Left cortical specialization for visual letter strings predicts rudimentary knowledge of letter-sound association in preschoolers

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Reading, one of the most important cultural inventions of human society, critically depends on posterior brain areas of the left hemisphere in proficient adult readers. In children, this left hemispheric cortical specialization for letter strings is typically detected only after approximately 1 y of formal schooling and reading acquisition. Here, we recorded scalp electrophysiological (EEG) brain responses in 5-y-old (n = 40) prereaders presented with letter strings appearing every five items in rapid streams of pseudofonts (6 items per second). Within 2 min of recording only, letter strings evoked a robust specific response over the left occipito-temporal cortex at the predefined frequency of 1.2 Hz (i.e., 6 Hz/5). Interindividual differences in the amplitude of this electrophysiological response are significantly related to letter knowledge, a preschool predictor of later reading ability. These results point to the high potential of this rapidly collected behavior-free measure to assess reading ability in developmental populations. These findings were replicated in a second experiment (n = 26 preschool children), where familiar symbols and line drawings of objects evoked right-lateralized and bilaterally specific responses, respectively, showing the specificity of the early left hemispheric dominance for letter strings. Collectively, these findings indicate that limited knowledge of print in young children, before formal education, is sufficient to develop specialized left lateralized neuronal circuits, thereby pointing to an early onset and rapid impact of left hemispheric reentrant sound mapping on posterior cortical development.

EEG | letter strings | children | cortical specialization | left hemisphere

Adult expert reading, a complex yet effortless and fast process (i.e., occurring at an average of 200 ms per word; ref. 1), critically depends on the left ventral occipito-temporal cortex (2). This left hemispheric specialization is thought to arise during children's reading acquisition through reentrant mapping of sound representations in the left temporal and frontal cortices to letter representations in ipsilateral posterior areas (3–5). Even though the exact onset of this leftward specialization is not known, this process appears to take considerable time during formal reading acquisition (6–8).

Functional magnetic resonance imaging (fMRI) reveals the typical left lateralized adult-like brain pattern for letter strings only in proficient readers (ref. 9 for a metaanalysis) and in natural settings, significant left lateralization appears only when children have already acquired formal reading ability, approximately at 7 y of age (10). In developmental studies with direct measures of brain activity (electro/magneto-encephalography, EEG/MEG), the typical reading adult occipito-temporal response evoked by letter strings at approximately 200 ms after stimulus onset (i.e., N1 or N170; refs. 11 and 12) is absent in preschool children, even if they can already categorize or name letters. Typically, sensitivity to print has been shown after 1 y (13), or 1.5 y of schooling (14), thus, after formal reading education. Moreover, whereas N1 tuning for letter strings can be induced in preschool children with relatively short grapho-phoneme training, this tuning is neither left-lateralized nor long-lasting, disappearing within a few weeks after training interruption (15). Collectively, these findings, as well as the relatively small amount of available data in preschool children, suggest that the left hemispheric specialization for letter strings emerges only after formal instruction or intensive training. That is, a relatively high level of automatization in letter-speech sound associations appears necessary for left hemispheric posterior lateralization to print, taking time, cognitive resources, and explicit teaching. This process could occur either through phonological mapping (16) or audiovisual integration (7).

The apparent late onset of left cortical specialization for print is quite surprising, because preschool children typically present some letter knowledge, this knowledge being one of the most important predictors of subsequent reading proficiency (17, 18). Thus, if letter knowledge is not only perceptual but also involves grapho-phoneme associations, neural specialization for print would be expected to start earlier and/or take place much faster than usually thought. Unfortunately, fMRI is not well-suited for young (preschool) children, making clarification of the onset time of left cortical specialization for print difficult (19, 20). As for standard EEG approaches, they require many trials to reach acceptable levels of signal-to-noise ratio (SNR) and, thus, may be unable to detect this early left cortical specialization in young children in short recording sessions. Being able to do so would have important theoretical and societal consequences, because it would reveal that rudimentary letter knowledge following exposure in natural settings suffices to induce cortical specialization for this category of stimuli. Furthermore, it could open new perspectives to assess reading at an early age and throughout development.

Here, we test the hypothesis of an early left lateralized specialization for print in preschool children (experiment 1: $n = 40$, mean age = 5.5; experiment 2: $n = 26$, mean age = 5.8) by means

Significance

This study reports a robust and specific marker of sensitivity to print in 5-y-old prereaders, in the form of an electrophysiological response recorded over visual areas of the left hemisphere in only 2 min. The significant correlation with rudimentary letter knowledge in preschoolers, a behavioral measure taken independently, suggests rapid domain-specific specialization of neuronal circuits, beyond mere visual familiarity. These findings also highlight the potential of an objective and highly sensitive behavior-free approach to assess letter knowledge, a precursor of reading ability, in developmental populations.

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of a recently developed EEG approach in which deviant stimuli ("oddball") are inserted periodically within rapid periodic streams of standard stimuli ("base") (Fig. 1 and Movie S1). Compared with standard event-related potential (ERP) measures, this Fast Periodic Visual Stimulation (FPVS) approach is highly sensitive (i.e., high SNR; refs. 21–23). Hence, in a recent study, it provides a posterior left-lateralized differential response between words and control characters (pseudofonts) in adults, which is significant in every participant, in a few minutes only (24). Here, in experiment 1 with preschool children, we contrast letter strings (words or pseudowords) inserted periodically (1/5 items) within pseudofonts, as well as words within pseudowords, at a fast rate of 6 items per second (Fig. 1). In experiment 2, we compare letter strings discrimination to the discrimination of other high contrast/spatial frequency stimuli varying in visual familiarity: familiar keyboard symbols vs. pseudosymbols, unfamiliar foreign script vs. pseudoscript, and line drawings of objects vs. pseudodrawings. In all conditions, if oddball stimuli are discriminated from base stimuli, a response is expected exactly at 1.2 Hz (i.e., 6 Hz/5) and its harmonics (such as 2.4 Hz), providing an objective (i.e., experimentally predefined) marker of visual discrimination in the EEG spectrum (e.g., ref. 24).

Testing preschool children with this approach before formal reading acquisition also provides a unique opportunity to evaluate the relationship between a putative early left cortical specialization for letter strings and behavioral measures of prereading ability (Table 1 for description of behavioral results). Although an early left lateralization may be due to low-level visual feature sensitivity (e.g., high spatial frequencies; ref. 25), its association with individual differences in letter knowledge, together with a bilateral or right lateralization to familiar symbols that are not associated to sounds (as tested in experiment 2), would instead favor the view of an early onset and/or rapid reentrant phonological mapping process during development, carrying important theoretical and societal implications.

Results

Oddball Responses. For words and pseudowords inserted in pseudofonts, scalp topographies and EEG spectra of grand-averaged data showed a clear (i.e., SNR > 1.6, >60% increase of signal; sum of baseline-corrected amplitudes > 1.4 μV) discrimination response at 1.2 Hz (first harmonic), 2.4 Hz (second harmonic) and 3.6 Hz (third harmonic) over the left lateral occipital electrode O1 (Fig. 2*A*). In these two conditions, we found significant responses at one or several harmonics from 1.2 Hz to 4.8 Hz (F/5–4F/5) at seven posterior electrodes (O1, O2, Oz, P7, P8, PO3, PO4). However, unlike the pattern found in adults (24), there was no discrimination response for words inserted in pseudowords sequences (Fig. 2). All electrodes were ranked according to their largest amplitude values for the sum of baseline corrected amplitudes computed on four harmonics (1.2 Hz, 2.4 Hz, 3.6 Hz, 4.8 Hz, all P values <0.005) as determined by grand-averaged data (F/5–4F/5; *Materials and Methods*). The largest response was recorded at electrode O1 for both pseudofont (PF)-word (W) and PF-pseudoword (PW) conditions.

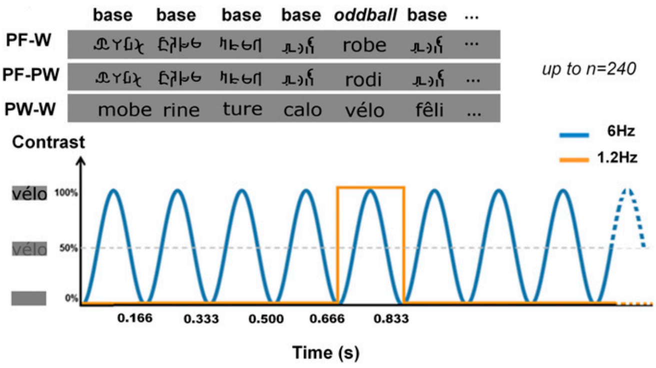

Fig. 1. Experimental paradigm (experiment 1). Two sequences were presented in each condition, for 96 oddball stimuli in total. Stimuli were sinusoidally contrast modulated at 6 Hz during 40 s, each stimulus reaching full contrast after 83 ms (i.e., one cycle duration = 166 ms). Stimulation alternated between base stimuli (b) and oddball (o) such as: *bbbbobbbbobb*. Base stimuli were either pseudofonts (*Top* and *Middle*), or pseudowords (*Bottom*), and oddball stimuli were either words (*Top* and *Bottom*), or pseudowords (*Middle*) appearing every fifth item (6/5 Hz = 1.2 Hz). Stimuli were randomly selected with no immediate repetition.

Table 1. Descriptive statistics for behavioral tests of reading (experiment 1)

	Data		Norms
Behavioral tests	Min–max	Mean (SD)	Mean (SD)
Grapheme-phoneme knowledge			
Total production score /52	0–42	6.5 (7.9)	NA
Letters /26	0–22	5.5 (4.9)	
Simple syllables /11	0–8	0.5 (1.7)	
Complex syllables /15	0–12	0.4 (2.1)	
Grapheme recognition /26	1–24	9.7 (5.7)	
Phonological awareness /12	0–12	7.4 (3.4)	5.6 (3.2)
Vocabulary			
Production scores /30	10–29	24.4 (3.6)	22.5 (3.7)
Recognition scores /20	12–18	15.1 (1.6)	14.3 (2.7)

Based on this observation, the sum of baseline-corrected amplitudes was analyzed in experiment 1 with a repeated-measures ANOVA with 3 (conditions: PF-W, PF-PW, PW-W) × 2 (hemisphere: O1, O2) levels. There was a main effect of condition [$F(2, 78) = 6.221$; $P < 0.003$], and a main effect of hemisphere [$F(1,39) = 6.444$; $P < 0.015$], responses being larger in the left than in the right hemisphere. There was no interaction between these factors [$F(2, 78) = 1.113$; $P = 0.31$]. Post hoc comparisons (Bonferroni corrected for multiple comparisons) revealed that PF-W and PF-PW did not differ ($P > 0.99$), both conditions giving rise to a significantly stronger response than the PW-W condition ($P < 0.01$), which showed no oddball response (i.e., $Z < 1.64$ at all harmonics).

Relationship Between Prereading Ability and Letters String Sensitivity. The two letter string conditions were grouped ("pseudofont-letters", PF-letters) and a lateralization index [(R−L)/(R+L)] was computed. Two behavioral measures significantly correlated with the O1 oddball response in PF-letters: the grapho-phoneme recognition score (i.e., pointing to the correct letter when hearing a phoneme) (Spearman $\rho = 0.505$; $P < 0.0001$) and the grapho-phoneme production score (i.e., reading aloud) (Spearman $\rho = 0.364$; $P < 0.011$) (Fig. 3*A* and Fig. S1). These two measures of prereading (GP recognition and production) were neither correlated with the EEG response on O2 (Spearman ρ: 0.128, $P = 0.213$; 0.016, $P = 0.462$, respectively), nor with the base rate response (6 Hz and significant harmonics) on Oz (Spearman ρ: –0.10; $P = 0.27$, $P = -0.157$; $P = 0.16$, respectively) or O1 (Spearman $\rho = -0.093$; $P = 0.285$; –0.194; $P = 0.109$, respectively). A combined score (average of production + recognition) correlated with the O1 response (Spearman $\rho = 0.49$; $P < 0.001$), as well as with the lateralization index ($\rho = -0.32$; $P < 0.01$), but not with response on O2 ($\rho = 0.05$; $P = 0.376$). Other measures of phonological processing (26) or vocabulary (27) did not correlate with the O1 oddball response (phonological processing: Spearman $\rho = 0.138$; $P = 0.19$; vocabulary: Spearman $\rho = 0.101$; $P = 0.259$), but both grapheme-phoneme (GP) recognition and production scores correlated with phonological awareness (Spearman $\rho = 0.463$, $P < 0.001$; Spearman $\rho = 0.394$; $P < 0.005$, respectively).

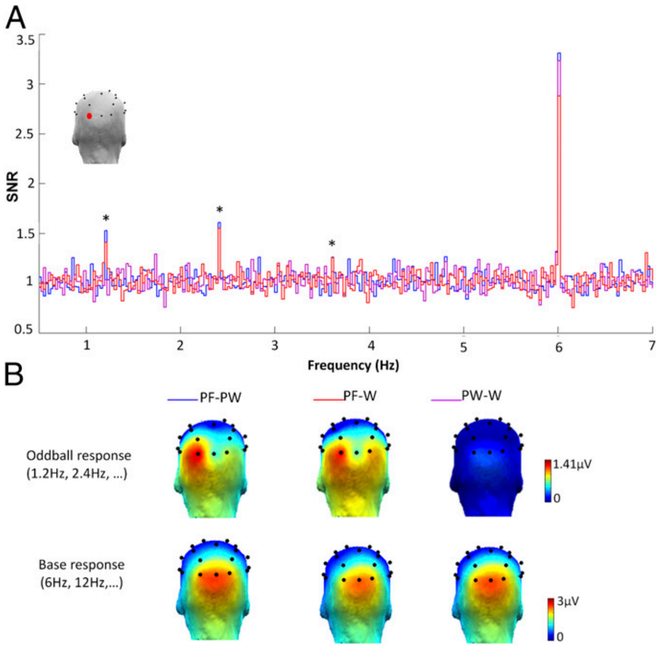

Fig. 2. Grand-averaged (n = 40) SNR EEG spectra and scalp topographies (back of the head) at oddball (1.2 Hz, 2.4 Hz, 3.6 Hz, 4.8 Hz) and base (6 Hz) frequencies. (*A*) SNR spectra on O1 (left occipito-temporal electrode, red dot on the scalp map) for the three conditions, at the different stimulus frequencies. The oddball responses to words and pseudowords are significant on this channel at 1.2 Hz, 2.4 Hz, and 3.6 Hz (*). Conditions PF-W (in red) and PF-PW (in blue) do not differ, and there is no response for PW-W (in purple). The response for letter strings (PW and W) is greater in the left hemisphere (O1). (*B*) Scalp topographies for the response in each condition at the base and oddball frequencies. The topographies are based on the sum of baseline subtracted amplitudes at significant harmonics.

Impact of Visual Familiarity. In experiment 2, the sum of baseline-corrected amplitudes was analyzed with a repeated-measures ANOVA with 4 [conditions: PF-letters, visual control (VC)-symbols, VC-script, VC-drawings; Fig. 4] × 2 (hemisphere: O1, O2) levels. There was a significant main effect of condition [$F(3,75) = 13.43$; $P < 0.008$], no main effect of hemisphere [$F(1,25) < 1$], and a highly significant interaction between these two factors [$F(3,75) = 4.57$; $P < 0.005$]. In all conditions, responses were significantly different from 0 (P values <0.0001) at both O1 and O2, except for the response on O1 for symbols [$t(25)=1.08$; $P = 0.29$], and for both electrodes in the VC-script condition ($P > 0.06$) (Fig. 4 and Fig. S2). In the VC-drawings condition, responses on O1 and O2 did not differ [2.06 µV vs. 2.09 µV; $t(25) = -0.13$; $P = 0.89$]. For PF-letters, the response was stronger on the left hemisphere than the right hemisphere [LH: 1.64 µV vs. RH: 1.24 µV; $t(25) = 2.07$; $P < 0.04$]. For the VC-symbols condition, the response was stronger in the right hemisphere (RH: 0.89 µV vs. LH: 0.27 µV; t (25) = −2.80; P = 0.010), whereas there was no significant lateralization in the VC-script condition (t (25) = 0.60; P = 0.5).

Discussion

Within only 2 min of recording, we obtained a clear left lateralized posterior response specific to letter strings in prereaders. The amplitude of this response varies across individuals and correlates with prereading abilities as measured by grapho-phoneme recognition and production. These findings agree with the left posterior hemispheric dominance in processing letter strings, as found in adults with a variety of approaches (11, 28, 29) including the paradigm used here (24). However, it challenges the view that left-hemispheric specialization emerges relatively late in natural settings, that is, after at least 1 y of formal reading instruction (13, 14). At the theoretical level, this finding indicates that minimal knowledge of grapheme-phoneme association is sufficient to induce neural changes, suggesting rapid plasticity in establishing connections between posterior visual and anterior phonological regions during development. From a societal point of view, it opens perspectives regarding the evaluation of reading acquisition, with a highly sensitive and objective approach that does not require explicit behavioral responses.

Evidence for Early Left Hemispheric Lateralization with a Sensitive Approach. To our knowledge, previous studies did not find a specific left hemispheric dominance for letter strings processing as early as in preschool children without formal instruction or intensive and prolonged training. One fMRI study (19) found a greater left fusiform/infero-temporal response to single symbols (letters and digits) than single objects in 4- to 5-y-old children, but pseudoletters were not tested. Another study (20) found a larger left fusiform response to single letters than pseudoletters and shapes, but a similar effect was also found in the right anterior fusiform gyrus, and the interaction with hemisphere was not tested. Moreover, because single letters may not engage similar linguistic processing as strings of letters (30), they may not be processed by the same neural structures. Following visuomotor and grapheme-phoneme training, preschool children may also show an increased EEG and/or fMRI response to single letters (20) or even letter strings (15) compared with symbols. However, hemispheric lateralization was not tested statistically or did not reach significance in these studies, and the tuning response may disappear within a few weeks (15). In addition, the relationship between letter knowledge and hemispheric specialization in preschool children has so far remained unclear. Although a right hemispheric N1 print tuning was found in prereading children with high letter knowledge (31), the reverse finding (i.e., right increased N1 tuning related to poor reading outcomes) was also found (32), and no relation between tuning and letter knowledge (15, 19).

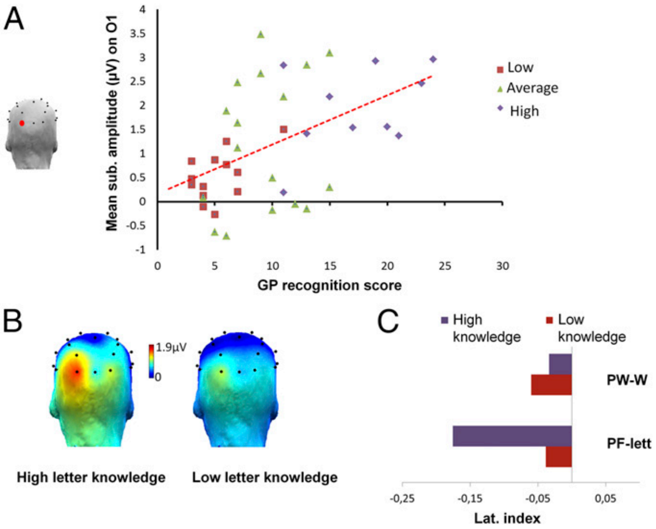

Fig. 3. Relation between individual performance and amplitude of the EEG discrimination responses. (*A*) Scatter plot of positive correlation data between the mean amplitude response on O1 for letter discrimination (in microvolts) and grapho-phonemes recognition. (*B*) Topographies of the discrimination response (baseline subtracted amplitudes) to letters among pseudofont (PF-letters) for children with low and high letter knowledge selected on the basis of performance. (*C*) Lateralization indexes (LI), where groups differ for the PF-letters condition. LI differs significantly from zero only for PF-letters in the high letter knowledge group.

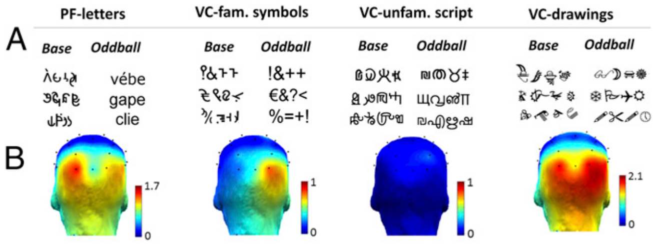

Fig. 4. Examples of stimuli and topographical maps (experiment 2). Examples of base and oddball stimuli (*A*), and topographical maps for each condition (*B*) (1. pseudofont-letters, 2. visual control-familiar symbols, 3. visual control-unfamiliar script, and 4. visual control-line drawings). Scalp topographies represent the discrimination response (baseline subtracted amplitudes) to letters, symbols, script, and line drawings among their respective visual control stimuli.

Here, the highly significant left lateralized response observed in preschool children's electrophysiological responses may be due to several critical aspects of the present approach. First, each letter string is backward- and forward-masked by pseudofonts. Hence, the EEG response of interest reflects an inherent contrast between letter strings and pseudofonts, without subtraction. Moreover, the large number and wide diversity of the pseudofonts used, as well as their size variations, virtually eliminate the contribution of low-level cues to the specific response to letter strings. Also, the fast presentation rate (i.e., slightly less than 166 ms per string) forces letter string detection at a single glance, further isolating this process from general perceptual and cognitive functions. We note that a similar logic has been used in the "rapid stream stimulation paradigm," giving rise to a "recognition potential" (RP) for visually presented words inserted in various "background" stimuli presented at approximately 4 Hz (33, 34). This RP is left lateralized in adults and increases with the level of discrimination required by the compared stimuli (e.g., ref. 35). However, in the present frequency-domain approach, the SNR (i.e., sensitivity) is dramatically increased by confining the response to a known specific frequency rather than spreading it over broadband frequency ERP components (21–23).

Early Left Lateralization for Print: Stimulus Properties or Functional Processes. The left lateralized response to print in prereading children is in line with the pattern found in adults with the same paradigm. Although there is no direct comparison between the two groups, children's discrimination response seems more posterior than the occipito-temporal response found in in adults (24). A similar developmental difference has been observed in fMRI, where sensitivity for words in children was found in more posterior brain regions compared with adults (36). This effect is thought to reflect children's reliance on a more posterior section of the visual word form system (VWFS) until whole-word recognition becomes automatized (37–39). Because the present FPVS-EEG approach does not require explicit processing of the words, and is thus less—or not—affected by motivation and comprehension, as well as by attentional and decisional processes, this hypothesis could be relatively easily tested with the exact same recording measure across development.

The correlation between neural measures of letter discrimination with behavioral measures of prereading abilities supports the view that these specific visual patterns are already associated as grapho-phoneme correspondences in young children. Indeed, spoken language circuits are already left-lateralized in infants' perisylvian areas (40). Hence, during reading acquisition, mapping between graphemes and phonemes, or orthographic-phonological binding (7), could generate the ipsilateral left hemispheric engagement of posterior brain regions to letter strings. This view is supported by spatial constraints in establishing intrahemispheric vs. interhemispheric connections (8, 16) and by privileged and/or preexisting connectivity with language areas as suggested by functional connectivity analyses in fMRI (41) and tractography (37, 42).

Importantly, the findings of our second experiment exclude another possibility: that the left hemispheric specialization to letters is due to a general visual mechanism that operates on any script with similar characteristics in terms of line junctions, foveal position, and high spatial frequencies. Moreover, for three reasons at least, these findings also show that the left hemispheric specialization for letter strings is not due to visual processes merely tracking the transition between two classes of high spatial frequency stimuli with different low-level properties. First, the discrimination response is observed only in children who know a few letters at least. Also, this left-lateralized response depends on the nature of the stimuli and is not found for letter-like symbols. Finally, although children with a better letter knowledge have presumably been more exposed to prints, this mere visual exposure cannot account for the left hemispheric specialization. Indeed, our findings show that visually familiar symbols not associated with phonological representations rather activate the right hemisphere preferentially, perhaps due to the right-hemispheric dominance in expertise/familiarity with visual shapes (43, 44).

At the theoretical level, this finding makes at least two important contributions to our understanding of how the human brain's circuitry develops. First, because minimal knowledge of grapheme-phoneme association is sufficient to induce neural changes, it implies early establishment of functional connections between posterior visual and anterior phonological regions during development, which may be relying on preexisting structural connectivity (41, 42). Second, because familiar, but not unfamiliar, symbols trigger a (right-lateralized) discrimination response, it shows that limited knowledge of certain classes of visual stimuli suffice to develop circuits that are specialized for processing these stimuli.

Rapid Evaluation of (Pre)Reading Abilities. Beyond their theoretical implications, our findings have potential implications for evaluating reading abilities across development. Here, we were able to objectively register individual differences in letter strings' sensitivity in only 80 s of recording and to replicate this finding in a second sample of children (experiment 2, 120 s). Importantly, the FPVS approach does not require any explicit response, thus allowing disentangling stimulus-related and response-related processes that are usually conflated with each other in behavioral measures. Moreover, this approach eliminates or minimizes the contribution of task comprehension factors, as well as attentional, motivational, and decisional processes, which can vary considerably across individuals and across development. This sensitive (i.e., high SNR) approach thus provides a powerful tool to rapidly evaluate the development of prerequisites in learning to read. From a clinical and educational neuroscience perspective, because early interventions in dyslexia result in much better outcomes (45), developing sensitive measures before the start of formal education is extremely important. Admittedly, to be useful as a clinical tool, the approach still needs to be further improved, demonstrating its test-retest consistency (i.e., reliability) with more stimulation sequences and above-noise EEG responses in all individuals tested (*SI Materials and Methods*).

To summarize, our study provides unambiguous evidence that prereading 5-y-old children already engage the left posterior hemisphere for letter string discrimination, and that the amplitude of this brain response is significantly associated with prereading abilities, i.e., letter knowledge. These observations point to an early interaction between phonological and visual processes, shaping the functional organization of the left hemisphere during development.

Materials and Methods

Participants.

Experiment 1. Forty-three children (23 males, mean age = 5.48 y; range = 5.01–5.94 y) were studied, of whom 3 were excluded (see below). They were in third year of kindergarten with normal/corrected-to-normal vision, and were tested after the parents gave informed consent for a study approved by the Biomedical Ethical Committee of the University of Louvain. Children were unaware of the goal of the study and that a change of stimulus type occurred at a periodic rate during stimulation.

Experiment 2. Twenty-six children (14 males, mean age = 5.82 y; range = 5.13–6.09), were tested.

Behavioral Testing.

Experiment 1. Children underwent a screening battery comprising subtests of the WISC (cubes and symbol search), verbal span, and vocabulary (ELO; ref. 27). On this basis, data of one child who scored abnormally low in several tasks (vocabulary: $Z = -3.38$, verbal span: $Z = -2.57$, and WISC subtests (standard notes: 1 and 4) were excluded (Fig. S3). For reading-related measures, we tested phonemic awareness (initial phoneme identification, N-EEL; ref. 26), grapheme recognition (by pointing), and grapheme-phoneme production (i.e., letter reading), reading simple and complex syllables (BELO; ref. 46) (Table 1). Letters were presented in lowercase. Both letter names and sounds were considered correct. Z scores were computed to remove outliers within the distribution of the current sample. One child's data were removed (grapho-phoneme production: $Z = +4.48$). For details of testing and results, see Table 1 and *SI Materials and Methods*.

Experiment 2. Children were tested on visuo-attentional capacities, vocabulary, grapheme-phoneme production, and recognition.

EEG Testing Stimuli.

Experiment 1. Three categories of 15 stimuli (words, pseudowords, pseudofonts) were made of four-symbol items (letters or pseudofont). In a first condition, "base" stimuli were pseudofonts, and "oddball" stimuli were words (PF-W) (Fig. 1). In the second condition, oddballs pseudowords were inserted in the pseudofonts (PF-PW). This condition was used to rule out any potential contribution of semantic processing to a putative left lateralized discrimination response between words and pseudofonts. In the last condition, oddballs words were inserted in pseudowords as base stimuli (PW-W), enabling assessment of lexical retrieval of orthographic representations (24). French words [frequent common nouns (estimated frequency: 242.01 per million) in singular form] were selected from the *Manulex* database (47). Pseudowords were built by rearranging the first and last bigrams (adjacent letters) of the words (e.g., the words "joli" ("cute") and "fête" ("party") could give rise to the pseudowords jote and fêli). Average bigram frequencies did not differ for words (5,586, SD: 927.48) and pseudowords {6,278, SD: 924; [$F(1,28) < 1$; $P = 0.6$]}. Pseudowords were pronounceable and respected the phonological rules in French. Pseudofont items were built on an item-by-item basis. Each word was vertically flipped and its letters were segmented into simple features by using Adobe Photoshop. These segments were then rearranged to form pseudoletters, respecting the total number of characters (4) and the overall size (width × height) of the original word (24). Pseudoletters therefore contained junctions, ascending/descending features, and close-up shapes (Fig. 1 for examples of stimuli). Each word thus had a corresponding PW and PF, containing the exact same amount of black-on-white contrast, so that all conditions were comparable in terms of low-level visual properties.

Experiment 2. Fifteen stimuli were built for each category of items, as well as their corresponding paired 15 visual control stimuli. For all conditions, the visual control items were built exactly in the same manner as described in experiment 1, so that each oddball stimulus had a paired visual control stimulus made of its rearranged segments. In the condition PF-PW, 15 pseudowords of 4 letters were presented as oddball stimuli. In the second condition, keyboard symbols (& € § ! % ? = + < > *) were arranged into four elements sequences, where repetition of the same symbol within the sequence was allowed (to mimic repetition of the same letter within a word or pseudoword). In the third condition, elements of the Kartika, Cyrillic, and Greek fonts (word processor) were selected, randomly mixed and arranged into four elements sequences. Finally, line drawings from the "Wingdings" font were chosen (with the exclusion of shapes filled in black, of faces, and of variations of the same shape). In both experiments, stimuli were presented centrally in Verdana font (except for script and drawings) on a cathode ray tube (CRT) display set at 800 × 600 screen resolution and 60 Hz refresh rate. Images varied in height between 40 and 78 pixels and in width between 92 and 184 pixels, depending on the shape of the individual letters. At a viewing distance of 1 m, stimuli ranged from 3.1 to 6.3 (width) and 1.1–2.2 (height) degrees of visual angle.

Procedure. Each stimulation sequence started with a fixation cross-displayed for 2–5 s, 2 s of gradual stimulation fade in, 40 s of stimulation sequence, and 2 s gradual fade out. Stimuli were presented by means of sinusoidal contrast modulation at a base frequency rate of 6 Hz (i.e., one item every 166.66 ms, hence each item reached full contrast after 83 ms) (Fig. 1 and Movie S1). Given that the stimulus can be recognized at low contrast (i.e., 20% or less), the actual duration of stimulus visibility is close to 140 ms. Every fifth (oddball frequency of 1.2 Hz, thus every 833 ms) item of the sequence was a word (PF-W and PW-W sequences) or a pseudoword (PF-PW sequence). MATLAB 7.8 (The Mathworks) with PsychToolbox (ref. 48; see psychtoolbox.org/) was used for stimulus display. Because the approach has a high SNR and stimuli are presented rapidly, in experiment 1 only two stimulation sequences of 40 s were used per condition, because one of the objectives of the study was to obtain selective responses to visual words in a minimal amount of time. Considering a total of 40 s (sequence duration) × 2 (repetitions) × 3 (conditions), 4 min of stimulation were presented in total. In experiment 2, each sequence was presented 3 times, for a total of 40 s (sequence duration) × 3 (repetitions) × 4 (conditions), thus 8 min of stimulation. There was a pause of approximately 30 s between each of the stimulation sequences, which were initiated manually to ensure low-artifact EEG signals.

During visual stimulation, children fixated a central cross and were instructed to press the space bar for any brief (200 ms) color change of the fixation cross (blue to red; six changes randomly timed per sequence). This orthogonal task was used to maintain a constant level of attention throughout the stimulation. Children performed this task almost at ceiling (91–95%), showing high attention to the stimulation, and without differences between conditions in response times (PW-W: 650 ms; PF-PW: 665 ms; PF-W: 672 ms) [$F(2,62) < 1$].

EEG Acquisition and Preprocessing. Children were seated comfortably at 1 m from the computer screen in a quiet room of the school. EEG was acquired at 1,024 Hz by using a 32-channel Biosemi Active II system (Biosemi), with electrodes including standard 10–20 system locations. The magnitude of the offset of all electrodes, referenced to the common mode sense, was held below 50 mV. All EEG analyses were carried out by using Letswave 5 and Matlab 2012 (The Mathworks). After fast Fourier transform (FFT) band-pass filtering at approximately 0.1 and 100 Hz, EEG data were segmented to include 2 s before and after each sequence, resulting in 44-s segments (−2–42 s). Data files were then resampled to 250 Hz to reduce file size and data processing time. Artifact-ridden or noisy channels were replaced by using linear interpolation. All channels were rereferenced to the common average. EEG recordings were then segmented again from stimulation onset until 39.996 s, corresponding exactly to 48 complete 1.2 Hz cycles within stimulation. This duration corresponds to the largest amount of complete cycles of 833 ms at the oddball frequency (1.2 Hz) within the 40 s of stimulation period.

Frequency Domain Analysis. To increase SNR, the trials of each condition were averaged in the time domain for each individual participant. A FFT was applied to the averaged time windows, and normalized amplitude spectra were extracted for all channels. This procedure yielded EEG spectra with a high frequency resolution (1/39.996 s = 0.025 Hz), increasing SNR (22) and allowing unambiguous identification of the response at the exact frequencies of interest (i.e., 6 Hz for the base stimulation rate and 1.2 Hz and its harmonics for the oddball stimulation). To estimate SNR across the EEG spectrum, amplitude at each frequency bin was divided by the average amplitude of 20 surrounding bins (10 on each side) (49). To quantify the responses of interest in microvolts, the average voltage amplitude of the 20 surrounding bins (i.e., the noise) was subtracted out (e.g., ref. 50).

Based on the grand-averaged amplitude spectrum for each condition, Z scores were computed at every channel to assess the significance of the response at the oddball frequency and harmonics, and at the base rate and harmonics (24, 49). Z scores larger than 2.58 ($P < 0.005$, one-tailed, signal > noise) were considered significant. A conservative threshold was used because the response was evaluated on all channels (although we expected responses at posterior channels), and to be distributed on several harmonics as in the adult study with letter strings (24), or similar studies with faces (49). An identical number of harmonics was selected across all conditions and electrodes based on the condition in which the highest number of consecutive harmonics (#4) was significant on any electrode. Finally, to quantify the periodic response distributed on several harmonics, the baseline subtracted amplitudes of significant harmonics (excluding the base stimulation frequency) were summed for each participant (50). One child's data were removed because his response (3.92 μV) was above 2 SDs of the group's mean response (1.25 μV, SD = 1.2 μV).

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