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# The Visual Word Form Area remains in the dominant hemisphere for language in late-onset left occipital lobe epilepsies: A postsurgery analysis of two cases

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ABSTRACT

Automatic recognition of words from letter strings is a critical processing step in reading that is lateralized to the left-hemisphere middle fusiform gyrus in the so-called Visual Word Form Area (VWFA). Surgical lesions in this location can lead to irreversible alexia. Very early left hemispheric lesions can lead to transfer of the VWFA to the nondominant hemisphere, but it is currently unknown if this capability is preserved in epilepsies developing after reading acquisition. In this study, we aimed to determine the lateralization of the VWFA in late-onset left inferior occipital lobe epilepsies and also the effect of surgical disconnection from the adjacent secondary visual areas. Two patients with focal epilepsies with onset near the VWFA underwent to surgery for epilepsy, with sparing of this area. Neuropsychology evaluations were performed before and after surgery, as well as quantitative evaluation of the speed of word reading. Comparison of the surgical localization of the lesion, with the BOLD activation associated with the contrast of words–strings, was performed, as well as a study of the associated main white fiber pathways using diffusion-weighted imaging. Neither of the patients developed alexia after surgery (similar word reading speed before and after surgery) despite the fact that the inferior occipital surgical lesions reached the neighborhood (less than 1 cm) of the VWFA. Surgeries partly disconnected the VWFA from left secondary visual areas, suggesting that pathways connecting to the posterior visual ventral stream were severely affected but did not induce alexia. The anterior and superior limits of the resection suggest that the critical connection between the VWFA and the Wernicke's Angular Gyrus cortex was not affected, which is supported by the detection of this tract with probabilistic tractography. Left occipital lobe epilepsies developing after reading acquisition did not produce atypical localizations of the VWFA, even with foci in the close neighborhood. Surgery for occipital lobe epilepsy should take this into consideration, as well as the fact that disconnection from the left secondary visual areas may not produce alexia.



## 1. Introduction

A significant effort has been dedicated to understanding the neurobiological basis of word recognition (reviewed by Wandell [1] and Dehaene [2]), a fundamental basis for reading. An important concept that has emerged is the Visual Word Form Area (VWFA), which was first proposed by Cohen [3] as a specialized cortical localization able to perform automatic word recognition from letter strings. A variety of sources of information ranging from lesion analysis [4,5], cortical stimulation [6], functional magnetic resonance imaging (fMRI) [7,8], and evoked potentials [9,10] to outcome of surgery for epilepsy [11] converge on the demonstration of a consistent localization for the VWFA in the middle fusiform gyrus of the left hemisphere [12]. In testing with fMRI, several contrasts are effective in activating the VWFA, ranging from the contrast between words and phase-scrambled words [13]; familiar and unfamiliar characters [14]; and letter strings, words, and checkboards [15,16] as well as false fonts; frequent and infrequent letters; and real words [17]. A bilateral ventral occipitotemporal activation is expected to be observed mostly in the left hemisphere. This asymmetric activation is expected when using verbal stimuli presented in the middle of the vision field [13,17].

This strong anatomical–functional relationship has important consequences for surgery for occipital and temporal lobe epilepsies, which

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place the patient at risk for development of postsurgical alexia [11]. This type of language impairment adds to the well-known risk of left side anterior fusiform gyrus resections [18,19].

Several studies have demonstrated a strong correlation between the hemispheric localization of the VWFA and the lateralization of language in healthy subjects [9,20], suggesting that the late specialization of the VWFA at the time of reading acquisition occurs in close relationship with the development of language networks in the same hemisphere. There are some data suggesting that despite left-hemisphere dominance for language, the specialization of the VWFA can localize to the right hemisphere when the original left side localization suffered a lesion in early childhood [21]. There are no data, however, about the effect of an epileptic focus developing in the neighborhood of the VWFA after reading acquisition. This piece of information would be of importance to assess the surgical risk of alexia. In view of the irreversible effect of late VWFA lesions [10], this is of obvious medical relevance.

Another important point concerning the organization of reading is whether the VWFA requires a functional connection with the neighbor secondary visual areas or is autonomous from them, a question that cannot be fully answered by correlational methods such as fMRI but that is well suited to lesional analysis. Nevertheless, an extended portion of the ventral occipitotemporal region is recruited in reading; Jobard [12] suggested that within the VWFA, there is a spatial hierarchal organization, with the most anterior part the one mostly recruited to process real words, but a potential disconnection within the VWFA and subsequent impairment in this “hierarchal organization” was not discussed. Important white matter bundles connecting these areas are the inferior longitudinal fasciculus (ILF) on the left [22] and a transcallosal bundle from the right hemisphere [23]. Interruption of one of these projection pathways has been postulated to lead to alexia limited to the contralateral visual hemifield [24].

We report on two patients who underwent to surgery for epilepsy arising in the inferior occipital cortex, in the immediate neighborhood of the VWFA, partially disconnecting this region from adjacent secondary visual areas. From the analysis of reading capabilities before and after surgery and comparison with similar cases from the literature, we draw conclusions regarding surgical decisions and the preservation of reading in late-onset occipital lobe epilepsies.

## 2. Methods and subjects

### 2.1. Clinical cases

#### 2.1.1. Patient 1

He is a right-handed 15-year-old boy, who had a normal development and was healthy until the age of 7 years, at which time he developed epilepsy with daily complex partial seizures, which proved refractory to medical therapy. The EEGs revealed a normal background with a very active spike focus on the left occipital–temporal area. The MRIs failed to demonstrate any structural lesion. The neurological examination was normal, including the confrontation visual fields.

With the onset of epilepsy, there was a significant decrease in school performance, which had previously been excellent, with more consistent problems in reading ability. He was previously an excellent reader, and the mother stated: “he was always selected to perform public reading of the Bible at the local church. He barely understood the meaning of some of the words but could read them perfectly. With the onset of seizures he lost completely the ability to read and had to learn again from scratch. At the present time he reads normally, but never again recovered the previous performance”.

#### 2.1.2. Patient 2

He is a right-handed 16-year-old boy, with a good development and no significant health problems until the 8th year of life, at which time a severe epilepsy became apparent, with rapid evolution to multiple daily seizures consisting of repeated and brief episodes of head drops and consciousness impairment which produced a major impact in daily activities and school performance. The EEG exposed a very active left occipital–temporal focus with secondary propagation to the frontal areas. No lesion was demonstrated with MRI studies. The neurological examination was normal, including the visual fields.

### 2.2. Neuropsychology

The neuropsychological evaluation consisted of three different parts: general intelligence assessment, specific cognitive domain evaluation, and specific language assessment.

The Portuguese version of the Wechsler Intelligence Scale for Children, III Edition (WISC-III) was used as a measure of general intelligence; and Coimbra's Neuropsychological Assessment Battery (CNAB), a set of 16 well-known tests, was used to evaluate specific cognitive functions (memory, language, attention, and executive functions) [25]. This comprehensive battery was previously subject to normalization in a representative sample of 1104 Portuguese children and adolescents from 5 to 15 years of age [26] (Table 1). Handedness was assessed using the Edinburgh Inventory [27].

Language was assessed with selected tests from the Portuguese version of Psycholinguistic Assessments of Language Processing in Aphasia [28,29] with an emphasis in Repetition, Naming, Comprehension, Writing, and Reading abilities. This comprehensive battery is used not only to assess acquired deficits [30,31] but also to detect more subtle developmental language deficits such as developmental dyslexia [32,33].

In order to test automatic reading versus letter-by-letter reading strategies, we analyzed the time taken to read short and long words with the same phonetic extension taken from PALPA-P (Subtest 29), which comprises a group of 24 words ranging from 3 to 6 letters. Reading speed was assessed by measuring the time taken to read each one of the 36 phrases of reading tests of PALPA-P. Reading times for each sentence were recorded and converted to reading speed in words per minute using the methodology suggested by Chung [34]. The reading speeds of the two patients were compared with the recommended goal for 9th grade students according to the Portuguese Education Ministry [35]. The difference taken to read the shortest (3-letter words) and longest (6-letter words) words was also analyzed, comparing the time taken to read the six shortest words, with the time taken to read the six longest ones.

### 2.3. Imaging

#### 2.3.1. Anatomical analysis

Imaging was performed on a 1.5-T GE Signa HDxt scanner, using an 8-channel head coil. Structural imaging, both before surgery and after surgery, was obtained with a 3D T1 Spoiled Gradient Recalled Echo (SPGR) sequence of the whole brain (FOV $= 240 \times 240$ mm$^2$, reconstruction matrix $= 256 \times 256 \times 248$, in-plane resolution $= 0.94 \times 0.94$ mm$^2$, slice thickness $= 1.2$ mm$^2$). The postsurgery MRIs were coregistered with their presurgical version, using a rigid body (6 DOF) transformation in the FLIRT software. The brain volume removed by the surgery was quantified by drawing regions of interest (ROIs) in the presurgery MRI using two methods: an “*uncorrected volume*” was obtained by taking into account the difference with the overlapping postsurgical MRI; a “*corrected volume*” was obtained by drawing the surgical ROI on the basis of sulcal and gyral pattern landmarks of the postsurgery MRI (Fig. 1). The latter method provided a larger volume, hopefully closer to the real brain volume removed, due to the correction for the brain shift after surgery. Critical to the purpose of our paper, the latter correction allowed an estimation of the shift along the longitudinal axis of the ventral occipital–temporal cortex.

The overlap of the surgical lesions with the retinotopic areas was obtained after coregistration to the MNI space and a comparison with atlas representations of V1, V2, and V3–V4–V5 obtained from the Julich histological atlas [36] available within FSL [37] (Fig. 2).