HHS Public Access

Author manuscript

*J Am Acad Child Adolesc Psychiatry*. Author manuscript; available in PMC 2020 October 01.

Published in final edited form as:

*J Am Acad Child Adolesc Psychiatry*. 2019 October ; 58(10): 948–960. doi:10.1016/j.jaac.2018.11.007.

# Reading Acquisition in Children: Developmental Processes and Dyslexia Specific Effects

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## Abstract

**Objective:** Reduced activation to print in the left ventral, dorsal and anterior pathways has been implicated in readers with dyslexia (DR) but is also characteristic for typical beginning readers. As the majority of studies compared DR to their age-matched peers, the observed results could either represent a dyslexia phenotype or a developmental delay. We aimed to disentangle reading and dyslexia effects by employing two control groups: age and skill matched, and a longitudinal design.

**Method:** We compared brain response for print in DR with typical readers (TR) who at the beginning of schooling (TP1, 6-7 years) read on average 3 words per minute, such as DR at TP1,

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Disclosures: Drs. Dębska, Łuniewska, Marchewka, Pugh, Jednoróg, Ms. Chyl, and Mr. Kossowski report no biomedical financial interests or potential conflicts of interest.

All authors served as statistical experts for this research.

but improved reading to an average level; and advanced readers (AR) who at TP1 read as well as DR two years later (TP3, 8-9 years). The TR and DR groups were tracked longitudinally to observe neurodevelopmental changes.

**Results:** At TP1, DR did not differ from TR. Along with time, only TR developed neural circuit for reading in the left inferior frontal and fusiform gyri. At TP3, DR hypoactivated these areas compared to both age- (TR TP3) and reading-matched (AR TP1) controls. At TP3, TR hypoactivated left frontal and bilateral ventral occipital regions when compared to AR, but these effects were non-overlapping with DR hypoactivations and are partly explained by IQ.

**Conclusion:** Decreased activation of the left fusiform and inferior frontal gyri to print in DR results from an atypical developmental trajectory of reading and cannot be explained solely by lower reading skills.

### Keywords

dyslexia; reading acquisition; reading development; dyslexia debate; longitudinal fMRI

## INTRODUCTION

The neural processes underlying reading have long been at the center of dyslexia research and debate. However, most neuroimaging studies examining children with dyslexia compare them to age-matched peers who have significantly better reading skills. In such comparisons, differences found in patterns of brain activity could reflect dyslexia-specific effects but may also be a consequence of reduced reading expertise, reading acquisition failure, reduced exposure to print, compensatory mechanisms or the deviant learning path of readers with dyslexia (DR)[1]. To overcome the natural issues related to experiential and performance related differences in some studies, an additional, younger reading-matched control group was examined. The idea behind this approach was to study dyslexia-specificity, not just reading-performance dependent differences, including those that are neuroanatomical[2-3] and functional[4-5]. To our knowledge, only two studies address the question of dyslexia specificity in the context of print processing: one with an emphasis on phonological awareness[6] and the other on sentence comprehension[7].

A coherent picture has emerged from a number of publications reviewing the neural pathways employed for reading in dyslexia[8-11]: DR fail to reorganize posterior and anterior cortical regions of the left hemisphere (LH) in a highly organized way that allows typically developing controls to effortlessly and rapidly process printed words and sentences. It is agreed that three LH neural systems tuned for reading are hypoactivated when processing print in DR: the anterior (inferior frontal gyrus, IFG), ventral (ventral occipitotemporal area, vOT) and dorsal systems (angular/supramarginal gyri). However, the importance and involvement of each of these systems may also depend on developmental changes, reading experience, stimuli type and the experimental instruction.

For example, initial work suggested that the left IFG activity can be both reduced (in children[12]) and increased (in adults[10,13-14] and children[15]) in response to print in DR. Increased activation of the left IFG was linked to covert articulatory processes[16],

phonological recoding[9], and more effortful reading[13]. However more recent work based on two metaanalyses[8,17] provided evidence for a distinction between left IFG underactivation and a close-by left precentral region overactivation in DR. The former is implicated in access to lexical and sublexical phonological representations, and the latter in silent articulatory reading processes[18]. Activation in left IFG during reading is also positively correlated with reading skills in young children and adolescents[19]. Many studies have shown that DR or poor readers hypoactivate the left vOT during reading[20-21]. However, reduced activation in the left vOT is reported more often in adults with dyslexia than children with dyslexia, when compared to their age matched controls[17], implicating developmental and/or reading proficiency factors. Generally, the ventral stream is regarded as the most mature and efficient system for reading, allowing for rapid recognition of visual word forms[20] and linking visual or other sensory information to higher-order representations[22]. Thus, it seems natural that the specialization for print in this system emerges only with higher reading expertise and is positively related with performance[23-24]. Nonetheless, there are also findings of early recruitment of the left vOT for non-impaired reading development[25-28] , also in response to phonological task [29] Finally, the implicated dysfunction of the phonological left dorsal system in dyslexia is also quite complex, as consistent hypoactivation in the posterior superior temporal cortex was found only in adults, whereas inferior parietal hypoactivation has only been shown in studies on children[17]. Additionally, the latter result was mostly driven by an increase in task-negative activation characterizing DR[7]. Dorsal pathway involvement can also be related to the orthographic transparency of the given language: it was shown that transparent orthography (Italian) readers employed dorsal pathways, while opaque orthography (English) readers employed ventral and anterior areas[30].

In sum, all three LH subsystems for reading have somewhat different functions, and their activation seems (1) orthography- or task-dependent, (2) to be related to the current reading expertise and/or developmental stage of the participant, and (3) to reflect a functional disruption characteristic for dyslexia. In many cases, it is difficult or even impossible to disentangle the effects of poor (but improving) reading skills of a young reader from dyslexia specificity itself, especially at the early stages of literacy acquisition. In other words, as impaired reading is present in all DR (since dyslexia is a reading impairment per se), it is often impossible to assess whether the observed effects stem from the disorder, or possibly from other factors, such as smaller exposure to print and limited reading experience.

In the current study, we attempted to separate the effects of reading skill and dyslexia on the brain network that supports reading by comparing DR to age-matched and skill-matched controls (typical readers: TR). We retrospectively matched the groups so that at the beginning of reading acquisition TR read on the same level as DR, but outperformed DR two years later. We longitudinally traced the non-impaired and disrupted developmental trajectories of the neural processes underlying reading. A direct retrospective comparison between TR and DR allowed an assessment of the developmental phase in which differences can be observed. However, the effects observed in this comparison (like in many other studies on reading in dyslexia) could be considered both as some trait typical for dyslexia (dyslexia-specific effect) but also as an effect evoked by the unequal reading level of the

groups (reading-specific effect). In this study, we attempted to separate these effects by including an additional age-matched control group which outperformed both TR and DR in reading in the first stage of the study, and was able to read as many words as DR two years later (advanced readers; AR). To observe reading-specific effects, we compared two control groups of the same age but with reading at a significantly different level (TR and AR). For the dyslexia-specific effects, we aimed to compare DR and the control groups who were reading at the same level at the selected time point (TP1 AR and TP3 DR).

We hypothesized that dyslexia specific effects (differences between DR and controls) are present only after acquisition of basic literacy, as we cannot expect differences in response to print between TR and DR at the pre-reading stage. Reading related effects emerge at the very beginning of literacy and are also present later on, reflecting either reading acquisition or proficiency effects. Dyslexia related effects are reflected in underactivation of left IFG (anterior), vOT (ventral) and inferior parietal (dorsal) regions in line with the model of impaired LH reading network in DR based on quantitative meta-analyses[18]. We further explore if dyslexia and reading related effects are distinct. Different neurodevelopmental trajectories are expected in DR and TR matched for age and reading skills at the start of formal reading acquisition, with higher activity in the LH neural systems tuned for reading develop only in the non-impaired group[25].

## METHOD

### Participants

The children selected for the current analysis were part of a cohort examined in a longitudinal study on early diagnosis of dyslexia, approved by the Warsaw University Ethical Committee. All participants were Polish-speaking monolinguals, born at term, right-handed and characterized by normal IQ (controlled with Raven's Colored Progressive Matrices[31]). None of the participants reported any history of neurological illness, brain damage or symptoms of ADHD. Children were tested at three time points (TP1, TP2, TP3), each one year apart. Since TP1 was conducted during the introduction of educational reforms in Poland, some of the six-year-old children were in the first grade and some were in kindergarten (based on parental decision). Formal literacy training was supposed to start in elementary school, but children were already taught letters in kindergarten. TP1 and TP3 involved both behavioral and MRI sessions and TP2 was limited to behavioral testing.

A total of 120 children were recruited for the study at TP1, and 109 completed all three TPs. At TP3, a formal diagnosis of dyslexia was conducted to enable the selection of DR (n = 25). Next, the Hungarian optimization algorithm was implemented and a custom MATLAB script was used to select subjects suitable for the control groups[32] (The Math-Works Inc. Natick, MA, USA). The algorithm was set to find a pair for each DR such that a total distance between variables of interest in paired subjects (words per minute (WPM), age, IQ, SES) would be minimal. For the typical readers group (TR; n = 25), the algorithm sought children who would match DR for WPM score at TP1, as well as demographic measures (age, IQ, SES). After TR group assignment, the script was run again to look for advanced readers (AR; n = 25) among the remaining children. Children for the AR group were supposed to match DR across time points, with the AR TP1 reading score being similar to

the TP3 reading score of the DR. However, we failed to match AR and DR for IQ and SES, with AR having significantly higher scores than DR (SES) or both DR and TR (IQ). As a result, a total of 75 children were included in the behavioral analysis. Demography of the groups is given in Table 1.

## Behavioral tasks and questionnaires

This report is a part of a larger study and only selected the most relevant tests and questionnaires. However, in Supplements 1-2 and Tables S1-S4, available online, a brief overview of all the applied tools is given.

At TP1, all parents were asked to complete the Adult Reading History Questionnaire[33] (ARHQ). When possible, we collected ARHQ from both biological parents. Children defined as FHD+ (with familial history of dyslexia) had at least one parent who reported reading difficulties and scored greater than 40 points in the ARHQ questionnaire[34]. Socioeconomic status score was based on Hollingshead's index of social position, where education level and occupation reported by both parents are considered[35]. At TP1, IQ was assessed with Raven's Colored Progressive Matrices[31]. A low score in Raven could be used as an exclusion criterion at this time, but all screened children were in the normal or above-normal range.

Every year, children participated in 1-2 individual experimental sessions in which cognitive abilities were tested, and the most relevant tests were repeated throughout all TPs: a Decoding Test with subscales of sight word and pseudoword reading per minute, phonological awareness with phoneme analysis and phoneme deletion[36]; The Orthographic Awareness Test in which children were asked to select a letter string that looks most familiar to Polish[37]; and the Rapid Automatized Naming Test[38] (subscales of objects and colors). For the cross-TPs group comparisons, raw scores were used (norms were not available or not applicable due to the educational reforms). The results of the behavioral tests applied at each TP or at only one of the TPs are provided, respectively, in Table S2 and Table S4, available online.

At TP3, all participants were tested with the standardized battery for the dyslexia diagnosis[39]. Detailed information about the diagnostic tool and methods used for dyslexia identification are presented in Supplement 1, available online.

## fMRI task and procedure

After completing the TP1 and TP3 behavioral sessions, children were familiarized with the task in a mock scanner and successively took part in the fMRI session. The same experimental procedure in the same laboratory environment was used at TP1 and TP3. The whole experimental procedure, with both visual and auditory stimuli, is described in our previous publication,[23] Supplement 3 and Table S5, available online. Only visual conditions of the fMRI task were analyzed in the current study, and thus only those will be described in this section.

Children were asked to pay attention to the stimuli appearing on the screen: high-frequency printed Polish words (e.g., "banan") were matched with symbols (e.g., "♌♋■♋■").

explicit task was given to the participants. On each trial, four different stimuli from the same condition were presented in rapid succession in a 'tetrad' designed to evoke strong activation with a relatively short imaging time. Each visual stimulus was presented for 250 ms, followed by a 200 ms blank screen. 'Jittered', intertrial intervals were employed with occasional 'null' trials resulting in ITIs ranging from 4 to 13 s (6.25 s on average). The whole audio-visual task was performed in two runs, each lasting 5 minutes and 2 seconds. All conditions were presented in each run, with 48 trials per run presented pseudorandomly, with no condition allowed to repeat more than three times in a row. This results in 24 total trials per condition, and 96 total stimuli per condition. Stimuli were presented using Presentation software (Neurobehavioral Systems, Albany, CA).

### fMRI Data Acquisition and Analyses

fMRI data were acquired on a 3T Siemens Trio scanner using a whole-brain echo planar imaging sequence with a 12-channel head coil (32 slices, slice-thickness 4 mm, TR = 2000 ms, TE = 30 ms, flip angle = 80°, FOV= 220 mm2, matrix size: 64 × 64, voxel size 3 x 3 x 4 mm). Anatomical data were acquired using a T1 weighted sequence (176 slices, slice-thickness 1 mm, TR = 2530 ms, TE = 3.32 ms, flip angle= 7°, matrix size: 256 × 256, voxel size 1 x 1 x 1 mm).

The neuroimaging data pre-processing and analyses were performed using Statistical Parametric Mapping (SPM12, Welcome Trust Center for Neuroimaging, London, UK) run on MATLAB R2016b (The Math-Works Inc. Natick, MA, USA). Images in all four runs (2 x TP1, 2 x TP3) were realigned to the mean. Next, a pairwise longitudinal registration was performed on T1-weighted images from two TPs and a midpoint average image was created. The outcome of the pairwise longitudinal registration was co-registered to the mean functional image. Co-registered images were segmented using pediatric tissue probability maps, while the Template-O-Matic toolbox[40] was used for this purpose with the matched pairs option. The functional images were normalized using compositions of flow fields and a group-specific template. Finally, the normalized functional images were smoothed with an 8 mm isotropic Gaussian kernel. The data were modeled for each fMRI run using the canonical hemodynamic response function convolved with the experimental conditions. Artifactual volumes were identified in the ART toolbox using a scan-to-scan movement threshold of 3 mm and a rotation threshold of 0.05 radians, similarly to previous publication[41], and modeled in the design matrix (with each artifactual volume represented as a separate regressor). Participant data were excluded from the fMRI data analysis if greater than 20% of volumes in one run exceeded these motion tolerances, and in effect one TR and one DR child was excluded from the fMRI analysis leaving 24 DR, 24 TR and 25 AR children in the whole-brain analyses. In other subjects, motion-affected volumes were modeled in the single-subject GLM and excluded from the analysis. Detailed description of this step is given in Supplement 4, available online, and statistical tests used to compare motion between the groups are reported in the Table S5 available online.

The general linear approach was used to analyze the data, contrasting experimental and rest trials in each subject. For each subject, contrasts were computed to examine word (print>rest) and word-specific effects (print>symbols). Additionally, the response for the

control condition (symbols>rest) was estimated. At the group level, two sample t-tests were applied to analyze the effect of reading (not associated with reading problems) and the effects of dyslexia (not associated with reading performance). The developmental trajectories of the DR and TR groups were analyzed by means of paired t-tests. Additionally, interactions between group and time were tested with a 2×2 flexible factorial model. The results are reported at a significance level of $p < .005$ uncorrected, and an extent threshold of 50 voxels[41] corresponding to the threshold of $p < .05$, corrected for multiple comparisons using a cluster size algorithm resulting from Monte Carlo simulations (3dClustSim, AFNI, http://afni.nimh.nih.gov). For all models, we report only task positive activations[42] – all the results were masked with the map of positive activations for all subjects in the respective condition (print, symbols, print > symbols). Significant clusters were labeled using the Automated Anatomical Labeling (AAL) Atlas implemented in xjView toolbox (http://www.alivelearn.net/xjview).

# RESULTS

## Behavioral Results

Depending on the variable either ANOVA or Ch2 was applied to test for behavioral and demographic differences between the three groups (see Table 1 for demographics and Table S2 [available online] for behavioral scores). Age, SES, Raven's IQ and TP1 sight word reading were similar between DR and TR, since those variables were used as the pairwise matching criteria. Other reading-related skills at TP1 were similar between the DR and TR groups. No differences were found in letter knowledge, phonological awareness tasks (phoneme deletion, phoneme analysis), vocabulary and verbal working memory (digit and syllable span). However, the DR group was slower in the rapid automatized naming task and less accurate in the orthographic awareness task. At TP2, 12 months after the first testing, the groups differed in several other tests, i.e., sight word reading, pseudoword reading and phonological awareness, with the DR group lagging behind TR. Differences in orthographic awareness persisted, along with longer naming times in RAN in the DR. At TP3, the DR group scored lower in sight word and pseudoword reading, phonology, RAN, selective visual attention task, and orthographic awareness, as presented in Figure 1.

AR children were of similar age to DR and TR children at the TP1. However, throughout the experiment, they were consistently better than the two other groups in reading, phonological awareness, rapid automatized naming, and orthographic awareness. However, their performance in reading and reading-related tests at TP1 was similar to that of DR at TP3 (see Table S3, available online).

Figure 1 presents five tests repeated with the same items and testing procedures at each measurement point (sight word reading, pseudoword reading, phonological awareness task, rapid automatized naming task, orthographic awareness task). Other testing procedures, as well as the results of the tests used throughout the experiment, are reported in Supplement 2 and Tables S2-S4, available online

## fMRI Results

Two-sample t tests performed for the DR and TR group at TP1 revealed no differences between the groups in any of the conditions. Significant differences were found at TP3 (Table 2 and Figure 2). For print, TR showed a stronger response in the bilateral IFG and left vOT, while for the word specific contrast (print > symbols), their response was stronger only in the bilateral IFG. An opposite pattern with DR being more active than TR was found only for print in the left Precentral gyrus (PrCG). Since a difference between DR and TR in the left vOT was expected and present in response to words (print > rest contrast) but no longer significant in the word specific contrast (print > symbols), we computed an additional two-sample t-test to examine group differences for symbols. We found that TR activated the left vOT for symbols more than the DR group. This cluster was in the same anatomical location as the cluster showing a group difference for words (print > rest contrast).

To examine the developmental trajectories of DR and TR children who were behaviorally and neurally similar at TP1 and diverged later on, we performed a series of paired t-tests that compared the patterns of activation at T1 and T3 (Table 2 and Figure 2). For words, TR children in the TP3 > TP1 comparison showed more activation in the left vOT, bilateral IFG and precentral gyri (PrCG), left supplementary motor area (SMA), bilateral superior parietal lobule and right angular gyrus, while DR children showed more activation in the left PrCG and inferior and middle occipital gyri on the right. Word specific activation was enhanced with time in the left PrCG in the DR group and in the left IFG in the TR group. Additionally, DR showed more activity in the bilateral calcarine gyrus in the word specific contrast, and TR - in the left superior parietal lobule and right angular gyrus for symbols.

Group x TP interactions were examined with a 2×2 flexible factorial model with the DR and TR groups and both TPs included. A significant interaction between group and time was found only for words. In TR, the activity of the left IFG grew with time, while it remained on a similar level in the DR group (Figure 2, Table 2).

To tease apart the differences that reflect reading skills from those that reflect dyslexia, we performed another series of two-sample t-tests comparing all three groups. To extract the neural regions related to dyslexia, we compared the neural response of the DR group at TP3 to the AR group at TP1 when their reading performance was similar (TP3 DR – $M_{wpm}$= 33.52, SD = 10.78, range = 3-49; TP1 AR – $M_{wpm}$= 37.52, SD = 16.16, range = 16-69), and the TR group, who read better than DR at TP3 ($M_{wpm}$ = 69.28, SD = 18.04, range = 37-107) but were more similar in all demographic measures (i.e., age, IQ and SES). For words, DR compared to the control groups (TR and AR) showed overlapping hypoactivation in the left IFG (108 voxels) and left vOT (44 voxels), while for the word specific contrast an overlapping hypoactivation was present in the bilateral IFG (left IFG - 201 voxels, right IFG – 102 voxels). Interestingly, for symbols, an overlapping hypoactivation (62 voxels) was present in the same left vOT cluster as that observed for words activation (see Figure 3 and Table 2). To examine whether the differences observed for the DR and TR groups are related to different reading skills, we compared AR with TR at TP3 (when both groups acquired reading). The AR group was consistently more proficient in reading and reading-related skills than TR at each TP. At the brain level, for words, even though AR showed stronger activity in the bilateral vOT and left IFG when compared to TR, the clusters were in

somewhat different locations than the hypoactivation clusters in DR compared to control groups. We did not find any areas of overlap in any of the contrasts. For symbols, a similar pattern of was found as for words. No significant differences between AR and TR groups were found for the word specific contrast (see Figure 3 and Table 2).

To test if neural differences related to the reading level can be observed at any stage of reading development, we compared our two control groups at the first stage of the study (TP1, when TR were still mostly pre-readers). We found that AR, when reading words, activated bilateral IFG and left SMA more strongly than TR children. The word specific contrast showed stronger activity of the bilateral IFG and STG in the AR group (for TP3, see Figure 3; for TP1, and see Supplement 5 and Figure S1, available online).

Finally, since IQ and reading are tightly connected during typical reading development[43], children selected to the AR group had higher IQ scores than the TR and DR groups. These children also had significantly higher parental SES than DR children. To control for these confounds, we introduced covariates to the group analyses (see Supplement 6, Figure S2, and Table S6, available online). At TP1, after controlling for IQ, the two control groups no longer differed in the bilateral IFG for word or right IFG and left STG for word specific activation. At TP3, IQ also partially accounted for the difference between AR and TR, but at the same time additional clusters appeared in the left IFG for words and symbols.

Interestingly, controlling for IQ and SES did not affect differences in the left vOT activation between AR and DR. However, the difference in response to symbols between AR and DR shifted from the left vOT to the left inferior temporal cortex when IQ and SES were covaried. Similarly, differences between AR and DR in the left IFG for print were no longer significant after controlling for IQ and SES.

## DISCUSSION

We explored the neurodevelopmental trajectories for reading in children matched for age and reading skill at the beginning of formal literacy acquisition, half of whom developed dyslexia two years later, and half of whom developed typical reading skills. Having an additional group of advanced readers who at the beginning of the study had reading skills similar to DR with two years of literacy education enabled us to separate dyslexia specific effects from reading skill effects in the neural processes underlying reading.

Typical readers matched with DR for reading skills, age and other demographics at the beginning of the study read better and had superior phonological skills than DR one and two years later. At the beginning of literacy acquisition, DR lagged behind TR in rapid naming and orthographic awareness tasks, and this pattern persisted over the next years (for details see Figure 1, Supplements 1, 2, and Table S4, available online). No differences in brain response to print were found at the first stage of the study, when the groups read on average 3 words per minute and 14 children in each group could not yet read. A possible explanation of this finding is that at this stage the neural circuit for reading is not yet “tuned up” in both TR and DR children. Even though two previous studies reported reduced activation for print processing in pre-readers at risk for dyslexia[44-45], smaller number of children, more liberal

thresholds and the lack of the follow-up with the dyslexia diagnosis limit their implications. Here, all DR children indeed developed dyslexia two years later (since this was the fundamental principle of the groups assignment), and at this time clear differences emerged. TR, when exposed to print, employed the bilateral IFG and left vOT more strongly than DR, while PrCG showed more activity in DR than TR. Time effect analysis show that two years of reading instruction increased activation to print in the left vOT, SMA, PrCG, and bilateral IFG in typical readers. In DR, increased activation was observed only in the left PrCG and occipital cortex. Additionally, an interaction between group and time was found in the left IFG: while the engagement of this area in the reading process increased in the TR group, it remained at a similar level in DR across two measurement points.

As expected, we observed the emergence of higher activity in the LH anterior (IFG) and ventral (vOT) neural systems tuned for reading only in children who developed typical reading skills. DR instead employed the left PrCG to a larger extent. We have previously shown that young readers widely employ the left PrCG for print processing, and its activity is positively correlated with the level of literacy at the beginning of literacy acquisition[23]. Processes underlying left PrCG activity may be related to serial letter-by-letter decoding and effortful covert articulatory processes, but in normal reading development, this strategy is replaced early on by phonological recoding and whole word recognition processes[19,24,46-48]. Our results show that DR still use this strategy when non-impaired readers already build up more mature pathways for reading in the ventral (vOT) and anterior (IFG) areas of the left hemisphere. The inefficiency of the strategy employed by DR is reflected by slower reading speed and lower accuracy, as observed in the behavioral data.

For word-specific (print > symbols) contrast, the group difference in the left vOT together with an increase of left vOT activity with time in TR were no longer significant, in line with evidence of equivalent sensitivity, but reduced specificity in the left vOT at the beginning compared to adult readers[49]. Further examination of the control condition (symbols) showed that the left vOT in typical readers was similarly active for symbols as for print, thus in the print > symbols contrast this effect was cancelled out. This result suggests that the left vOT in non-impaired readers is responsive not only to stimuli other than visual[50], but also to those other than words, such as symbol strings[51]. However, in DR, the left vOT was not activated by symbols, and was the only region that differentiated the groups for symbols when they were directly compared. Nonetheless, the control condition of symbols was not purely non-linguistic, since some of the symbols could be named easily (e.g.,↗≏●○□♦) We may hypothesize that children could engage themselves in some sort of implicit, automatized naming, a process that is often disrupted in DR[52-53].

In line with previous studies, we found clear differences between typical readers and DR in the neural processes underlying reading[8,13,17]. However, these effects could be potentially attributed to the fact that DR at this point were already reading significantly poorer than TR, using strategies suitable for the earlier stages of reading development. To identify the neural differences that are characteristic of the DR sample and not just of the lower literacy level, we compared brain responses of the DR group with advanced readers (AR) who already two years earlier were able to read at a similar level as DR at TP3. This comparison revealed hypoactivation in several brain areas in DR, which partially overlapped with the effects

found in comparison with TR. Overlap was present in the left IFG in a similar anatomical location for word and word-specific contrasts. Additionally, for print and symbols, an overlap was observed in the left vOT. Controlling for IQ and SES removed differences between AR and DR in the left IFG for words but not for word specific contrast, while the difference in the left vOT for symbols was shifted more anteriorly to the inferior temporal gyrus. The observed differences between younger AR and older DR cannot be accounted for by a varying level of literacy, because both groups were reading with a similar speed and accuracy of approximately 30 words per minute. The differences could be ascribed to neural functioning characteristic of the DR group, who hypoactivate the anterior language system specifically for written words. This result is not surprising given the broad literature implicating the left IFG in early reading stages[46]. It is thought to reflect the problem that DR have in accessing phonological output representations[54-55]. In addition, the left IFG has strong reciprocal connections and interacts with the left vOT cortex during non-impaired reading[56-58]. The left vOT cortex, associated with both visual-orthographic whole-word processing and serial grapheme-phoneme conversion[18], also showed hypoactivation in DR compared to both control groups. Surprisingly, the hypoactivation was not specific to words, but to some extent was also present for symbols, suggesting a more general visual object processing deficit in dyslexia. The word-specificity of the left vOT has been disputed before[59-61], and higher activation for unfamiliar compared with familiar letter strings was interpreted as a reflection of sustained task-related top-down processing[20] or of greater prediction error (i.e., the difference between bottom-up visual information and top-down predictions[51]. The top-down predictions are assumed to be generated automatically from prior experience in higher cortical levels that contribute to representing phonology, semantics, and actions. In this context, hypoactivation in the left vOT in DR could reflect a failure to establish hierarchical connections and access top-down predictions.

No differences between DR and controls were found in the dorsal stream, in contrast to previous studies, where dyslexia-specific effects were found in the bilateral parietal areas in the basic sentence reading[7] and visual word rhyming task[6]. In contrast to these studies, where reading comprehension or phonological decisions were required, we employed passive single word reading, which is less likely to involve the dorsal stream[62]. Furthermore, we focused on task positive activations[42], as dyslexia specific hypoactivation in the inferior parietal cortex could be partly explained by task negative activations[6-7]. Hypoactivation due to deactivation in dyslexia may have a different functional role compared to reduced activation[17]. However, the significance of this difference has yet to be understood and some studies excluded foci which resulted from differences in deactivation[22].

Finally, we examined reading skill related effects by comparing two control groups at two stages of reading development. At TP1, when TR were still mostly pre-readers, AR presented increased activity in in bilateral IFG for words and also in the bilateral STG for word specific contrasts. Differences in IFG were in a similar location to changes related to reading acquisition in TR, supporting the notion that the emergence of a neural circuit for reading parallels typical reading acquisition[63]. At TP3, no differences were observed for word specific contrast, while for words, increased activity was found in left IFG and bilateral visual cortex. Interestingly, when differences in IQ between the two control groups were controlled for, IFG overactivation in was no longer significant for words in the TP1. Thus, it

seems that among typically reading children, brain response to print is related to their cognitive capacities, but given the general nature of this measure the mechanism is not clear. At the same time, differences in IQ or SES cannot account for reduced left vOT activation to print in children with dyslexia.

Current study has several limitations. Most importantly, the results of the comparisons, including AR, should be interpreted with caution, since this group has a significantly higher IQ than the other two groups and comes from high SES families. However, it seems natural that children who were able to master reading very quickly are characterized by high cognitive functioning and probably have considerable support from their highly educated parents. There is also evidence that IQ and reading are tightly connected in typical reading development[43]. After IQ or IQ and SES were controlled for, some of the effects changed, especially in the comparison between the two control groups. Another potentially limiting factor is the high number of FHD+ children present in the control groups. We cannot exclude the possibility that by using ARHQ as a measure of parental risk instead of a dyslexia diagnosis (which was not common in Poland when participants' parents were attending school), we overestimated "dyslexia risk". Even though the number of FHD+ children was similar across the groups, the observed results could be more robust if only FHD- children were included as controls. An additional disadvantage of the current study is that no normalized tests measuring reading and reading-related skills were available for children at TP1 or TP2. Therefore, group assignment, including dyslexia diagnosis, was based only on TP3 scores from a normalized battery for the dyslexia diagnosis. Finally, the break between fMRI scan and the behavioral sessions when reading and other skills were measured was on average 44 days (SD 25.32, range 5-127) at the TP1 and 23 days (SD = 23.73, range = −45-85) at the TP3. Future studies on reading acquisition in children should aim at reducing this gap, since at this developmental stage one could expect a steep increase in reading performance within the period of 2-3 months.

To conclude, this study's results indicate that hypoactivation of the left ventral occipito-temporal and inferior frontal cortex characteristic of the brain response to print in dyslexia cannot be explained solely by lower reading skills. We thus confirm that these two brain modules, which emerge in parallel to reading development in typical readers, are impaired in dyslexia. Therefore, the classical models of reading-related brain activation that involve the dorsal tempo-parietal cortex need to be updated.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

The authors would like to thank all of the families that participated in this study.

Funding

This work was funded by grants from the Polish Ministry of Science and Higher Education (IP2011 020271), the National Science Center (2014/N/HS6/03515, 2011/03/D/HS6/05584, 2015/17/N/HS6/03013 and 2014/14/A/HS6/00294), grants from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (P01 HD 001994 to Haskins Laboratories and P01 HD 070837 to Georgia State University). The project was

realized with the aid of CePT research infrastructure purchased with funds from the European Regional Development Fund as part of the Innovative Economy Operational Programme, 2007–2013. Funding sources were not involved in the experiment realization, data collection, data analysis, or writing of the report.

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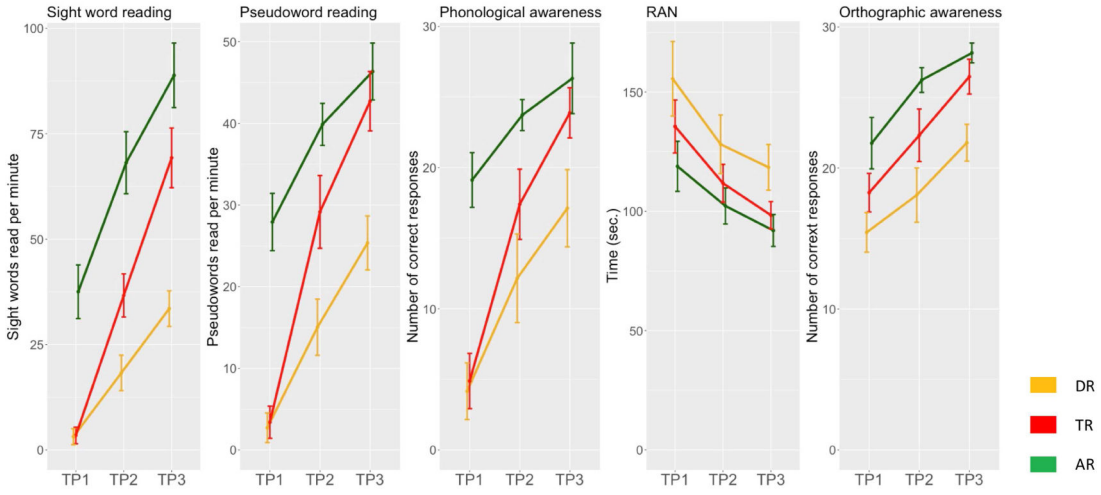


**Figure 1: Changes in Reading and Reading-Related Skills Across Time**

Note: Reading (sight word reading and pseudoword reading) and reading-related skills (phonological awareness, rapid automatized naming, and phonological awareness) of DR, TR and AR across three time points. 95% confidence intervals are represented for each data point. Raw scores are reported for all measures. AR = advanced readers; DR = readers with dyslexia; TP1 = time point 1; TP2 = time point 2; TP3 = time point 3; TR = typical readers.

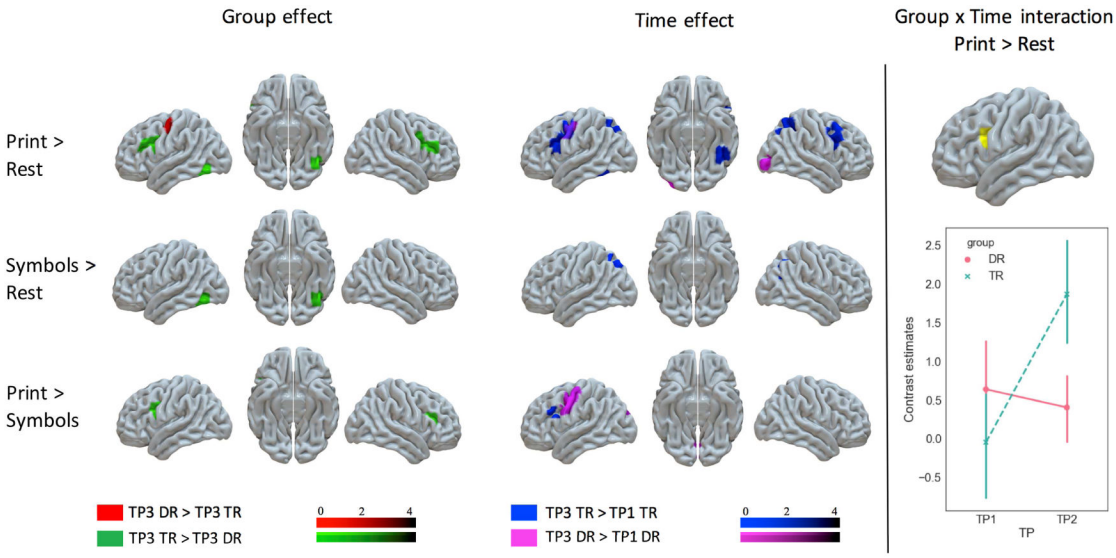


**FIGURE 2. Group Effects, Time Effects, and Their Interaction**

Note: Group effect: Word (Print > Rest), Symbol (Symbol > Rest) and word-specific (Print > Symbols) activations contrasted for DR and TR at TP3. Time effect: BOLD signal increases over time (TP3 > TP1) in the word activation (Print > Rest) and word specific activation (Print > Symbols) in DR and TR. Interaction: interaction between group (DR, TR) and time (TP1, TP3) for Print > Rest. 95% confidence intervals are represented for each data point. AR = advanced readers; BOLD = blood-oxygen level dependent; DR = readers with dyslexia; TP1 = time point 1; TP3 = time point 3; TR = typical readers.

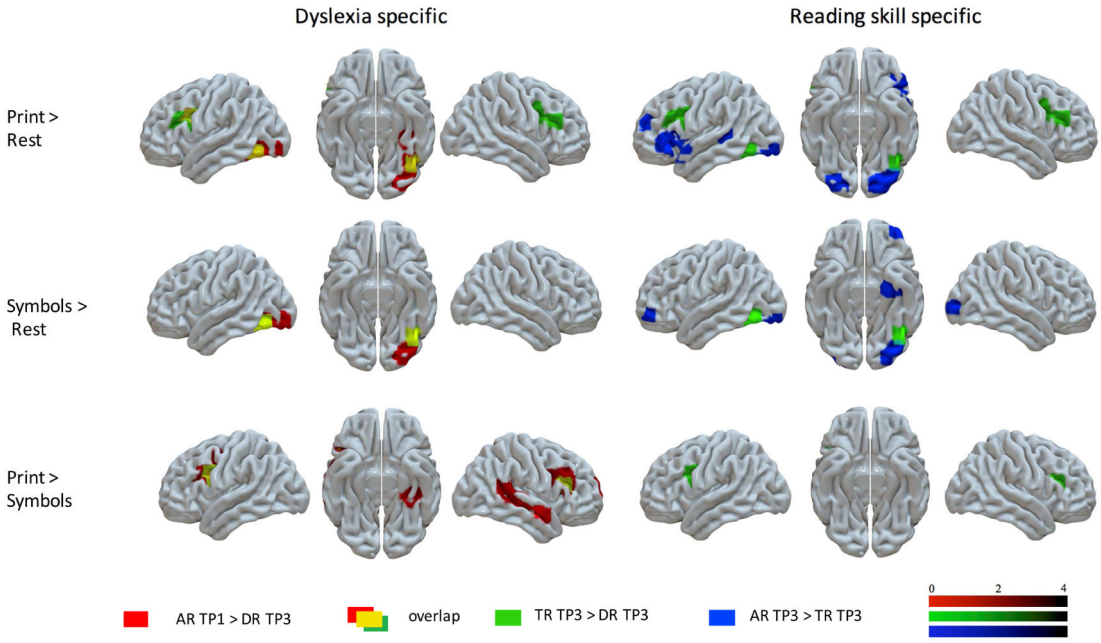


**FIGURE 3: Dyslexia Specific Effects and Reading Skill Specific Effects**

Note: Differences between groups of interest showing regions discriminating groups for dyslexia (Dyslexia specific: AR TP1 > DR TP3) or poorer/better reading (Reading skill specific: AR TP3 > TR TP3). AR = advanced readers; DR = readers with dyslexia; TP1 = time point 1; TP3 = time point 3; TR = typical readers.

**TABLE 1:**

Participant Demographic Information

| Characteristic | DR | TR | AR | F/_$\chi^2$ | direction |
|---|---|---|---|---|---|
| **n** | 25 | 25 | 25 | | |
| **Age in years at TP1** | M = 6.75<br>SD = 0.54 | M = 6.75<br>SD = 0.45 | M = 6.98<br>SD = 0.44 | F(2,72) = 2.032<br>ns | |
| **Age in years at TP3** | M = 8.79<br>SD = 0.53 | M = 8.78<br>SD = 0.45 | M = 9.03<br>SD = 0.46 | F(2,72) = 2.192<br>ns | |
| **Sex** | B = 14<br>G = 11 | B = 9<br>G = 16 | B = 9<br>G = 16 | $\chi^2$= 2.725<br>ns | |
| **School grade at TP1** | K = 12<br>E = 13 | K = 8<br>E = 17 | K = 5<br>E = 20 | $\chi^2$= 4.440<br>ns | |
| **FHD status** | FHD+ = 19<br>FHD− = 6 | FHD+ = 13<br>FHD− = 12 | FHD+ = 14<br>FHD− = 11 | $\chi^2$= 3.486<br>ns | |
| **ARHQ mother** | M = 35.84<br>SD = 17.74 | M = 29.60<br>SD = 15.51 | M = 33.40<br>SD = 14.30 | F(2,72) = 0.969<br>ns | |
| **ARHQ father** | M = 42.05<br>SD = 14.71 | M= 36.23<br>SD = 17.42 | M = 32.83<br>SD = 17.01 | F(2,63) = 2.079<br>ns | |
| **SES** | M = 40.37<br>SD = 13.31 | M = 45.71<br>SD = 11.63 | M = 51.79<br>SD = 8.78 | F(2,72) = 6.286<br>§ | AR>DR§ |
| **Raven IQ (sten score)** | M = 6.84<br>SD = 1.52 | M = 7.08<br>SD =1.26 | M = 8.44<br>SD = 0.96 | F = 11.617<br>*** | AR> DR ***<br>AR>TR§ |

Note: Demographic information of DR, TR and AR are reported, with M and SD. Statistical tests used to compare the groups are ANOVA and Chi2. ANOVA = analysis of variance; AR = advanced readers; ARHQ = adult reading history questionnaire; B = boys; Chi2 = chi-squared test; $\chi^2$ = chi-squared test score; DR = readers with dyslexia; E = first grade of elementary school; F = f-test statistics; FHD = familial history of dyslexia; G = girls; IQ = intelligence quotient; K = kindergarten; M = group mean; n = number of individuals in the subsample; ns = non significant; SD = standard deviation; SES = socioeconomic status; sten = sten scores; TP1 = time point 1; TP2 = time point 2; TR = typical readers.

*** $p < .001$;

§ $p < .005$.

**Table 2:**

Brain Activation for Effects of Group, Time Point, and Their Interaction

| | Brain region | H | x | y | z | t | V |
|---|---|---|---|---|---|---|---|
| | **PRINT > REST** | | | | | | |
| **Group effects** | | | | | | | |
| TR TP3 > DR TP3 | Inferior Frontal (tri, oper), Precentral | L | −34 | 10 | 32 | 4.13 | 472 |
| | Fusiform | L | −42 | −62 | −12 | 3.85 | 52 |
| | Inferior Frontal (oper), Precentral | R | 40 | 2 | 26 | 3.29 | 97 |
| | Inferior and Middle Frontal | R | 48 | 28 | 22 | 3.21 | 152 |
| DR TP3 > TR TP3 | Precentral | L | −46 | −12 | 50 | 3.97 | 63 |
| AR TP1 > TR TP1 | Supplementary Motor Area | L | −6 | 6 | 56 | 3.80 | 109 |
| | Inferior Frontal (oper, tri), Precentral | L | −36 | 8 | 22 | 3.49 | 121 |
| | Inferior frontal (oper), Middle frontal | R | 44 | 20 | 36 | 3.33 | 64 |
| | Precentral | L | −48 | 0 | 56 | 3.24 | 133 |
| AR TP3 > TR TP3 | Inferior Frontal (tri, orb) | L | −46 | 30 | −4 | 4.17 | 459 |
| | Inferior Occipital, Lingual, Cerebellum (crus 1), Fusiform | L | −38 | −80 | −18 | 3.74 | 407 |
| | Middle Temporal | L | −50 | −38 | 4 | 3.59 | 51 |
| | Middle Frontal | L | −30 | 58 | 22 | 3.58 | 68 |
| | Lingual, Inferior Occipital | R | 26 | −88 | −8 | 3.56 | 108 |
| AR TP1 > DR TP3 | Inferior Occipital, Fusiform | L | −40 | −64 | −12 | 4.88 | 147 |
| | Inferior Temporal | L | −36 | −38 | −12 | 3.96 | 50 |
| | Inferior Occipital | L | −30 | −86 | −8 | 3.48 | 70 |
| | Inferior Frontal (oper, tri), Middle Frontal | L | −30 | 10 | 30 | 3.37 | 144 |
| **Time effects** | | | | | | | |
| DR TP3 > TP1 | Inferior and Middle Occipital | R | 38 | −96 | −4 | 4.62 | 96 |
| | Precentral | L | −56 | 2 | 40 | 3.80 | 116 |
| TR TP3 >TP1 | Precentral | L | −56 | 4 | 46 | 6.99 | 254 |
| | Inferior Frontal (oper), Precentral, Middle Frontal | R | 42 | 2 | 26 | 4.52 | 322 |
| | Inferior Temporal, Fusiform | L | −44 | −50 | −20 | 4.39 | 137 |
| | Superior Parietal Lobule | L | −30 | −74 | 56 | 4.17 | 100 |
| | Supplementary Motor Area | L | −4 | 6 | 58 | 4.12 | 166 |
| | Superior Parietal Lobule, Angular, Inferior Parietal | R | 40 | −60 | 62 | 4.08 | 268 |
| | Inferior Frontal (oper, tri), Precentral | L | −34 | 6 | 26 | 3.97 | 362 |
| **TP x group interaction** | | | | | | | |
| TR and DR TP1 and TP3 | Inferior Frontal (oper) | L | −44 | 8 | 22 | 12.11 | 126 |
| | **SYMBOLS > REST** | | | | | | |
| **Group effects** | | | | | | | |
| TR TP3 > DR TP3 | Inferior Occipital Gyrus, Fusiform Gyrus, Inferior Temporal Gyrus | L | −42 | −64 | −12 | 3.93 | 82 |
| AR TP1 > DR TP3 | Inferior Occipital Gyrus, Fusiform Gyrus, Middle Occipital Gyrus | L | −42 | −64 | −14 | 4.41 | 311 |

| | Brain region | H | x | y | z | t | V |
|---|---|---|---|---|---|---|---|
| DR TP3 > AR TP1 | Middle Occipital Gyrus | L | −48 | −84 | 12 | 3.83 | 72 |
| | Insula, Inferior Frontal Gyrus (orb, tri) | L | −36 | 6 | 0 | 3.63 | 156 |
| AR TP3 > TR TP3 | Parahippocampal Gyrus, Fusiform Gyrus, Hippocampus | L | −28 | −10 | −28 | 4.39 | 108 |
| | Lingual Gyrus, Fusiform Gyrus, Cerebellum (crus I) | L | −36 | −82 | −18 | 3.55 | 146 |
| | Middle Orbital Frontal | L | −38 | 54 | −8 | 3.33 | 53 |
| | Middle Occipital, Calcarine | R | 32 | −98 | 2 | 3.55 | 73 |
| **Time effects** | | | | | | | |
| TR TP3 > TP1 | Superior and Inferior Parietal Lobule | L | −32 | −74 | 54 | 5.78 | 91 |
| | Angular | R | 34 | −60 | 28 | 4.35 | 95 |
| | **PRINT > SYMBOLS** | | | | | | |
| **Group effects** | | | | | | | |
| TR TP3 > DR TP3 | Inferior Frontal (oper), Precentral, Middle Frontal | L | −28 | 8 | 30 | 4.36 | 230 |
| | Inferior Frontal (tri) | R | 36 | 26 | 22 | 3.74 | 106 |
| AR TP1 > TR TP1 | Precentral, Inferior Frontal (oper, tri) | L | −50 | 6 | 42 | 5.57 | 1172 |
| | Middle and Superior Temporal, Supramarginal | L | −58 | −44 | 10 | 4.22 | 382 |
| | Supplementary Motor Area | L&R | −8 | 8 | 54 | 4.21 | 306 |
| | Superior Temporal | R | 60 | −38 | 14 | 4.19 | 209 |
| | Middle and Superior Occipital, Superior Parietal | L | −26 | −64 | 36 | 3.66 | 202 |
| | Inferior Frontal (tri, oper) | R | 40 | 16 | 26 | 3.05 | 87 |
| AR TP1 > DR TP3 | Inferior Frontal (tri, oper), Precentral, Middle Frontal | L | −28 | 6 | 30 | 5.55 | 505 |
| | Fusiform, Inferior Temporal | L | −34 | −34 | −16 | 5.36 | 111 |
| | Middle and Superior Temporal | R | 60 | −8 | −12 | 4.92 | 67 |
| | Middle and Superior Temporal | R | 50 | −26 | 2 | 4.53 | 365 |
| | Inferior Frontal (tri, oper), Middle Frontal | R | 40 | 24 | 30 | 4.36 | 489 |
| | Medial Superior Frontal | R | 10 | 70 | 12 | 4.14 | 79 |
| | Precuneus | R | 6 | −50 | 60 | 3.30 | 53 |
| **Time effects** | | | | | | | |
| DR TP3 > TP1 | Precentral, Postcentral | L | −42 | −8 | 50 | 5.39 | 595 |
| | Calcarine (L&R), Cuneus (L) | L&R | −8 | −88 | 36 | 3.81 | 377 |
| TR TP3 > TP1 | Inferior Frontal (tri) | L | −52 | 10 | 28 | 4.60 | 57 |
| | Supplemenary Motor Area | L | −8 | 12 | 54 | 3.42 | 57 |

Note: Results of word (print > rest), symbol (symbol > rest) and word-specific (print > symbols) contrasts are reported, including hemisphere, MNI coordinates, t-statistic and the number of voxels. Direct comparisons are shown for DR, TR and AR at TP1, TP3 and across time points (group effects). Time-related changes are shown in DR and TR (time effects). Results are reported at a significance level of $p < .005$ uncorrected, and an extent threshold of 50 voxels. AR = advanced readers; DR = readers with dyslexia; H = hemisphere; L = left hemisphere; MNI coordinates = Montreal Neurological Institute coordinates, x, y, z; orb = pars orbitalis; oper = pars opercularis; R = right hemisphere; t = t-test statistic; TP1 = time point 1; TP3 = time point 3; TR = typical readers; tri = pars triangularis; V = number of voxels.