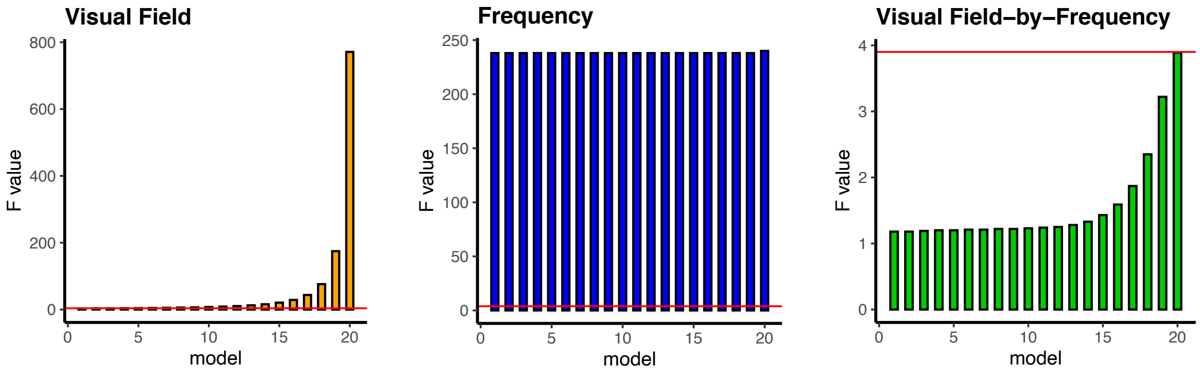

Figure 5.4 | F values for the effects of Visual Field/Hemisphere, Frequency, and the Visual Field-by-Frequency interaction in 20 the mixed ANOVAs on simulated RTs for the noiseless model simulating the LH and the 20 noisy models simulating the RH. The red line indicates the critical F value (3.902) for 1 and 155 degrees of freedom and alpha threshold set to .05.

Post-hoc pairwise comparisons revealed that low-frequency words processed in the LVF/RH were associated with longer simulated RTs than high-frequency words processed in the LVF/RH ($t(155)= -15.515$, $p < 0.001$) and that low-frequency words were processed slower in the LVF/RH than in the RVF/LH ($t(76)= 19.888$, $p < 0.001$). In addition, a one-sample t-test revealed that across the 60 simulations conducted for model 20, the magnitude of the frequency effect was significantly smaller than that observed for the "noiseless" LH simulation ($t(59)= 2.622$, $p = 0.011$).

Simulated RTs for model 20 (with scaling factors comprised between 0.01 and 0.05) also turned out to be significantly positively correlated with human RTs for stimuli projected in the LVF/RH (Spearman's *rho*= 0.275, $p < 0.001$, Figure 5.5).

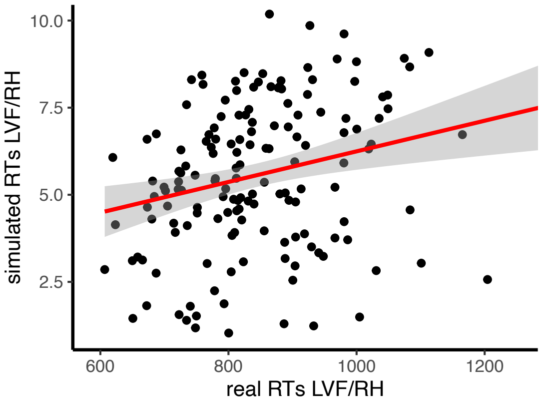

Figure 5.5 | Correlation between real (right-handed subjects) RTs in the LVF and simulated RTs in the "noisy" model of RH lexicon with scaling factors comprised between 0.01 and 0.05.

Descriptive statistics for human and simulated data are reported in table 5.2.

Table 5.2 | Descriptive statistics for real and simulated data. Simulated data refer to the "noiseless" model for the LH and to the noisy model with scaling factors comprised between 0.01 and 0.05 for the RH.

		Real data		***Simulated data***	
		High Frequency	Low Frequency	High Frequency	Low Frequency
Left Visual Field/RH	mean	817.463	878.967	3.900	7.318
	sd	116.808	128.641	1.447	1.335
Right Visual Field/LH	mean	740.025	843.345	3.787	7.22
	sd	94.337	102.670	1.424	1.333

In Table 5.3 details of the ANOVAs for real data and simulated data (noiseless learning simulating the LH and model 20 to simulate noisy learning in the RH) are reported.

Table 5.3 | Mixed ANOVA (Visual Field -by- Frequency) for human data (upper part) and simulated data (lower part).

Repeated Measures ANOVA

Human data

Within Subjects Effects	**Sum of Squares**	**df**	**Mean Square**	**F**	**p**
Visual Field	0.363	1	0.363	29.94	< .001
Visual Field -by- Frequency	0.068	1	0.068	5.610	0.019
Residual	1.881	155	0.012		

Note. Type 3 Sums of Squares

Between Subjects Effects	**Sum of Squares**	**df**	**Mean Square**	**F**	**p**
Frequency	0.811	1	0.811	35.900	< .001
Residual	3.499	155	0.023		

Note. Type 3 Sums of Squares

Repeated Measures ANOVA

Simulated data

Within Subjects Effects	**Sum of Squares**	**df**	**Mean Square**	**F**	**p**
Visual Field	0.86904	1	0.86904	771.290	< .001
Visual Field ✻ Frequency	0.00438	1	0.00438	3.890	0.050
Residual	0.17465	155	0.00113		

Note. Type 3 Sums of Squares

Between Subjects Effects	**Sum of Squares**	**df**	**Mean Square**	**F**	**p**
Frequency	921	1	921.200	240	< .001
Residual	596	155	3.850		

Note. Type 3 Sums of Squares

Discussion

In this computational modelling study, the stable state (Danks, 2003) of consolidation of lexical orthographic knowledge was simulated through Naïve Discriminative Learning. This approach has been adopted by Baayen and colleagues (2011) to simulate word recognition, through a two-layer network in which input units were letter bigrams, and output units were lexical-semantic units (see also Milin et al., 2017). In the context of the present investigation, the same two-layer structure was used to simulate lexical orthographic consolidation by modelling the relationship between orthographic cues (letters, bigrams) and orthographic lexical outcomes (words) in the two cerebral hemispheres. The goal of this study was to replicate the effects of Visual Field and Frequency observed in human data (described in Chapters 3 and 4) during lateralized lexical decision, as well as to simulate the compression of the frequency effect in the LVF/RH relative to the RVF/LH. To do so, I simulated efficient, "noiseless" consolidation of lexical orthographic representations in the LH, and inefficient, "noisy" learning in the RH. Simulated lexical decision RTs (computed as in Baayen et al., 2011) for the LH "noiseless" model were significantly positively correlated with human RTs of right-handed subjects for stimuli projected in the RVF/LH, supporting the face-validity of the adopted simulation method.

The progressive addition of noise (by attenuating cue-outcome association weights through their multiplication by scaling factors comprised from 0 -maximum attenuation- to 1 -minimum attenuation-) had a positive exponential effect on simulated RTs (i.e., longer RTs), and a negative exponential effect on the simulated frequency effect (i.e.: greater compression of the frequency effect).

Simulated RTs for the RH "noisy" model of RH lexicon with scaling factors comprised between 0.01 and 0.05 -combined with the noiseless model simulating orthographic consolidation in the LH- managed to replicate the main effects of Visual Field (i.e. longer RTs for stimuli projected to the LVF/RH than to the RVF/LH) and Frequency (i.e. longer RTs for low-frequency than for high-frequency words) described in human data, as well as the Visual Field-by-Frequency interaction, although for simulated data this interaction barely missed formal significance (p= 0.050). Also, simulated RTs of the noisy model with scaling factors comprised between 0.01 and 0.05 were positively correlated with human RTs for stimuli projected to the LVF/RH.

Taken together, these results suggest that "noisy learning" in the RH orthographic lexicon could represent a plausible mechanism underlying both the visual field effect and the compression of the frequency effect in the RH described for human data in Chapters 3 and 4, provided that a considerable amount of noise is introduced to attenuate the relationship between orthographic cues and lexical orthographic representations in the RH. Indeed, RH models 1 to 19 proved to be ineffective in simulating the Visual Field-by-Frequency interaction described in human data. Moving beyond the pure attempt of explaining behavioral data described in previous chapters, these findings could have implications for the interpretation of how the LH dominance for reading comes about. The present computational model was run assuming that orthographic information could be -in principle- stored in both hemispheres, according to the idea (supported by previous neuropsychological data and evidence presented in Chapters 2,3, and 4 of this thesis) of the existence of "two orthographic lexicons" in the brain (Coltheart, 1980; 2000; Saffran et al., 1980; Saffran & Coslett, 1998, Luzzatti, Rumiati & Ghirardi, 1998; Luzzatti, 2003). However, in running these simulations, I also assumed that consolidation of lexical knowledge could be substantially less efficient in the RH than in the LH. Basing on results on simulated data, I suggest these two basic features of distribution and consolidation of lexical knowledge across hemispheres could contribute in giving rise, on the one hand, to the ubiquitous LH advantage over the RH for reading and to the visual field effect commonly observed in lateralized reading tasks (e.g.: Leiber, 1976; Babkoff & Ben-Uriah, 1983; Chiarello, Senehi & Soulier, 1986; Hernandez, Nieto & Barroso, 1992; Chiarello et al., 2005; Willemin et al., 2016; De Clercq & Brysbaert, 2020). Therefore, the present study provides a possible computational definition of how a *relative* dominance of the LH could come about: through the different efficiency with which orthographic representations are consolidated in the input lexical stores of the two cerebral hemispheres.

On the other hand, the existence of two orthographic lexicons with poor consolidation of lexical orthographic knowledge in the RH could also explain poor performance for low-frequency words processed in the RH, as suggested by neuropsychological literature (Saffran et al., 1980; Saffran & Coslett, 1998, Luzzatti, Rumiati & Ghirardi, 1998; Luzzatti, 2003). Remarkably, this study suggests that the RH orthographic lexicon is "poorer" than that of the LH, but instead of advocating a lack of lexical orthographic representations for low-frequency words in the RH (as apparently suggested by Saffran et al., 1980 and Saffran & Coslett, 1998, see also Coltheart, 1980 for a similar view on imageability), it rather suggests that orthographic representations are weaker in the RH the in the LH due to inefficient learning, and low-frequency words are consequently particularly difficult to activate (i.e.: giving rise to the longest RTs).

Of course, this study leaves open a series of questions that will need to be addressed by future studies. The first and most obvious one concerns the mechanism underlying noisy learning in the RH. One possible reason underlying such noise could be inter-hemispheric inhibition exerted on the RH by the LH (Landis et al., 1983; see also Cook, 1984 and Van der Knaap & Van der Ham, 2011) to optimize reading development.

In previous studies, it was proposed that learning to read implies the progressive binding of orthographic information with previously existing lexical phonological representations (see Ziegler, Perry & Zorzi, 2014) that are typically already left-lateralized before the acquisition of reading (see Sowman et al., 2014). This binding mechanism is highly efficient in the LH due to short intra-hemispheric connections (Plaut & Behrmann, 2011; Behrmann & Plaut, 2015). Conversely, in the RH such binding is undoubtedly weaker because, on the one hand, intra-hemispheric connections between orthographic and phonological lexicons are less beneficial in the RH than in the LH since fewer lexical phonological representations are localized in the RH than in the LH. On the other hand, inter-hemispheric connections from the RH orthographic lexicon to the LH phonological lexicon are highly inefficient, due to the need for long and indirect neuronal pathways. Indeed, given its possibility of connecting with (and therefore activating) phonological and semantic representations derived from spoken language, the LH orthographic lexicon would be more efficient than the RH in mediating access to meaning and word sounds since the earliest phases of reading development. Inhibition of consolidation of orthographic knowledge in the RH could therefore maximize reading development while minimizing the required resources to perform the task. Although reasonable, such interpretation is merely speculative. A future development of this computational model including prior lexical phonological knowledge and inter-hemispheric inhibitory connections during learning will be required to shed light on this link.

Another point that could provide input for future research concerns the role of inter-hemispheric interactions during lexical consolidation and during reading performance proper. Indeed, for the sake of simplicity, the present model treated the two hemispheres as if they were completely independent from each other. However, behavioral (Iacoboni & Zaidel, 1996), computational (Weems & Reggia, 2004) and neurofunctional (Chu & Meltzer, 2019) studies have suggested that massive inter-hemispheric interactions occur during reading. Therefore, future implementations of this model will need to simulate these interactive processes, with a particular focus on how orthographic processing in two hemispheres is integrated in order to provide one single behavioral response.

Finally, the inclusion of a semantic component will be required in future developments of this model, in order to explore how combined effects of frequency and imageability can emerge in the residual reading abilities of patients with a LH lesion impairing the visual word form system (as described in Chapter 2 of the present work). The literature on patients with optic aphasia anticipates that verbal semantic knowledge should be lateralized to the LH, whereas visual semantic knowledge should be available to both hemispheres (Luzzatti, Rumiati & Ghirardi, 1998; Luzzatti, 2003).

References

Arppe, A., Hendrix, P., Milin, P., Baayen, R. H., & Shaoul, C. (2014). NDL: Naive discriminative learning. *R package versions 0.1, 6*(0.2), 16.

Baayen, R. H., Milin, P., Đurđević, D. F., Hendrix, P., & Marelli, M. (2011). An amorphous model for morphological processing in visual comprehension based on naive discriminative learning. *Psychological Review, 118*(3), 438.

Babkoff, H., & Ben-Uriah, Y. (1983). Lexical decision time as a function of visual field and stimulus probability. Cortex, 19(1), 13-30.

Behrmann, M., & Plaut, D. C. (2015). A vision of graded hemispheric specialization. *Annals of the New York Academy of Sciences, 1359*(1), 30-46.

Bertinetto, P. M., Burani, C., Laudanna, A., Marconi, L., Ratti, D., Rolando, C., & Thornton, A. M. (2005). CoLFIS (Corpus e Lessico di Frequenza dell'Italiano Scritto). http://www. istc. cnr.it/material/database, 67-73.

Chiarello, C., Senehi, J., & Soulier, M. (1986). Viewing conditions and hemisphere asymmetry for the lexical decision. *Neuropsychologia, 24*(4), 521-529.

Chiarello, C., Shears, C., Liu, S., & Kacinik, N. A. (2005). Influence of word class proportion on cerebral asymmetries for high-and low-imagery words. *Brain and Cognition, 57*(1), 35-38.

Chu, R. K., & Meltzer, J. A. (2019). Interhemispheric connectivity during lateralized lexical decision. *Human Brain Mapping, 40*(3), 818-832.

Coltheart, M. (1980). Deep dyslexia: a right-hemisphere hypothesis. In Coltheart, M., Patterson, K., & Marshall, J.C. (Eds.), *Deep Dyslexia*. London: Routledge and Kegan Paul.

Coltheart, M. (2000). Deep dyslexia is right-hemisphere reading. *Brain and Language, 71*(2), 299-309.

Cook, N. D. (1984). Homotopic callosal inhibition. *Brain and Language*, *23*(1), 116-125.

Crepaldi, D., Keuleers, E., Mandera, P., & Brysbaert, M. (2013). SUBTLEX-IT. *Retrieved from http://crr.ugent.be/subtlex-it/.*

Danks, D. (2003). Equilibria of the Rescorla–Wagner model. *Journal of Mathematical Psychology, 47*, 109 – 121.

De Clercq, P., & Brysbaert, M. (2020). The influence of word valence on the right visual field advantage in the VHF paradigm: time to adjust the expectations. *Laterality,* 1-23.

Ellis, A. W. (2004). Length, formats, neighbours, hemispheres, and the processing of words presented laterally or at fixation. *Brain and Language, 88*(3), 355-366.

Ellis, A. W., Young, A. W., & Anderson, C. (1988). Modes of word recognition in the left and right cerebral hemispheres. *Brain and Language, 35*(2), 254-273.

Goslin, J., Galluzzi, C., & Romani, C. (2014). PhonItalia: a phonological lexicon for Italian. *Behavior research methods, 46*(3), 872-886.

Hernandez, S., Nieto, A., & Barroso, J. (1992). Hemispheric specialization for word classes with visual presentations and lexical decision task. *Brain and Cognition,* 20(2), 399-408

Iacoboni, M., & Zaidel, E. (1996). Hemispheric independence in word recognition: Evidence from unilateral and bilateral presentations. *Brain and Language, 53*(1), 121-140.

Landis, T., Regard, M., Graves, R., & Goodglass, H. (1983). Semantic paralexia: A release of right hemispheric function from left hemispheric control?. *Neuropsychologia, 21*(4), 359-364.

Leiber, L. (1976). Lexical decisions in the right and left cerebral hemispheres. *Brain and Language, 3*(3), 443-450.

Luzzatti, C. (2003). Optic aphasia and pure alexia: contribution of callosal disconnection syndromes to the study of lexical and semantic representation in the right hemisphere. In Zaidel, E., & Iacoboni, M. (Eds.), *The Parallel Brain: The Cognitive Neuroscience of the Corpus Callosum* (pp. 479-499). Cambridge, MA: MIT Press.

Luzzatti, C., Rumiati, R. I., & Ghirardi, G. (1998). A functional model of visuo-verbal disconnection and the neuroanatomical constraints of optic aphasia. *Neurocase, 4*(1), 71-87.

Milin, P., Feldman, L. B., Ramscar, M., Hendrix, P., & Baayen, R. H. (2017). Discrimination in lexical decision. *PloS one, 12*(2), e0171935.

Plaut, D. C., & Behrmann, M. (2011). Complementary neural representations for faces and words: A computational exploration. *Cognitive neuropsychology, 28*(3-4), 251-275.

Rescorla, R.A. & Wagner, A.R. (1972). A theory of pavlovian conditioning: variations in the effectiveness of reinforcement and nonreinforcement. In Black, A.H., & Prokasy, W.F. (Eds.), *CLASSICAL CONDITIONING II: Current Theory and Research*, New-York: Meredith Corporation.

Saffran, E. M., Bogyo, L. C., Schwartz, M. F., & Marin, O. S. M. (1980). Does deep dyslexia reflect right-hemisphere reading? In Coltheart, M., Patterson, K., & Marshall, J.C. (Eds.), *Deep Dyslexia* (pp. 381-406) London: Routledge and Kegan Paul.

Saffran, E. M., & Coslett, H. B. (1998). Implicit vs. letter-by-letter reading in pure alexia: A tale of two systems. *Cognitive Neuropsychology, 15*(1-2), 141-165.

Sowman, P. F., Crain, S., Harrison, E., & Johnson, B. W. (2014). Lateralization of brain activation in fluent and non-fluent preschool children: a magnetoencephalographic study of picture-naming. *Frontiers in human neuroscience, 8,* 354.

Van der Knaap, L. J., & Van der Ham, I. J. (2011). How does the corpus callosum mediate interhemispheric transfer? A review. *Behavioural Brain Research, 223*(1), 211-221.

Weems, S. A., & Reggia, J. A. (2004). Hemispheric specialization and independence for word recognition: A comparison of three computational models. *Brain and Language*, *89*(3), 554-568.

Willemin, J., Hausmann, M., Brysbaert, M., Dael, N., Chmetz, F., Fioravera, A., ... & Mohr, C. (2016). Stability of right visual field advantage in an international lateralized lexical decision task irrespective of participants' sex, handedness or bilingualism. *Laterality: Asymmetries of Body, Brain and Cognition, 21*(4-6), 502-524.

Ziegler, J. C., Perry, C., & Zorzi, M. (2014). Modelling reading development through phonological decoding and self-teaching: Implications for dyslexia. *Philosophical Transactions of the Royal Society B: Biological Sciences, 369*(1634), 20120397.

Chapter 6

General discussion

After more than 100 years from the first anatomo-clinical attempts of localizing the function of reading in the brain (Dejerine, 1891; 1892), the dominance of the LH over the RH for reading is still unchallenged. A considerable amount of neuropsychological, neurofunctional, and behavioral evidence has been provided in this direction. However, it is still not completely clear whether this LH advantage is underlaid by a complete word-blindness of the RH (in this case the dominance would be *absolute*), or by poorer orthographic processing abilities of the RH compared to the LH (in this case the dominance would be *relative*). In this thesis, I formally compared these two frameworks in three experimental studies (Chapters 2, 3 and 4). Results provided evidence in favor of a *relative* account of LH dominance over the RH for reading, according to the assumption that "two orthographic lexicons" exist in the brain, with that of the RH containing poorer/weaker representations than those of the LH. In Chapter 5, I provided a possible computational description of how such *relative* dominance of the LH could develop as the result of more efficient consolidation of orthographic lexical representations in the LH than in the RH. In what follows, after a brief summary of the context in which these studies were conducted and of their main results, theoretical implications of these findings as well as future directions are discussed.

Reading in the brain and elusive the role of the right hemisphere

Since the late XIX century, when Skwortzoff (1881) and Dejerine (1891, 1892) first associated reading deficits with brain damage occurring to the left angular gyrus, much effort has been put in the domain of cognitive neuroscience in the attempt of characterizing the set of brain regions whose activity gives rise to the function of reading. Although this localizationist approach was criticized by Pierre Marie (1897), who claimed that it is illogical to presume that specialized centers evolved for purpose of reading (being reading a recent breakthrough in human history), a considerable amount of evidence has accumulated in the last 100 years linking reading with the activity of left posterior ventral regions of the brain (see for instance Marshall & Newcombe, 1973; Dérouesné & Beauvois, 1979; Behrmann & Bub, 1992; Ripamonti et al., 2014; Baldo et al., 2018). In the last three decades, functional neuroimaging techniques have provided a set of methods to localize the mental operations necessary to derive sound and/or meaning from print in the healthy brain (for a review, see Price, 2012). Remarkably, in 2000, Cohen and colleagues associated orthographic processing with the activity of a left ventral temporo-occipital complex that they defined as "visual word form area". More recently, the correlates of a *lexical-semantic* route, as well as of a *sub-lexical* reading route (Coltheart et al., 2001; see also Ziegler, Perry & Zorzi, 2014)[1] have been unraveled: the former, that allows reading known words through access to an *orthographic lexicon* to activate its visual representation, retrieval of its meaning in the semantic system, and through access to its sound representation in the *phonological lexicon,* has been associated with the activity of ventral occipital-temporal cortices, anterior fusiform and middle temporal gyri; conversely, the sub-lexical route, that allows reading unknown words (pseudowords) through a grapheme-to-phoneme conversion system, has been associated with the inferior parietal cortex, and with the inferior frontal gyrus for phonological output resolution (Jobard et al., 2003; Taylor, Rastle & Davis, 2013). A prominent feature emerging from all these studies is the apparent dominance of the LH over the RH for reading. Such dominance is evident also in behavioral studies on lateralized reading, in which the crossed arrangement of the visual system is used (through tachistoscopic lateralized visual stimulation) to investigate the functional processing of each cerebral hemisphere. According to evidence from neuropsychology and neuroimaging, divided

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[1] For a different perspective, see Plaut et al. (1996) and Harm & Seidenberg (2004)

visual field reading paradigms have consistently reported a processing advantage for stimuli projected to the RVF (and therefore first processed by the LH) on stimuli projected to the LVF (and therefore first processed by the RH), known as the "visual field effect" (Leiber, 1976; Babkoff & Ben-Uriah, 1983; Chiarello, Senehi & Soulier, 1986; Hernandez, Nieto & Barroso, 1992; Chiarello et al., 2005; Willemin et al., 2016; De Clercq & Brysbaert, 2020).

Nevertheless, it is not completely clear whether the LH dominance over the RH for reading is underlaid by the complete inability of the RH to process orthographic information (i.e., such dominance is *absolute,* to use the wording of Rutherford & Lutz, 2004), or by a different organization of orthographic knowledge between hemispheres, with the RH being characterized by weaker and/or poorer lexical orthographic representations than the LH (i.e.: *relative* dominance; see also Coltheart, 1980). From a cognitive point of view, the feature that differentiates these two accounts is the absence (according to the *absolute* view) vs. existence (according to the *relative* view) of orthographic lexical representations in the RH.

The predictions of these two frameworks differ macroscopically in two domains: (1) the interpretation of the visual field effect in lateralized reading and (2) the interpretation of residual reading abilities after a LH brain lesion damaging the visual word form system.

As far as the interpretation of the visual field effect is concerned, the first framework (Ellis, Young & Anderson, 1988; Ellis, 2004) suggests that it is due to the lack of lexical orthographic representations in the RH. Accordingly, to reach the "single orthographic (input) lexicon" located in the LH, orthographic stimuli projected to the LVF/RH must undergo stepwise conversion into abstract letter units (this process being unnecessary for reading words presented in a standard horizontal format in the RVF/LH) and interhemispheric transfer from the RH to the LH. These processes would occur prior to lexical access, implying a cost in performance proportional to the amount of orthographic information to process (see also Whitney, 2001). According to this framework, the effect of variables affecting pre-lexical processing stages (namely word length and N size) should maximally differ between visual fields/hemispheres. In particular, these pre-lexical effects are expected for stimuli projected to the LVF/RH and not to the RVF/LH.

Conversely, according to the "two orthographic lexicons" framework, complying with the idea of a *relative* dominance of the LH for reading, the visual field effect in lateralized reading is due to poorer/weaker lexical representations in the RH compared to those in the LH, especially for infrequent and/or abstract words (Coltheart, 1980; 2000; Saffran et al., 1980; Saffran &

Coslett, 1998; Luzzatti, Rumiati & Ghirardi, 1998; Luzzatti, 2003). In line with this account, performance should differ between hemispheres according to lexical-semantic factors, with infrequent and/or abstract stimuli that should be particularly difficult to process when targeting the LVF/RH.

From these two models, although indirectly, different interpretations of residual reading abilities after a LH brain lesion can also be derived. According to the "single orthographic lexicon" view, reading is impossible when the LH visual word form system is lesioned and both afferent and efferent connections with the rest of the LH are interrupted by the lesion. Therefore, for any residual reading ability to be present, the LH visual word form system must be at least partially active, and its connections with the rest of the brain must be spared. Conversely, according to the "two orthographic lexicons view" reading can occur even when the LH visual word form system is lesioned and both afferent and efferent connections with the rest of the brain are interrupted by the lesion, through RH -although far from perfect- mediation.

Hello from the other side: a neuropsychological, behavioral and computational exploration of hemispheric asymmetries in reading.

In this thesis, the predictions of the "single orthographic lexicon" (complying with an *absolute* view of LH dominance over the RH for reading: Ellis, Young & Anderson, 1988; Ellis, 2004) and of the "two orthographic lexicons" (complying with a *relative* view of LH dominance: Coltheart, 1980; 2000; Saffran et al., 1980; Saffran & Coslett, 1998, Luzzatti, Rumiati & Ghirardi, 1998; Luzzatti, 2003) models have been formally compared through a behavioral study complemented by a structural disconnectome approach on a patient with Pure Alexia, a behavioral lateralized lexical decision study on healthy right-handed subjects, and a behavioral lateralized lexical decision study in which performance of right-handed subjects was compared with that of a group of left-handers. Finally, a computational model of how a *relative* dominance of the LH over the RH for reading could develop was proposed. In what follows, aims and results of the studies contained in this thesis are summarized.

Study one (Chapter 2) was conducted with the aim of comparing the predictions of the "single orthographic lexicon" and "two orthographic lexicons" models on implicit reading abilities after a LH brain lesion. A patient with pure alexia due to occlusion of the left posterior cerebral artery was tested by means of a tachistoscopic lexical decision in which frequency and imageability were manipulated. In order to explore the structural disconnection pattern due to the lesion, a structural disconnectome analysis was conducted. Data revealed that, in spite of the inability to recognize words explicitly, the patient was able to identify accurately high-frequency concrete words as lexical strings. The lesion and disconnectome profile highlighted that the LH visual word form system was lesioned and both afferent and efferent connections with the rest of the LH were interrupted by the lesion.

Study two (Chapter 3) aimed at testing the existence of one vs. two orthographic lexicons in healthy young right-handed subjects, by means of a highly controlled divided visual field reading paradigm. In the attempt of replicating the lexical-semantic effects observed in patient AA, the experimental manipulation of word frequency and imageability was included. Also, pre-lexical experimental modulations were introduced, in order to test whether pre-lexical factors, rather than lexical-semantic factors determine hemispheric differences in reading. A Visual Field effect was detected, as well as a Visual Field-by-Frequency interaction. This latter effect was due to compression of the frequency effect in RTs for stimuli projected to the LVF/RH compared to stimuli projected to the RVF/LH. Pre-lexical effects didn't differ between visual fields/hemispheres.

Study three (Chapter 4) was conducted to exclude that the compression of the frequency effect in the LVF/RH observed in study two could only be due to a "floor" effect in performance. In addition, study three was designed to explore the extent to which the effects described in the previous experiment could be modulated by different patterns of hemispheric dominance. For these reasons, a sample of left-handed subjects (expected to be less likely than right-handers to show a "floor" effect in performance for stimuli projected to the LVF/RH) was compared with the sample of right-handed subjects described in study two in the same divided visual field reading task. An advantage of the RVF/LH over the LVF/RH was found in both groups, as well as a compression of the frequency effect in the LVF/RH, although performance of left-handed subjects was better than that of right-handers for stimuli projected to the LVF/RH.

Study four (Chapter 5) a computational modelling approach was adopted to simulate consolidation of lexical orthographic knowledge in the two hemispheres, assuming that learning could be less efficient in the RH than in the LH. In particular, noise attenuating the relationship between orthographic pre-lexical units (letters, bigrams) and lexical orthographic units (words) was introduced to simulate lexical consolidation in the RH, while "noiseless learning" was assumed to occur in the LH. As much as for human data (comparison with right-handed subjects) a Visual Field/Hemisphere effect was observed in simulated data, together with a Visual Field-by-Frequency interaction indicating a compression of the frequency effect in the (simulated) RH.

One or two orthographic lexicons in the brain?

Results of the study reported in Chapter 2 indicated that residual reading abilities could be present even when the LH visual word form system is lesioned and both afferent and efferent connections with the rest of the LH are interrupted by the lesion. Indeed, despite the lesion and disconnection pattern, patient AA showed 90% accurate performance (although without overt stimuli recognition) in the tachistoscopic lexical decision task for frequent concrete words. For the LH to account for this pattern, orthographic stimuli (initially processed by the RH due to LVF presentation) should have survived a considerable amount of sources of likely information loss due to the lesion and consequent disconnection (lesion of the callosum, lesion of LH occipital cortices, disconnection of the left Inferior Longitudinal Fasciculus, lesion of the left fusiform gyrus, disconnection of the left Inferior Fronto-Occipital, Arcuate and Superior Longitudinal Fasciculi) and still have allowed a 90% accurate performance for frequent and concrete words. Conversely, according to the framework advocating RH mediation of implicit reading, information could have flown in the RH without being affected by any lesion-related source of information loss. Therefore, these findings tip in favor of a RH account of implicit reading in patient AA, in line with previous studies (Coslett & Saffran, 1989, 1994; Saffran & Coslett, 1998; Shan et al., 2010) advocating a RH mediation of implicit reading in Pure Alexia. Interestingly, performance being accurate only for frequent and highly imageable items provides support to the idea that the RH is able to process proficiently only frequent and/or concrete words (Coltheart 1980; 2000; Saffran et al., 1980; Saffran & Coslett, 1998). Study two (Chapter 3) was conducted with the aim of exploring the extent to which these conclusions could also apply to healthy subjects. In the context of a lateralized lexical decision task on healthy right-handed subjects, the effect of pre-lexical factors (namely word length and N size) did not differ between visual fields/hemispheres, while performance between visual fields/hemispheres differed according to a lexical variable, namely word Frequency (the effect of Frequency being greater for stimuli presented in the RVF/LH than in the LVF/RH). These results do not comply with the "single orthographic lexicon" framework (Ellis, Young & Anderson, 1988; Ellis, 2004), advocating that mental operations occurring at a pre-lexical level in the LVF/RH -and not in the RVF/LH- determine the visual field effect in lateralized reading. Rather, these results support the idea that the visual field effect in lateralized reading is due to a weaker/poorer orthographic lexicon in the RH compared to that of the LH, as suggested by the "two orthographic lexicons" framework (Coltheart, 1980; 2000; Saffran et al., 1980; Saffran & Coslett, 1998, Luzzatti, Rumiati & Ghirardi, 1998; Luzzatti, 2003). Therefore, these results apparently support the *relative* account of LH dominance over the RH for reading.

However, it is worthy to note that, in study two, performance for low-frequency words projected to the LVF/RH was not significantly better than chance level. If on the one hand this result could simply mirror a "structural limit" of the lexical orthographic processing capabilities of the RH lexicon, on the other hand this could more simply indicate that the crucial effect pointing to a lexical interpretation of the visual field effect (namely the compression of the Frequency effect in the LVF/RH) is due to a "floor" effect in performance in the LVF/RH.

The results of the study reported in Chapter 4 suggested that the compression of the Frequency effect in the LVF/RH described in Chapter 3 did not simply depend on a "floor" effect in performance in the LVF/RH. Indeed, the same effects described in right-handed subjects (a visual field effect and the compression of the effect of Frequency in the LVF/RH) were replicated on a sample of left-handers, who showed better performance than right-handed subjects for stimuli projected to the LVF/RH.

The framework proposing the existence of "two orthographic lexicons" in the brain, with the RH one being limited with respect to that of the LH, provides a better explanation than that suggested by the "single orthographic lexicon" of implicit reading in patient AA, as well as of the visual field effect in lateralized reading in healthy subjects described in Chapters 3 and 4. Taken as a whole, these results support a *relative* view of LH dominance over the RH for reading, in line with studies on split-brain patients suggesting that, although limited it its capability of reading compared to the LH, the RH is not word-blind (Gazzaniga & Hillyard, 1971; Baynes, Tramo & Gazzaniga, 1992; Reuter-Lorenz & Baynes, 1992). The idea of an orthographic lexicon in the RH is also supported by recent findings suggesting the existence of a RH homologue of the “visual word from area” (Cohen et al., 2000) that could process orthographic information projected to the LVF in a partially independent way from the visual word form system of the LH (Rauschecker et al., 2012; Chu & Meltzer, 2019).

The development of a *relative* LH dominance over the RH for reading

One critical feature of the “two orthographic lexicons” framework is the possibility that lexical representations in the RH are limited to high frequency and/or concrete words. This claim is apparently supported by the results of studies 1, 2 and 3 of the present thesis. Indeed, patient AA showed accurate performance only for frequent concrete words, while for healthy subjects, performance was particularly low for low-frequency words projected to the RH. However, within the “two orthographic lexicons” framework, no explanations are provided on how a “limited” RH orthographic lexicon could develop (Coltheart, 1980, 2000; Saffran et al., 1980; Saffran & Coslett, 1998; Luzzatti, Rumiati & Ghirardi, 1998; Luzzatti, 2003).

One mechanism that may account for this phenomenon could be a sort of “gate” preventing low-frequency and/or abstract words from accessing the RH lexicon. However, this explanation is circular and not conservative, as it requires the existence of a module that should be sensitive to lexical properties of orthographic stimuli (i.e.: a lexicon) operating prior to access to the RH lexicon proper (“a lexicon before the lexicon”). An alternative explanation for the weak representation of lexical orthographic knowledge in the RH could be a poorer consolidation of orthographic information in the RH compared to the LH. Accordingly, in Chapter 5, the stable state (Danks, 2003) of efficient consolidation of orthographic knowledge in the LH and of inefficient learning in the RH was simulated through the Naïve Discriminative Learning approach (Baayen et al., 2011; Milin et al., 2017), based on a model of classical conditioning (the Rescorla-Wagner model of learning; Rescorla & Wagner, 1972). Inefficient, “noisy” learning in the RH was simulated by attenuating the connection weights from pre-lexical orthographic cues (letters and bigrams) to orthographic lexical representations (words). Remarkably, the pattern of results described in Chapters 3 and 4 (and in particular the main effects of Visual Field, Frequency and the Visual Field-by-Frequency interaction due to compression of the effect of Frequency in the LVF/RH) was replicated by the simulated data, provided that a significant amount of noise is introduced in the RH during the consolidation of orthographic knowledge.

These findings suggest that a *relative* account (supported by data presented in Chapters 2,3, and 4 of the present thesis) of LH dominance over the RH for reading, underlaid by the existence in the RH of weaker orthographic representations than those of the LH, could develop due to "noisy", inefficient consolidation of orthographic knowledge in the RH. However, it is worthy to note that, despite the face validity of this explanation, it is not clear what mechanism could generate such "noise" in the RH. On the other hand, if learning was "noiseless" also in the RH and lexical orthographic consolidation in the RH was as efficient as in the LH, the two orthographic lexicons in the two hemispheres would be equally proficient and they would likely be engaged in a constant competition for neurocognitive resources. As a result, reading would be a highly inefficient cognitive process. Therefore, inhibiting orthographic consolidation in one hemisphere could be reasonably helpful in assuring optimization of the neurocognitive circuitry underlying reading, ensuring that the most efficient reading pathway is consolidated, while the use of the most inefficient one is discouraged.

Assuming that the goal of reading is to retrieve meaning and/or a word's sound from its printed form, the greater efficiency of the LH pathway for reading would be due to the fact that the binding between lexical orthographic representations and pre-existing lexical phonological and semantic knowledge derived from spoken language (that is already left-lateralized before reading development; Sowman et al., 2014) is mediated by highly efficient intra-hemispheric connections (Plaut & Behrmann, 2011; Behrmann & Plaut, 2015). Conversely, for this associative process, the RH has to rely on intra-hemispheric connections with weaker RH phonological and/or semantic representations derived from spoken language or on inefficient inter-hemispheric connections with these representations in the LH. Therefore, inhibiting the consolidation of orthographic information in the RH would be helpful to optimize the neurocognitive network underlying reading.

In this regard, "noise" -giving rise to inefficient consolidation of orthographic knowledge in the RH- could represent the combined effect of LH inhibition and inefficient binding between lexical orthographic representations and pre-existing lexical phonological and semantic knowledge derived from spoken language. Nevertheless, the validity of this purely speculative explanation will need to be explored by future studies. In this regard, it is evident how a complete developmental account aiming at describing how LH dominance for reading develops will probably need to explore the cascade effect of lateralization of lexical and semantic knowledge derived from spoken language on the subsequent development and functional lateralization of reading, with a particular focus on the role of inter-hemispheric inhibition in mediating the development of written language.

A functional characterization of the right orthographic lexicon in the brain

If translated in the domain of functional neuroimaging, the results presented in this thesis imply that the activity of a RH homologue of the visual word form system should be observable during processing of orthographic stimuli, at least in case of a brain lesion impairing the visual word form system of the LH and in case of lateralized reading tasks. Data from previous studies support this suggestion: on the one hand, it was shown that in case of surgical removal of a left-temporo-occipital neoplasm, the right homologue of the visual word form area (Cohen et al., 2000) is activated during orthographic processing (Cohen et al., 2004; see also Cohen et al., 2003 and Henry et al., 2005)[2]. On the other hand, recent fMRI and MEG data from lateralized reading paradigms on healthy subjects have suggested that orthographic information projected to the LVF/RH can be processed by the RH visual word form system before being transferred to the LH (Rauschecker et al., 2011; Chu & Meltzer, 2019). Crucially, data presented in this thesis also suggest that the activity of the two visual word form systems in the two cerebral hemispheres (representing the neural correlates of the two orthographic lexicons) should display different sensitivity to word Frequency. Future studies adopting an experimental approach similar to that employed in Chapters 3 and 4, combined with functional neuroimaging techniques, will be required to provide a neurofunctional characterization of the different lexical orthographic abilities of the two hemispheres suggested in the present thesis[3].

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[2] It is worth considering that neoplastic pathologies typically evolve slowly. Therefore, a progressive reorganization of the reading system increasingly involving the RH due to a neoplastic formation in the LH should not be excluded (see for instance Tomasino et al., 2020).

[3] A lateralized lexical decision fMRI study on healthy subjects using high- and low-frequency words has been designed for this purpose. Unfortunately, data collection was stopped -due to the COVID-19 pandemic- before a sufficient sample size could be reached.

A role for orthographic regularity?

As a final remark, it is worthy to note that a critical common feature underlying the experimental and computational data presented in this thesis is the regularity of Italian orthography. Previous studies showed that learning to read in a regular orthography is less demanding than in irregular orthographies (Ellis & Hooper, 2001). It was also shown that the regularity of the Italian language makes reading faster than in opaque orthographies such as English (Paulesu et al., 2000). Therefore, the possibility of generalizing the present findings to orthographies in which grapheme-phoneme mapping is irregular should be considered with caution. In particular, it cannot be excluded that the lateralization of orthographic lexical knowledge could be influenced by the regularity of the orthography that has to be learned. This would explain why hemispheric differences in pre-lexical factors have been found in previous literature on irregular orthographies (see for instance Iacoboni & Zaidel, 1996; Ellis, Young & Anderson, 1988, Mano et al., 2010), apparently suggesting an *absolute* dominance of the LH over the RH for reading. In this regard, it cannot be ruled out that in regular orthographies LH dominance for reading could be *relative* while in irregular ones the dominance pattern is more similar to an *absolute* one. Unfortunately, literature on transparent orthographies has not provided conclusive evidence pointing to hemispheric differences in lexical-semantic factors in lateralized reading (e.g., Perea & Fraga, 2006; Perea, Acha & Fraga, 2008), suggesting that the relationship between orthographic regularity and lateralization of reading may not be straightforward. If anything, the evidence presented in this work coming from a regular orthography such as the Italian one suggests that LH dominance over the RH for reading <u>can</u> -in principle- be *relative.* Nevertheless, the impact of orthographic regularity on the lateralization of lexical orthographic knowledge in the brain will need to be clarified in order to formulate a general developmental theory of reading lateralization.

Conclusions

In the present thesis, I described how the dominance of the LH over the RH for reading has been defined throughout the history of cognitive neuroscience and I presented two neurocognitive models of reading supporting either an *absolute* or a *relative* view of LH dominance in reading. Evidence of residual (implicit) reading abilities for frequent concrete words in case of a LH visual word form system lesioned and with both afferent and efferent connections with the rest of the LH being interrupted by the lesion, together with evidence of lexical-semantic effects accounting for visual field/hemisphere differences in lateralized reading, supports the view of a *relative* LH dominance, according to the idea of the existence of a poorer/weaker orthographic lexicon in the RH. A computational modelling study suggested that weaker orthographic representations in the RH than in the LH -giving rise to such *relative* LH advantage for reading- could be due to inefficient consolidation of orthographic knowledge in the RH. Future studies will be required to shed light on the cause(s) of inefficient consolidation of orthographic representations in the RH. In this regard, I suggest that future research should explore the role of active inter-hemispheric inhibition from the LH and inefficient binding of orthographic information with previously existing lexical phonological and semantic representations on the development of lexical orthographic representations in the two cerebral hemispheres.

References

Baayen, R. H., Milin, P., Đurđević, D. F., Hendrix, P., & Marelli, M. (2011). An amorphous model for morphological processing in visual comprehension based on naive discriminative learning. *Psychological Review, 118*(3), 438.

Babkoff, H., & Ben-Uriah, Y. (1983). Lexical decision time as a function of visual field and stimulus probability. *Cortex, 19*(1), 13-30.

Baldo, J. V., Kacinik, N., Ludy, C., Paulraj, S., Moncrief, A., Piai, V., ... & Dronkers, N. F. (2018). Voxel-based lesion analysis of brain regions underlying reading and writing. *Neuropsychologia*, *115*, 51-59.

Baynes, K., Tramo, M. J., & Gazzaniga, M. S. (1992). Reading with a limited lexicon in the right hemisphere of a callosotomy patient. *Neuropsychologia, 30*(2), 187-200.

Behrmann, M., & Bub, D. (1992). Surface dyslexia and dysgraphia: Dual routes, single lexicon. *Cognitive Neuropsychology, 9*(3), 209-251.

Behrmann, M., & Plaut, D. C. (2015). A vision of graded hemispheric specialization. *Annals of the New York Academy of Sciences, 1359*(1), 30-46.

Chiarello, C., Senehi, J., & Soulier, M. (1986). Viewing conditions and hemisphere asymmetry for the lexical decision. *Neuropsychologia, 24*(4), 521-529.

Chiarello, C., Shears, C., Liu, S., & Kacinik, N. A. (2005). Influence of word class proportion on cerebral asymmetries for high-and low-imagery words. *Brain and Cognition, 57*(1), 35-38.

Chu, R. K., & Meltzer, J. A. (2019). Interhemispheric connectivity during lateralized lexical decision. *Human Brain Mapping, 40*(3), 818-832.

Cohen, L., Dehaene, S., Naccache, L., Lehéricy, S., Dehaene-Lambertz, G., Hénaff, M. A., & Michel, F. (2000). The visual word form area: spatial and temporal characterization of an initial stage of reading in normal subjects and posterior split-brain patients. *Brain, 123*(2), 291-307.

Cohen, L., Henry, C., Dehaene, S., Martinaud, O., Lehéricy, S., Lemer, C., & Ferrieux, S. (2004). The pathophysiology of letter-by-letter reading. *Neuropsychologia, 42*(13), 1768-1780.

Cohen, L., Martinaud, O., Lemer, C., Lehéricy, S., Samson, Y., Obadia, M., ... & Dehaene, S. (2003). Visual word recognition in the left and right hemispheres: anatomical and functional correlates of peripheral alexias. *Cerebral Cortex, 13*(12), 1313-1333.

Coltheart, M. (1980). Deep dyslexia: a right-hemisphere hypothesis. In Coltheart, M., Patterson, K., & Marshall, J.C. (Eds.), *Deep Dyslexia*. London: Routledge and Kegan Paul.

Coltheart, M. (2000). Deep dyslexia is right-hemisphere reading. *Brain and Language, 71*(2), 299-309.

Coltheart, M., Rastle, K., Perry, C., Langdon, R., & Ziegler, J. (2001). DRC: a dual route cascaded model of visual word recognition and reading aloud. *Psychological Review, 108*(1), 204.

Coslett, H. B., & Saffran, E. M. (1989). Evidence for preserved reading in pure alexia. *Brain, 112*(2), 327–359

Coslett, H. B., & Saffran, E. M. (1994). Mechanisms of implicit reading in alexia. In M. Farah & G. Ratcliff (Eds.), *The neuropsychology of high-level vision* (pp. 299–330). Lawrence Erlbaum Associates.

Danks, D. (2003). Equilibria of the Rescorla–Wagner model. *Journal of Mathematical Psychology, 47*, 109 – 121.

De Clercq, P., & Brysbaert, M. (2020). The influence of word valence on the right visual field advantage in the VHF paradigm: time to adjust the expectations. *Laterality,* 1-23.

Déjerine, J. (1891). Sur un cas de cécité verbale avec agraphie suivi d'autopsie. *Mémoires de la Société de Biologie*, *3*, 197-201.

Dejerine, J. (1892). Contribution à l'étude anatomopathologique et clinique des différents variétés de cécité verbale. *Mémoires de la Société de Biologie, 4*, 61-90.

Dérouesné, J., & Beauvois, M. F. (1979). Phonological alexia: three dissociations. *Journal of Neurology, Neurosurgery & Psychiatry*, *42*(12), 1115-1124.

Ellis, A. W. (2004). Length, formats, neighbours, hemispheres, and the processing of words presented laterally or at fixation. *Brain and Language, 88*(3), 355-366.

Ellis, A. W., Young, A. W., & Anderson, C. (1988). Modes of word recognition in the left and right cerebral hemispheres. *Brain and Language, 35*(2), 254-273.

Ellis, N. C., & Hooper, A. M. (2001). Why learning to read is easier in Welsh than in English: Orthographic transparency effects evinced with frequency-matched tests. *Applied Psycholinguistics, 22*(4), 571-599.

Gazzaniga, M. S., & Hillyard, S. A. (1971). Language and speech capacity of the right hemisphere. *Neuropsychologia, 9*(3), 273-280.

Harm, M. W., & Seidenberg, M. S. (2004). Computing the meanings of words in reading: cooperative division of labor between visual and phonological processes. *Psychological Review*, *111*(3), 662.

Henry, C., Gaillard, R., Volle, E., Chiras, J., Ferrieux, S., Dehaene, S., & Cohen, L. (2005). Brain activations during letter-by-letter reading: A follow-up study. *Neuropsychologia, 43*(14), 1983-1989.

Hernandez, S., Nieto, A., & Barroso, J. (1992). Hemispheric specialization for word classes with visual presentations and lexical decision task. *Brain and Cognition, 20*(2), 399-408.

Iacoboni, M., & Zaidel, E. (1996). Hemispheric independence in word recognition: Evidence from unilateral and bilateral presentations. *Brain and Language, 53*(1), 121-140.

Jobard, G., Crivello, F., & Tzourio-Mazoyer, N. (2003). Evaluation of the dual route theory of reading: a metanalysis of 35 neuroimaging studies. *Neuroimage, 20*(2), 693-712.

Leiber, L. (1976). Lexical decisions in the right and left cerebral hemispheres. *Brain and Language, 3*(3), 443-450.

Luzzatti, C. (2003). Optic aphasia and pure alexia: contribution of callosal disconnection syndromes to the study of lexical and semantic representation in the right hemisphere. In Zaidel, E., & Iacoboni, M. (Eds.), *The Parallel Brain: The Cognitive Neuroscience of the Corpus Callosum* (pp. 479-499). Cambridge, MA: MIT Press.

Luzzatti, C., Rumiati, R. I., & Ghirardi, G. (1998). A functional model of visuo-verbal disconnection and the neuroanatomical constraints of optic aphasia. *Neurocase, 4*(1), 71-87.

Mano, Q. R., Patrick, C. J., Andresen, E. N., Capizzi, K., Biagioli, R., & Osmon, D. C. (2010). Re-examining format distortion and orthographic neighbourhood size effects in the left, central and right visual fields. *Journal of Research in Reading*, *33*(4), 356-373.

Marie, P. (1897). L’évolution du langage considérée au point de vue de l’étude de l’aphasie. *Presse médicale*, 29.

Marshall, J. C., & Newcombe, F. (1973). Patterns of paralexia: A psycholinguistic approach. *Journal of Psycholinguistic Research, 2*(3), 175-199.

Milin, P., Feldman, L. B., Ramscar, M., Hendrix, P., & Baayen, R. H. (2017). Discrimination in lexical decision. *PloS one, 12*(2), e0171935.

Paulesu, E., McCrory, E., Fazio, F., Menoncello, L., Brunswick, N., Cappa, S. F., ... & Pesenti, S. (2000). A cultural effect on brain function. *Nature Neuroscience, 3*(1), 91-96.

Perea, M., & Fraga, I. (2006). Transposed-letter and laterality effects in lexical decision. *Brain and Language, 97*(1), 102-109.

Perea, M., Acha, J., & Fraga, I. (2008). Lexical competition is enhanced in the left hemisphere: Evidence from different types of orthographic neighbors. *Brain and Language, 105*(3), 199-210.

Plaut, D. C., & Behrmann, M. (2011). Complementary neural representations for faces and words: A computational exploration. *Cognitive Neuropsychology, 28*(3-4), 251-275.

Plaut, D. C., McClelland, J. L., Seidenberg, M. S., & Patterson, K. (1996). Understanding normal and impaired word reading: computational principles in quasi-regular domains. *Psychological Review*, *103*(1), 56.

Price, C. J. (2012). A review and synthesis of the first 20 years of PET and fMRI studies of heard speech, spoken language and reading. *Neuroimage, 62*(2), 816-847.

Rauschecker, A. M., Bowen, R. F., Parvizi, J., & Wandell, B. A. (2012). Position sensitivity in the visual word form area. *Proceedings of the National Academy of Sciences, 109*(24), E1568-E1577.

Rescorla, R.A. & Wagner, A.R. (1972). A theory of pavlovian conditioning: variations in the effectiveness of reinforcement and nonreinforcement. In Black, A.H., & Prokasy, W.F. (Eds.), *CLASSICAL CONDITIONING II: Current Theory and Research*, New-York: Meredith Corporation.

Reuter-Lorenz, P. A., & Baynes, K. (1992). Modes of lexical access in the callosotomized brain. *Journal of Cognitive Neuroscience, 4*(2), 155-164. doi: 10.1162/jocn.1992.4.2.155.

Ripamonti, E., Aggujaro, S., Molteni, F., Zonca, G., Frustaci, M., & Luzzatti, C. (2014). The anatomical foundations of acquired reading disorders: a neuropsychological verification of the dual-route model of reading. *Brain and Language, 134,* 44-67.

Rutherford, B. J., & Lutz, K. T. (2004). Conflicting strategies and hemispheric suppression in a lexical decision task. *Brain and Cognition, 55*(2), 387-391.

Saffran, E. M., Bogyo, L. C., Schwartz, M. F., & Marin, O. S. M. (1980). Does deep dyslexia reflect right-hemisphere reading? In Coltheart, M., Patterson, K., & Marshall, J.C. (Eds.), *Deep Dyslexia* (pp. 381-406) London: Routledge and Kegan Paul.

Saffran, E. M., & Coslett, H. B. (1998). Implicit vs. letter-by-letter reading in pure alexia: A tale of two systems. *Cognitive Neuropsychology, 15*(1-2), 141-165.

Shan, C., Zhu, R., Xu, M., Luo, B., & Weng, X. (2010). Implicit reading in Chinese pure alexia. *Brain and Language, 114*(3), 147–156

Skwortzoff N: *De la Cécité et de la Surdité des Mots dans l'Aphasie*. Paris, Delahaye et Lecrosnier, 1881.

Sowman, P. F., Crain, S., Harrison, E., & Johnson, B. W. (2014). Lateralization of brain activation in fluent and non-fluent preschool children: a magnetoencephalographic study of picture-naming. *Frontiers in Human Neuroscience, 8,* 354.

Taylor, J. S. H., Rastle, K., & Davis, M. H. (2013). Can cognitive models explain brain activation during word and pseudoword reading? A meta-analysis of 36 neuroimaging studies. *Psychological Bulletin, 139*(4), 766.

Tomasino, B., Ius, T., Skrap, M. e Luzzatti, C. (2020). Phonological and surface dyslexia in individuals with brain tumors: Performance pre-, intra-, immediately post-surgery and at follow-up. *Human Brain Mapping, 41,* 5015-5031.

Whitney, C. (2001). How the brain encodes the order of letters in a printed word: The SERIOL model and selective literature review. *Psychonomic Bulletin & Review, 8*(2), 221-243.

Willemin, J., Hausmann, M., Brysbaert, M., Dael, N., Chmetz, F., Fioravera, A., ... & Mohr, C. (2016). Stability of right visual field advantage in an international lateralized lexical decision task irrespective of participants' sex, handedness or bilingualism. *Laterality: Asymmetries of Body, Brain and Cognition, 21*(4-6), 502-524.

Ziegler, J. C., Perry, C., & Zorzi, M. (2014). Modelling reading development through phonological decoding and self-teaching: Implications for dyslexia. *Philosophical Transactions of the Royal Society B: Biological Sciences, 369*(1634), 20120397.

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