Tracking Adult Literacy Acquisition With Functional MRI: A Single-Case Study

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ABSTRACT— We evaluated neuro-functional changes associated with late acquisition of reading in an illiterate adult who underwent 20 longitudinal functional magnetic resonance imaging (fMRI) scans during 2 years, while the participant progressed from complete illiteracy to a modest level of alphabetical decoding. Initially, the participant did not activate neural circuits for reading when he was exposed to words; gradually, however, he began to present activation in left occipitotemporal cortex, at the visual word form area. This increase was accompanied by a decrease in face responses. Reading-related responses also emerged in language-related areas of the inferior frontal gyrus and temporal lobe. Additional activations in superior parietal lobe, superior frontal gyrus and posterior medial frontal cortex suggested that reading remained dependent on effortful executive attention and working memory processes. Nevertheless, the results indicate that adult plasticity can be sufficient to induce rapid changes in brain responses to written words and faces in an unschooled and illiterate adult.

Literacy is a fundamental skill in contemporary society, which is why the neural networks for expert reading have been widely studied (Dehaene, 2009; Jobard, Crivello, & Tzourio-Mazoyer, 2003). Little is known, however, about how the brain system evolves during the process of literacy acquisition, particularly in adults (Abutalebi et al., 2007; Dehaene, Cohen, Morais, & Kolinsky, 2015). In addition to the difficulty of recruiting and scanning illiterate children or adults, there are limitations in the types of data that have been used to explore reading acquisition. Adult functional magnetic resonance imaging (fMRI) studies comparing groups of literate versus illiterate subjects (Dehaene et al., 2010) exhibit imprecisions in localization caused by inter-subject normalization and smoothing, that can mask the details of the literacy acquisition process. Within-subject longitudinal data have been collected in children learning to read (Brem et al., 2010; Saygin et al., 2016), but they rarely offer more than two or three longitudinal data points, and they are still typically analyzed at the group rather than at the single-subject level. For those reasons, in the present work we aimed to acquire a significant amount of successive fMRI data and conduct a 23-month follow-up study of a single adult subject who was initially illiterate and who endeavored to learn to read in his primary language (Brazilian Portuguese).

Various models have tried to explain the process of recognizing words. Common among these models is the belief that learning to read requires a highly organized brain system capable of integrating orthographic, phonological, and lexico-semantic features (Sandak, Mencl, Frost, & Pugh, 2004). Fluent readers appear to use direct connections, both between orthographic form and semantic meaning, and between orthographic representation and phonological lexical representation (Jobard et al., 2003). Although phonological and lexical processes differ, they do interact (Ellis & Batista, 1995). The type of process the reader will use is determined by their level of competence and the linguistic characteristics of the stimulus (Pinheiro & Parente, 1999).

Prior research has determined that learning to read and write changes the brain's structure and function (Carreiras et al., 2009; Dehaene et al., 2010, 2015; Thiebaut de Schotten,

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Cohen, Amemiya, Braga, & Dehaene, 2012). Initial stages of reading acquisition rely primarily on a grapho-phonological decoding process, with resultant activation in areas responsible for letter recognition and for spoken phonology (Goswami, 2008). Very early on in reading acquisition, a specific brain area, located in the left occipitotemporal cortex, known as the visual word form area (VWFA; Cohen et al., 2002), begins exhibiting more intense activation when exposed to written stimuli (Brem et al., 2010) and becomes specialized for the specific script being acquired (Baker et al., 2007; Szwed, Qiao, Jobert, Dehaene, & Cohen, 2014). This specialization for reading is independent of the individual's cultural context, of the language and symbols used (Dehaene, 2009), and even of the modality employed to convey writing, including Braille and auditory sensory substitution in the blind (Reich, Szwed, Cohen, & Amedi, 2011; Striem-Amit, Cohen, Dehaene, & Amedi, 2012). The hypothesis is that this area is activated by the recognition of written words because it identifies elementary shapes and possesses direct connectivity to language areas in the temporal cortex (Bouhali et al., 2014; Cohen & Dehaene, 2004; Dehaene et al., 2015; Hannagan, Amedi, Cohen, Dehaene-Lambertz, & Dehaene, 2015; Mei et al., 2010). The theory of neuronal recycling proposes that literacy acquisition not only increases VWFA activity to reading-related stimuli, but may also negatively impact on the responses of this region to other categories, as reading invades areas dedicated to other functions. Indeed, previous studies have shown how, as reading level increases, the activation to faces and checkerboards decreases in the left hemisphere, and face responses shift toward the right hemisphere (Dehaene et al., 2010; Pegado et al., 2014). Another effect of literacy is to reduce the capacity for invariant recognition of mirrored images (Pegado et al., 2014).

The planum temporale also shows reading-related changes. Its activation to spoken language is nearly doubled in literate individuals compared to illiterate individuals (Dehaene et al., 2010). In expert readers, its activation also increases when the sight of a letter is compatible with a simultaneously heard phoneme (Van Atteveldt, Formisano, Goebel, & Blomert, 2004). This convergence of visual and auditory information is fundamental for literacy acquisition (Blomert, 2011).

Even in the early stages of reading acquisition, there is also activation in the left inferior frontal gyrus (IFG; Church, Coalson, Lugar, Petersen, & Schlaggar, 2008; Gaillard, Balsamo, Ibrahim, Sachs, & Xu, 2003). This region has been associated with various linguistic functions, such as speech planning and comprehension (Price, 2012), grapheme–phoneme conversion (Jobard et al., 2003), semantics (Binder & Desai, 2011), and lexical access (Heim, Wehnelt, Grande, Huber, & Amunts, 2013). Recent studies showed that there is a convergence among children and adults in IFG activation during reading, and a small left dorsal precentral gyrus cluster that showed heightened activation with increasing age (Martin, Schurz, Kronbichler, & Richlan, 2015).

In summary, in a fluent reader circuits emerge for the efficient extraction of both phonological and semantic information from the written word (Jobard et al., 2003). Only greater proficiency helps readers to identify all letters of a word simultaneously and relay this information to the anterior fusiform and middle temporal gyrus (Church et al., 2008). Jobard et al. (2003) postulate that direct access from word shape to meaning occurs through the coactivation of the prelexical occipitotemporal junction in the fusiform gyrus and semantic areas, such as the inferior temporal, the posterior middle temporal, and inferior frontal gyri.

In the present study, using fMRI, we aimed to probe whether some or all of those reading-induced brain changes could be detected at the single-subject level. We had the unique opportunity to study the fMRI correlates of reading acquisition in a single illiterate adult participant who voluntarily underwent 20 fMRI sessions over a 23-month period. Thus, we could monitor the progressive evolution of preferences for reading-related and reading-unrelated stimuli within the same identified voxels. Our goals were to (1) test whether adult brain plasticity allows for increasing activations to words, particularly in the VWFA, as an adult turns from illiterate to literate; and (2) evaluate whether this increase with literacy is accompanied by a decrease in nonreading-related activations for checkers and faces.

METHOD

Participant

The participant was a 45-year-old Brazilian illiterate, Portuguese language speaking, right-handed man, with no significant medical history; no neurological, sensory, or psychiatric disorders; and on no medications. Brain MRI showed no abnormalities. He worked as an assistant janitor, showed no problems performing his work duties, and was functional when handling money and practical matters of daily living. He was raised in a rural area, did not attend school or receive any formal education, and helped his family with farming chores. There are no reports of language or speech delays, nor of learning disabilities in practical situations common to the rural setting in which he was living at that time. His parents were illiterate, as was his grandfather, who raised him. In Brazil, there are still regions with high rates of illiteracy and populations with very limited formal education, particularly in the north and northeastern parts of the country (Instituto Brasileiro de Geografia e Estatística, 2015).

This research project was approved by the Ethics Committee of the SARAH Network of Neurorehabilitation Hospitals.

Measurement of Skill Acquisition

In order to verify the participant's reading skills prior to undergoing the reading acquisition process, he underwent a battery of simple neuropsychological tests as previously described (Dehaene et al., 2010). The Mini-Mental State Examination (MMSE) was used to screen for cognitive impairment, using data standardized for the illiterate population (Brucki, Nitrin, Caramelli, Bertolucci, & Okamoto, 2003).

For assessment and follow-up of the literacy acquisition process, the participant was given other specific neuropsychological tests, such as the phonological awareness test (PAT; Capovilla & Capovilla, 1998), to determine the individual's ability to manipulate speech sounds. When the participant started reading words, he was given a reading speed task with four lists (monosyllabic words, disyllabic words, monosyllabic pseudo-words, and disyllabic pseudo-words). Each list was comprised of 10 words and 10 pseudo-words that had to be read as quickly as possible. The assessment instruments were administered one day before the fMRI, done month to month.

Before intervention, the participant correctly named all the images on a picture-naming task and, from the 26-letter alphabet, could recognize only three capital letters ("A," "O," and "M"). He was able to just write the first letter of his name ("M"). On the MMSE, his performance was within the expected range for illiterates. The subject scored 0 in the reading and PAT tests. He also showed no mastery of grapheme–phoneme correspondences, or supra-segmental aspects of language (rhyme and alliteration).

Process of Literacy Acquisition

The participant was taught to read by two teachers during 1-hr classes twice weekly using a didactic approach developed by Paulo Freire which has been widely used in Brazil for teaching young adults and adults to read and write. This model centers on defining words associated with the student's real life setting (Brandão, 1981). The syllabic method, which combines syllables to form words (Corrêa, 2003), was used concurrently with the Freire model.

In the first 16 months of the literacy acquisition process, the participant began recognizing more letters and could write his own name. Thirteen fMRIs were run during this period. However, he still could not perform syllabic synthesis, because he had difficulty relating graphemes and phonemes (Table 1). Some aspects of phonological processing may not be spontaneously acquired because they are modulated by learning an alphabetic written language (Petersson, Reis, Askelöf, Castro-Caldas, & Ingvar, 2000). Thus, at month 17, we increased stimulation using the phonic method (Capovilla & Capovilla, 2007), which teaches how to read by correlating sounds with letters and groups of

Table 1

Performance in the Phonological Awareness Test (PAT)

Item set	Month			
	0	17th	23rd	25th
Syllabic synthesis	0	3	4	4
Phonemic synthesis	0	2	4	3
Rhymes	0	0	3	4
Alliteration	0	3	4	4
Syllabic segmentation	0	3	4	4
Phonemic segmentation	0	0	0	0
Syllabic manipulation	0	2	2	2
Phonemic manipulation	0	0	0	0
Syllabic transposition	0	2	2	4
Phonemic transposition	0	0	0	0
Total (max = 40)	0	15	23	25

Note. Month 0 = before start of literacy acquisition process; 17th month = start of phonological stimulation; 23rd month = end of phonological stimulation; 25th month = follow-up. Maximum points for each item set = 4.

letters; as well as specific stimulation of phonological awareness. This stimulation was conducted by two speech therapists, comprising two 50-min sessions weekly, for a period of 7 months.

As stimulation of the meta-phonological skills became more intense, we noticed better performance in syllabic tasks and increased supra-segmental skills (rhyme and alliteration) in relation to phoneme skills (Table 1).

Furthermore, we also added an assessment of reading speed at month 17, and noted steady improvement in the accuracy and speed of reading real words, monosyllabic and disyllabic words, although the participant remained unable to read pseudo-words (Table 2). After 23 months of literacy acquisition efforts, he had become a functional reader. The behavioral data showed gradual gains during the literacy process and changes in daily life were identified. As the subject's reading skills improved, so did his independence; he began needing less assistance from others when he wanted information about such things as public transportation, market items, and signs in public or work places.

fMRI Assessment

Stimuli

During each fMRI scanning session, five types of visual stimuli were used: sentences, faces, checkerboards, stars, and rest (fixation cross). Sentences were split in two parts, each comprising 1–3 written words (e.g., "the window … is new"). The entire sentence contained a maximum of five words and an average of 12 letters. Faces stimuli comprised two consecutive parts, each consisting of one picture of a human face. Checkerboards were a circular checkerboard constantly expanding by 1% every 25 ms. As in our previous work (Dehaene et al., 2010), the stars were presented to test the participant's attention: throughout the exam, he was

Table 2
Performance in Reading Speed Tasks (Number of Words Read per Minute)

Task item	Month							
	17th	18th	19th	20th	21st	22nd	23rd	25th
Monosyllabic words	3	5	3	4	4	4	5	6
Disyllabic words	2	2	3	4	3	4	6	7
Monosyllabic pseudo-words	0	0	0	0	1	0	0	1
Disyllabic pseudo-words	0	1	0	0	0	0	1	2

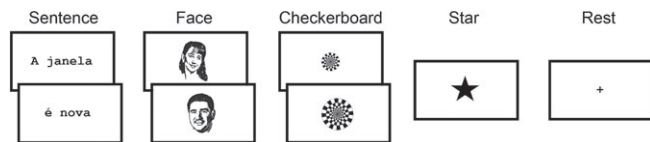*Notes.* 25th month = follow-up. Maximum points for each task item = 10.

Fig. 1. Examples of stimuli used for fMRI scanning.

asked to push a response button whenever a star appeared. Finally, at rest, the participant fixated on a central fixation cross (Figure 1). All of these stimuli were black against a white background and positioned in the center of the screen.

Experimental Design
The protocol involved fMRI runs that lasted about 4 min, each of which we ran five times on a given scanning session. The experiment used an event-related design, with the sequence of stimuli appearing in random order. Sentence, face, checkerboard, and rest trials appeared 10 times each; the star appeared five times. The participant was instructed to read the sentences silently and to simply watch the faces, checkerboards, and fixation cross. To reduce the possibility of stimulus-specific learning, each sentence was drawn from a database of 50 sentences and each face was drawn from a set of 43 images, both randomly without repetition.

Each sentence and face trial comprised a sequential presentation of stimuli in the following order: first part of the stimulus (2,000 ms); blank screen (100 ms); second part of the stimulus (2,000 ms); fixation cross (1,900 ms). A checkerboard trial consisted in: checkerboard (1,000 ms); blank screen (1,000 ms); checkerboard (1,000 ms); blank screen (1,100 ms); fixation cross (1,900 ms). The star trials included three sequences: a star (1,000 ms); a blank screen (1,100 ms); and a fixation cross (1,900 ms). Duration of the star stimulus, however, varied. When the participant pressed the response button, the star disappeared and was replaced by a blank screen. In the rest trial, a fixation cross was shown on the screen for 4,000 ms.

The protocol was written in e-Prime software (Psychology Software Tools) and was presented using the IFIS

Presentation Solution (MRI Device). Visual stimuli (images) appeared on an LCD screen (MRI-compatible 12×17 cm^2). An MRI-compatible response key was used to record the patient's responses.

fMRI Acquisition
Data were acquired on a SIEMENS Magnetom Trio A Tim System 3-Tesla MRI with 3 T Head Matrix. A 3D MPRAGE sequence was used for anatomical image (176 sagittal slices, FoV = 256 mm^2, slice thickness = 1 mm, gap = 0.5 mm). An EPI echo sequence was used for each run (33 slices, matrix = 64×64 mm^2, FoV = 192 mm^2, slice thickness = 4 mm, no gap, TR = 2,000 ms, TE = 30 ms). Two scans were added at the start of each run and discarded in the analysis.

Data Processing and Statistical Analysis
fMRI data analyses were performed using SPM12 (http://www.fil.ion.ucl.ac.uk/spm). For maximal accuracy, an anatomical template of the patient was created using all 20 anatomical volumes. First, all anatomical scans were separately normalized using SPM's standard T1 template. Then, the normalized anatomies were averaging to generate a participant-specific template, to which all data were then re-normalized. Functional images were corrected for motion and slice acquisition time and realigned to the participant's mean image. Imaging data were then normalized into standard stereotaxic MNI space (Montreal Neurological Institute, McGill University, Montreal, Canada). Images were resampled using fourth degree spline interpolation and smoothed with a 5-mm FWHM Gaussian kernel to increase signal-to-noise ratio in the images. The data were high-pass filtered (128 s) to remove low-frequency noise components and corrected for autocorrelation assuming an AR(1) process. Brain activity was convolved over all experimental trials with the canonical haemodynamic response function (HRF).

Because a single participant was scanned, the statistical analysis was performed by grouping all runs from the fMRI protocol in a single first-level general linear model (GLM).
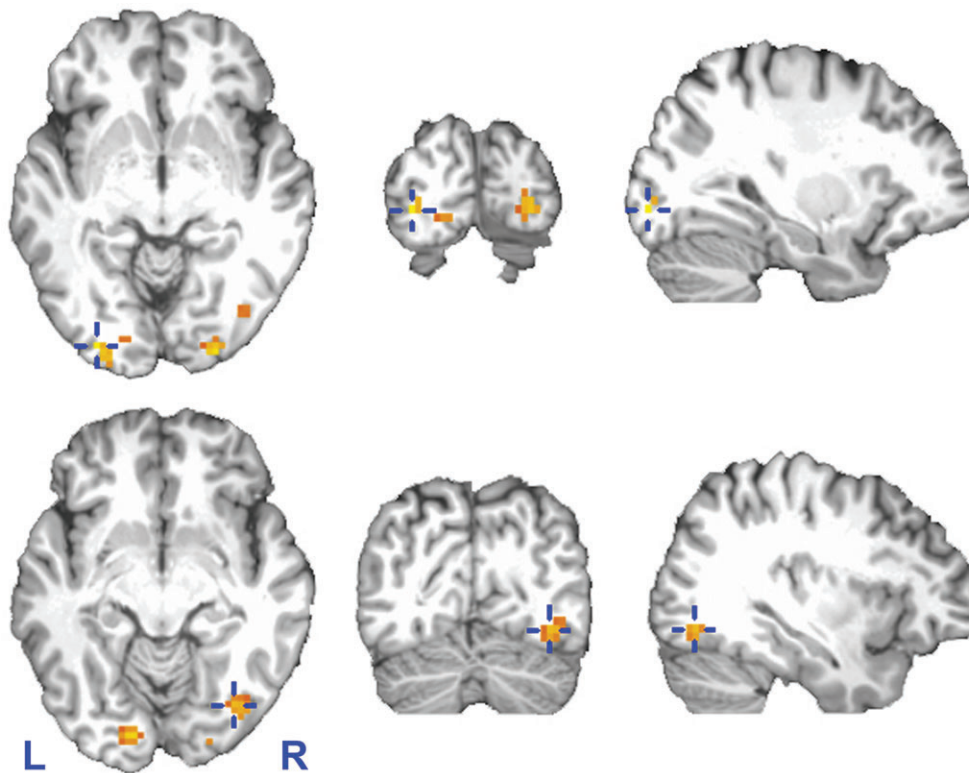
Fig. 2. Brain activation for the sentence versus rest contrast before literacy acquisition. Peak activations are at (−30, −91, −6) and (36, −73, −10).

The analysis was performed with a total of 100 runs (20 sessions, each comprising 5 runs). The sessions were divided into first session, last session, first phase (period before phonological intervention), and second phase (period during phonological intervention in the learning process). To identify voxels in which the fMRI signals evolved with time, each contrast (e.g., sentence—rest) was modulated with a mean-corrected covariate that was a linear function of the time elapsed since the first MRI (Ward, Brown, Thompson, & Frackowiak, 2006).

Resulting statistics were considered significant at voxelwise $p < .001$ (uncorrected) with a minimum cluster size of 10 voxels and clusterwise $p < .05$, corrected for multiple comparisons across the whole-brain volume using the false detection rate (FDR).

RESULTS

The results allowed us to monitor the progressive emergence of activation in the occipitotemporal region, as well as in other parts of the reading network, and to formulate hypotheses about the network that supported reading acquisition, in parallel with the progress evidenced in the behavioral data.

Emergence of the Reading Network

The first session before the start of literacy acquisition showed only bilateral activation in the middle occipital gyrus (Figure 2) for the sentences versus rest contrast (S > R).

Analysis of the linear growth of the same contrast (S > R) across time for all sessions showed the emergence of part of the reading network (Table 3). In the left hemisphere, one of the main activation sites was in the left inferior temporal gyrus, at coordinates close to the VWFA (−48, −55, −10), as well as a nearby but more mesial location in the fusiform gyrus (−27, −61, −10). Additional sites were found in the left middle frontal gyrus, in three regions of the left IFG (pars triangularis, rolandic operculum, and pars orbitalis), in the left precentral gyrus and in the right inferior occipital gyrus.

Despite more intense activation and a predominance of clusters in the left hemisphere, there was nonetheless considerable bilaterality (Figure 3), including right-hemispheric activations in areas homologous to Broca's region (pars opercularis and pars triangularis) and to the VWFA, as well as pars orbitalis and precentral gyrus.

Two large areas were recruited for reading sentences. The first extended from the middle occipital gyrus to the superior parietal lobe, in each hemisphere (Figure 4). The second comprised a series of clusters suggestive of an activation arc, from the left precentral gyrus, passing through the superior

Table 3
Activation Peaks of the Reading Network

Contrast	Brain region (area)	MNI			Cluster size	z score	Peak
		x	y	z			
Sentence vs. rest	LH fusiform gyrus (area FG1)	−27	−61	−10	380	>8	2
(S > R)	LH inferior temporal gyrus[a]	−48	−55	−10		6.93	1
Modulation over	LH precentral gyrus	−45	2	38	1080	>8	9
Time	LH precentral gyrus[a]	−45	−7	58		>8	8
(Mod time)	LH middle frontal gyrus[a]	−45	20	46		>8	3
	LH inferior frontal gyrus (area 45)[a]	−48	17	30		>8	4
	LH inferior frontal gyrus (area 45)[a]	−51	29	−2		>8	5
	LH inferior frontal gyrus, pars orbit.[a]	−45	35	−10		>8	7
	LH inferior frontal gyrus (area 44)[a]	−54	8	2		>8	6
	RH inferior frontal gyrus (area 44)	48	5	26	330	>8	11
	RH inferior frontal gyrus (area 45)[a]	51	20	18		>8	12
	RH inferior temporal gyrus	48	−55	−14	982	>8	13
	RH inferior frontal gyrus, pars orbitalis	45	32	−10	173	5.85	14
	RH precentral gyrus	54	−4	50	330	4.23	15
	LH superior parietal lobe (area 7A)	−27	−70	54	868	>8	16
	LH superior frontal gyrus	−24	−1	58	127	>8	17
	RH superior frontal gyrus	27	−1	54	111	>8	20
	LH posterior medial frontal	−3	8	54	305	>8	18
	RH posterior medial frontal[a]	6	11	54		>8	21
	RH superior occipital gyrus	30	−67	42	982	>8	19
	RH inferior occipital gyrus (Area V3d)[a]	27	−91	10		7.12	10
Sentence vs. rest	LH superior temporal gyrus	−54	−40	14	16	4.18	22
(S > R)	LH temporal pole	−45	14	−18	217	5.63	23
Modulation on	LH middle temporal gyrus[a]	−45	−4	−22		4.62	25
Monosyllabic score	LH middle temporal gyrus	−54	−49	14	34	3.79	24
(Mod monosyllabic)	RH middle temporal gyrus	54	−58	6	51	5.44	27
	RH temporal pole	57	14	−18	101	6.34	26
Sentences vs. checkerboard (S > C)	LH temporal pole	−48	14	−18	40	4.97	29
	LH superior temporal gyrus[a]	−51	−1	−10		3.67	28
(Mod monosyllabic)	LH middle temporal gyrus	−57	−10	−14	11	4.43	30
	RH temporal pole	45	17	−18	61	5.56	31
	RH temporal pole	57	14	−18	61	4.43	32
	RH middle temporal gyrus	57	−58	10	23	4.37	33
	RH middle temporal gyrus[a]	48	−49	14		4.31	34
Sentences vs. faces	LH temporal pole	−48	8	−18	76	5.02	36
(S > F)	LH superior temporal gyrus[a]	−51	−4	−14		3.66	35
(Mod monosyllabic)	LH middle temporal gyrus[a]	−57	−10	−14		4.21	37

Notes. LH = left hemisphere; MNI = Montreal Neurological Institute; RH = right hemisphere. Areas are based on the SPM Anatomy Toolbox (http://www.fz-juelich.de/inm/inm-1/DE/Forschung/_docs/SPMAnatomyToolbox/SPMAnatomyToolbox_node.html).
[a]Secondary peak.

frontal and the posterior medial frontal gyri, crossing over to the other hemisphere, through the same areas, up to the right precentral gyrus (Table 3).

Next, we examined whether the observed changes were specific to reading-related stimuli. The contrasts for a linear increase in activation to faces versus rest (F > R) or to checkerboard versus rest (C > R) with time for all sessions yielded no significant voxels. The same was true for both, faces versus checkerboard (F > C) and checkerboard versus faces (C > F). Further, the contrasts for a linear increase in sentences versus faces (S > F) or sentences versus checkerboards (S > C) with time yielded results virtually identical to those for the sentence versus rest contrast (Table 3). Thus, the observed increase was specific to written words.

Brain Activation as a Function of Reading Performance
During the last 7 months (second phase), as reading performance became measurable, we correlated brain activation with reading speed (Table 2). The S > R contrast, correlated with the number of monosyllabic words that could be read in 1 min, revealed activations in left posterior superior temporal gyrus, left temporal pole, and left middle temporal gyrus (Table 3). Again, despite the predominance of voxels in the left hemisphere, similar activations were seen at the right temporal pole and in the right middle temporal gyrus.

We examined the reproducibility of these results when comparing sentences with other categories of stimuli. The S > C and S > F contrasts, modulated by performance in reading monosyllabic words (second phase), exhibited more restricted activations in the temporal lobe (Table 3). S > C
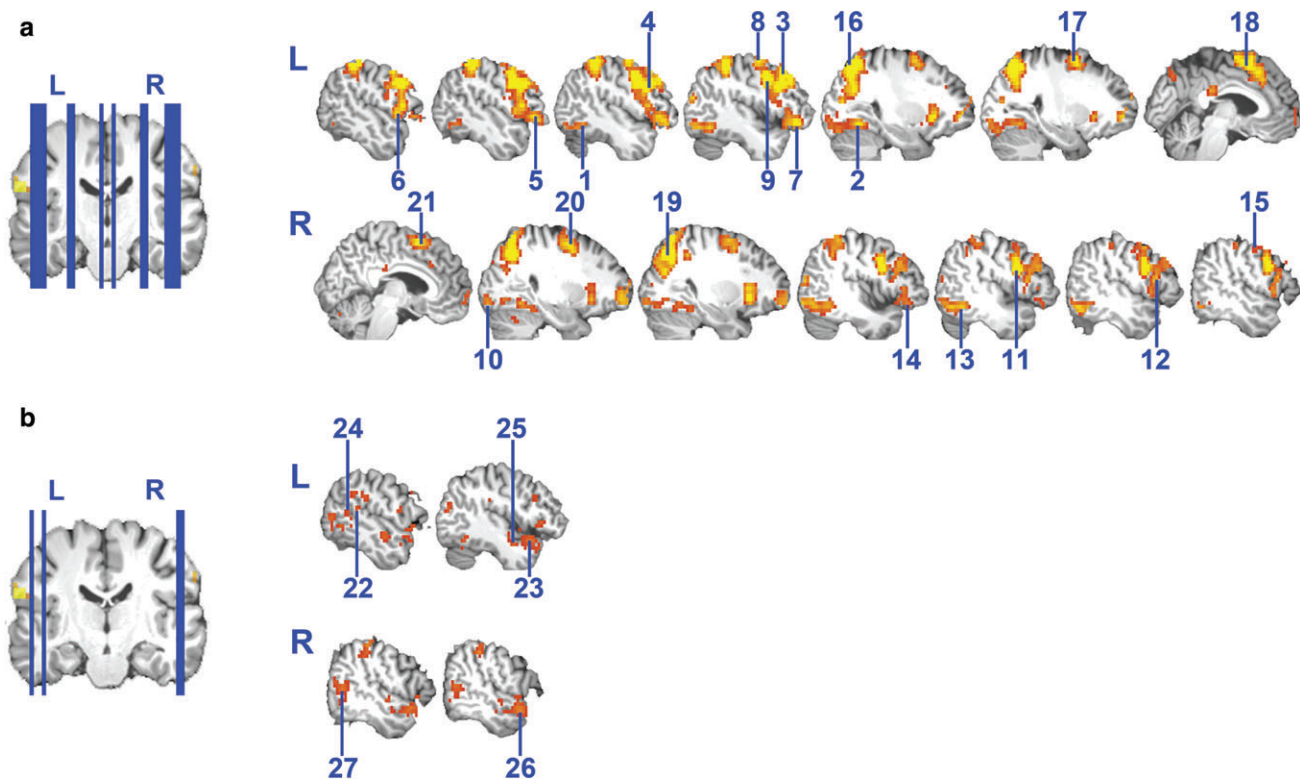
Fig. 3. Statistical map of activation sites for sentence stimuli. Peak numbers correspond to Table 3. Thresholded at $p < .001$ (uncorrected) and clusterwise $p < .05$, false discovery rate corrected. (a) Activations for the contrast S > R Mod Time. (b) Activations for the contrast S > R Mod Mono.

activated the left superior temporal gyrus, as well as temporal pole and middle temporal gyrus, both bilaterally. S > F showed activation in left superior temporal gyrus, left temporal pole, and left middle temporal gyrus. Again, face versus checkerboard (F > C) and checkerboard versus face (C > F), modulated by reading performance, yielded no significant voxels of activation.

Changes in the VWFA

We then focused on signal change at the VWFA site, as identified earlier (linear increase in S > R Mod Time). There were significant changes in the VWFA region (Figure 5). Initially, activations were confined to the occipital lobe. Over time, additional activations appeared more anteriorly in ventral occipitotemporal cortex. The same process occurred in the right hemisphere.

We plotted the contrast estimates of the activation signal at the VWFA site $(-48, -55, -10)$ where we had found a positive correlation between sentence processing and learning time (Figure 6). The activation was initially identical for words, faces, and checkerboards, but word-induced activity increased steadily with time. A significant increase was seen even from the first to the second scanning session. A slightly negative but nonsignificant correlation was observed

between time and the activation to faces $(r = -.36, p = .117)$ and to checkerboards $(r = -.36, p = .122)$.

Competition With Other Categories of Stimuli

We also examined whether reading acquisition resulted in a cortical competition with other stimuli (Dehaene et al., 2010; Dundas, Plaut, & Behrmann, 2013; Pegado et al., 2014). We assessed whether there were any changes in activation for faces. First, we used a whole-brain search to check if there was increased activation in F > R and F > C over time in all sessions. We did not find any. With regards to a decrease in the faces contrast (F > R) over time in the sessions before the phonological intervention (first phase), we did find a peak very near the VWFA area, only one voxel away from the main peak, at $(-48, -58, -10, z = 5.03)$. There was no decrease in faces relative to checkerboards (F > C).

Finally, we checked the linear decrease of C > R in all sessions, and found two bilateral clusters with secondary peaks close to the VWFA and its homologous location in the right hemisphere. The first peaked at $(27, -91, -6, Z > 8)$ with subpeak at $(45, -58, -22, Z = 5.40)$. The second peaked at $(-27, -64, -10, Z = 5.41)$ with subpeaks at $(-45, -70, -14, Z = 5.04)$ and $(-30, -49, -14, Z = 4.81)$.

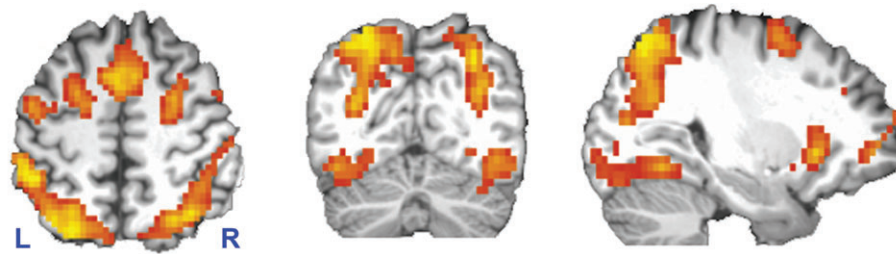**Fig. 4.** Increases in dorsal activation to sentences versus rest (S > R) as a function of time (−27, −70, 54). The image on the left (axial slice) also shows the activation arc passing through the left precentral gyrus, superior frontal, and right precentral gyrus.
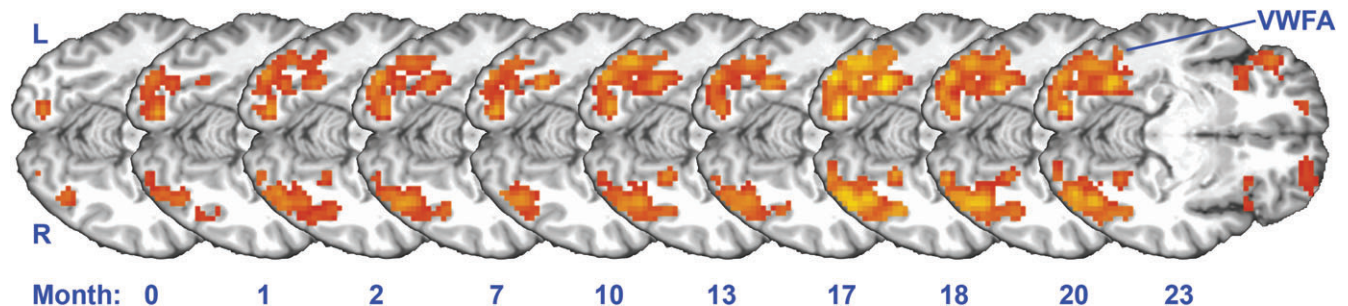

Fig. 5. Evolution of activation to sentences versus rest at and around the VWFA site. The image on the far left corresponds to the first session performed before literacy acquisition (month 0), while the image on the far right represents the last session (month 23).

DISCUSSION

The aim of this study was to explore the functional evolution of the neuronal network for reading when literacy is acquired during adulthood. The results showed that the participant began to gradually activate areas partially similar to those seen in fluent readers. The present findings confirm previous research in a group of ex-illiterate adults, which indicated that they used the same neuronal networks as individuals who learned to read as children (Dehaene et al., 2010).

The participant's reading skills evolved over the course of the study, from identifying only a few letters, to reading simple words. This progress was corroborated by the behavioral and functional findings. His reading skills still relied heavily on executive functions, resulting in a slow and effortful process of grapheme–phoneme decoding. There was, therefore, a consequent slowness to his reading, and the subject exhibit considerable difficulties in reading pseudo-words or complex syllabic pattern words. Adult learners should be able to read at least one short word every 1 or 2 seconds with about 95% accuracy at the end of a literacy course, although this performance level may be hard to attain (Abadzi, 2003). Few ex-illiterates are able to read more than 50 words per minute (Dehaene et al., 2015). The present subject, with a reading rate of 6–7 short words per minute, was clearly on the lower end of this spectrum.

Given those behavioral difficulties in acquiring reading, it is all the more striking that fMRI revealed a gradual activation of the whole word reading network. In particular, as predicted, the participant exhibited a progressive activation of the VWFA in the course of literacy acquisition. We previously reported group differences in the VWFA activation evoked by letter strings between illiterate and literate individuals, with ex-illiterates showing an intermediate level of activation in direct proportion to their intermediate reading skills (Dehaene et al., 2010). The present results, using a within-participant design, confirm and qualify those earlier findings. We observed that the VWFA activation appeared very early in the learning process (Figure 6), as also reported for young children (Brem et al., 2010). The VWFA is involved in visual recognition of letters (Cohen et al., 2002), so it might be expected to emerge prior to the areas that interpret sounds or words.

Previous results have also suggested that reading acquisition induces a competition for cortical space in and around the VWFA (Dehaene et al., 2010, 2015). Accordingly, we found a small but significant decrease in activation to faces right next to the left-hemispheric VWFA peak. This result fits with a growing list of experimental results (Dehaene et al., 2010, 2015; Dundas et al., 2013; Monzalvo, Fluss, Billard, Dehaene, & Dehaene-Lambertz, 2012; Pegado et al., 2014), which indicate that faces and written words occupy distinct but neighboring locations in the left occipitotemporal cortex, and that the growth of word-related responses induces a shift in the boundary between these two preferences and thus a relative decrease in the left-hemispheric
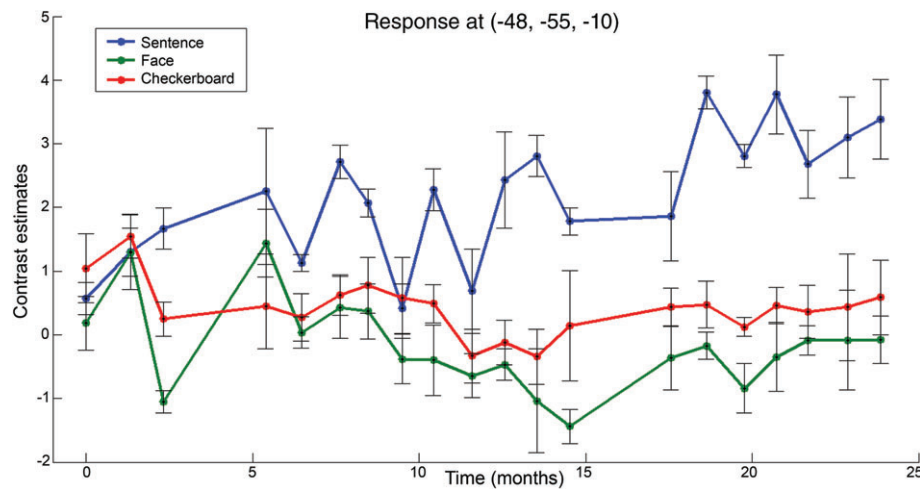
Fig. 6. Contrast estimates (*y*-axis) at the VWFA coordinates (−48, −55, −10) throughout the literacy acquisition process (*x*-axis).

response to faces. Importantly, however, we did not find any significant increase in activation to faces in the right hemisphere, as was reported when comparing early-schooled literates versus illiterates (Dehaene et al., 2010). This finding may suggest that this lateralization shift is dependent on childhood plasticity and/or more extensive practice with reading.

Interestingly, we found bilateral changes in the IFG, with predominance of the left hemisphere. Bilateral changes were also seen in the temporal pole and in the middle temporal gyrus. Unilaterally there was activation in the left posterior superior temporal gyrus. Changes in the superior temporal gyrus and in the inferior frontal may indicate that the participant started to understand the meaning of what he read (Moore & Price, 1999). With the improvement of reading skill, it has been suggested that there is a decrease in participation of the right hemisphere (Poldrack, Desmond, Glover, & Gabrieli, 1998). Supporting this hypothesis, tests conducted in 5-year-old children with preliteracy skills reported that they initially recruited bilateral temporoparietal regions (letters > false font). Later, they began activating only the left hemisphere, suggesting that literacy development requires greater participation of the right hemisphere during the early stages (Yamada et al., 2011), as in the case of the participant in this study.

One may suggest some similarities between the present study and the neuronal network activated when learning a second language. Comparisons between reading in one's native language (L1) and reading in a foreign idiom acquired in adulthood (L2) reveal that the same areas are used (Abutalebi, 2008). However, differences in intensity were noted between L1 and L2: while L1 provokes greater activation in the temporal regions, L2 activates more in the frontal and parietal regions (Feng, Chen, Zhu, He, & Wang, 2015). The participant in this study also demonstrated a similar pattern, with large clusters and intense activity in the frontal and parietal regions, as seen in the acquisition of a second language in adulthood. These activations in the frontal areas may be associated with a support system for learning, with the greater use of executive functions of self-monitoring and executive attention (Horowitz-Kraus & Hutton, 2015). Indeed, the participant showed intense bilateral activation in three areas related to effortful attention and learning: the superior parietal lobule, the posterior-medial frontal, and the superior frontal gyri. The superior parietal lobe is usually associated with sustaining attention (Klarborg et al., 2013) and the level of visual attention (Fiez et al., 1995). The posterior-medial frontal region participates in performance monitoring, evaluating responses, and signaling the need for adjustments (Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004). The superior frontal gyri, especially the left one, are involved in active manipulations in working memory tasks (Klingberg, Forssberg, & Westerberg, 2002). The results found in this study may suggest that these areas play an important role in learning when greater attention is needed because the words are not yet familiar. Given the complexity of the literacy acquisition process, which demands focused attention, rapid processing, error monitoring, and working memory for decoding the successive letters within a word, it seems unsurprising that effortful reading acquisition, in an illiterate adult, relies on executive functions (Horowitz-Kraus & Hutton, 2015).

Methodologically, the single-subject design that we used presents both advantages and problems. Finding a healthy adult at the start of a literacy process who is willing to undergo fMRI exams over a prolonged period is a rare opportunity, and it would not be easy to perform an equivalent group study. Furthermore, a single-subject longitudinal design proves that the very same voxel can change in a few

months during adult reading acquisition, thus alleviating the doubts arising from the smoothing and normalization inherent in traditional group fMRI studies. Still, a central difficulty is that, with a single case, we cannot ascertain whether the results would generalize to other individuals, especially given that our subject experienced somewhat unusual difficulties in acquiring reading and never became a fluent reader. Future studies should clearly attempt to explore literacy acquisition in a larger number of single subjects. Another important issue with single-case studies is the imperfect reliability of the fMRI data. One way to enhance the statistical power of fMRI results is to increase the number of trials (de Bertoldi et al., 2015). For this reason, five 4-min fMRI runs were acquired in each session, for a total of 20 sessions. The present study makes it very clear that, under those conditions, fMRI can be reliable at the single-subject level. This conclusion is, in fact, supported by other much shorter studies in educated adults, such as the single-subject 6-min localizer approach developed by Pinel et al. (2007). The key methodological aspect is to acquire enough data within each subject, and with a high signal-to-noise ratio. Recently single-case fMRI studies also used the approach of acquiring a large number of sessions within the same subject (Laumann et al., 2015; Poldrack et al., 2015).

Another limitation of the present study is that the patient was asked to read the stimuli mentally, and therefore we could not evaluate reading performance inside the scanner. In fact, given the presentation duration of 2 s per word, it cannot be taken for granted that the participant was able to fully read the words or even sentences. While this is unfortunate, presentation duration had to be determined at the beginning of our study, in order to monitor reading acquisition with a fixed design, and at that time 2 s per word seemed a reasonable value. Although the average reading time on the behavioral test was longer than the stimulus time in the scanner, we observed during classes that the participant was able to read simple words more quickly than average time (e.g., *bola* and *casa*, respectively *ball* and *house* in English). This variation in reading speed is consistent with the literacy acquisition process. Furthermore, given the activation that we observed in the WFA, left IFG, and left posterior superior temporal gyrus, it seems highly plausible that the participant at least attempted to read the words.

In summary, this study permitted a first analysis of the evolution of the reading network during its formation in a single, initially illiterate adult. The present results demonstrate that adult plasticity is sufficient for literacy acquisition at a late age, in the absence of any early schooling and literacy. They also show that, as the VWFA grows, there is a competition with face responses even in the adult brain. In addition, our data suggested that literacy development requires greater participation of the right hemisphere during the early stages and activation in the frontal areas that may

be associated with learning. It is still recommended that a larger sample be studied, in order to demonstrate the generality of the conclusions about the neuro-functional changes that occur during reading acquisition in adulthood.

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