

Dysfunction of Rapid Neural Adaptation in Dyslexia

Highlights

- We found reduced neurophysiological adaptation in adults and children with dyslexia
- In dyslexia, adaptation to speech from a consistent voice was significantly reduced
- Repetition of words, objects, and faces also elicited less adaptation in dyslexia
- Reading skills in dyslexia were related to the degree of neural adaptation

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In Brief

Perrachione et al. studied neurophysiological adaptation to stimulus repetition in adults and children with dyslexia, finding reduced adaptation across a variety of diverse stimuli. Dysfunctional adaptation in representing consistent features of stimuli may be a core neural signature of dyslexia.



Dysfunction of Rapid Neural Adaptation in Dyslexia

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SUMMARY

Identification of specific neurophysiological dysfunctions resulting in selective reading difficulty (dyslexia) has remained elusive. In addition to impaired reading development, individuals with dyslexia frequently exhibit behavioral deficits in perceptual adaptation. Here, we assessed neurophysiological adaptation to stimulus repetition in adults and children with dyslexia for a wide variety of stimuli, spoken words, written words, visual objects, and faces. For every stimulus type, individuals with dyslexia exhibited significantly diminished neural adaptation compared to controls in stimulus-specific cortical areas. Better reading skills in adults and children with dyslexia were associated with greater repetition-induced neural adaptation. These results highlight a dysfunction of rapid neural adaptation as a core neurophysiological difference in dyslexia that may underlie impaired reading development. Reduced neurophysiological adaptation may relate to prior reports of reduced behavioral adaptation in dyslexia and may reveal a difference in brain functions that ultimately results in a specific reading impairment.

INTRODUCTION

Dyslexia is a neurological disorder that specifically impairs the development of expert reading skills (Gabrieli, 2009; Lyon et al., 2003). However, because reading is a relatively recent cultural invention rather than an adaptation honed by natural selection, any impairment in reading development must arise from some other, more fundamental difference in the structure or function of the dyslexic brain. Research in functional brain imaging has elaborated a core system of visual and language areas that underlie reading (Price, 2012; Rueckl et al., 2015; Schlaggar and McCandliss, 2007; Wandell et al., 2012) and shown that this reading network is altered in individuals with dyslexia (Norton et al., 2015; Paulesu et al., 2014; Pollack et al., 2015; Shaywitz et al., 1998), but so far has produced scant evidence for how

basic neurobiological processes may be disrupted in individuals with dyslexia in a way that explains how the cognitive or perceptual precursors to reading are impaired. Behavioral research has not gone much further: although impaired reading development is most commonly associated with disordered phonological processing (Bradley and Bryant, 1983), this leaves open the question of how such processing itself came to be impaired.

Learning to read is a complex process, involving many aspects of vision, language, motor control (eye movements), and attention. It is unlikely, therefore, that there is a single mechanistic explanation for dyslexia. Nevertheless, there is a large body of evidence that, on average, individuals with dyslexia show deficits in rapid perceptual and motor learning on nonverbal tasks. Unlike typical readers, who demonstrate enhanced perceptual thresholds in discrimination tasks when a target stimulus is held constant throughout an experiment (Braidia et al., 1984), such perceptual enhancements are frequently reduced or absent in dyslexia (Ahissar et al., 2006). This failure to “anchor” to perceptual consistency in dyslexia has also been observed for a wide variety of stimuli and tasks (Ben-Yehudah and Ahissar, 2004; Oganian and Ahissar, 2012) and has been advanced as a potential core deficit in this disorder (Ahissar, 2007). Similarly, individuals with dyslexia tend to exhibit reduced implicit learning in both perceptual (Gabay and Holt, 2015) and perceptual-motor tasks (Lum et al., 2013; Menghini et al., 2006; Stoodley et al., 2008). In general, individuals with dyslexia tend to exhibit a reduced ability to exploit regularities in stimuli to enhance performance.

These nonverbal deficits in individuals with dyslexia may be related to known cortical mechanisms of perceptual learning in animals. Rapid neural adaptation to perceptual context has been associated with improved detection behaviors in animal models (Edeline et al., 1993; Fritz et al., 2003; Jääskeläinen et al., 2007). Moreover, neural adaptation in sensory cortices to the consistent features of perceptual noise has been shown to be an important mechanism for improving perception in adverse conditions (Atiani et al., 2009). A large behavioral literature now shows that perceptual noise is significantly more detrimental to individuals with dyslexia than controls across auditory, visual, verbal, and nonverbal tasks (Chait et al., 2007; Sperling et al., 2005, 2006; Ziegler et al., 2009), with neural evidence also showing noise-exclusion deficits in dyslexia (White-Schwoch et al., 2015; Zhang et al., 2013). Based on these

behavioral effects in dyslexia, and corresponding neurophysiological effects in animal models and humans, we hypothesized that rapid neural adaptation may be dysfunctional in individuals with dyslexia.

Neural adaptation can be assessed in human participants via fMRI paradigms that measure the difference in blood oxygenation level dependent (BOLD) signals between blocks of repeated stimuli ("adaptation") and blocks of numerous, distinct stimuli without repetition (Grill-Spector and Malach, 2001; Krekelberg et al., 2006). Adaptation fMRI is a powerful tool for investigating neurophysiological function in vivo: there is a strong correspondence between regionally localized BOLD adaptation effects and the stimulus selectivity of individual neurons (Bell et al., 2011; Sawamura et al., 2005, 2006), and adaptation paradigms have been used extensively to map stimulus selectivity in visual and auditory cortices (Chandrasekaran et al., 2011; Weiner et al., 2010). Adaptation paradigms in fMRI also have several advantages over alternative methods for interrogating neural adaptation, such as the mismatch negativity (MMN) and other scalp electrophysiology measures: namely, adaptation fMRI can ascertain not only the magnitude of adaptation, but also its precise spatial localization. Likewise, it can assess diverse perceptual domains while using consistent stimulation paradigms.

A prominent, ecological example of rapid perceptual adaptation in human behavior is adaptation to a speaker's voice. Listeners rapidly learn the correspondence between a speaker's idiosyncratic phonetics and their long-term phonological representations, which makes speech perception faster and more accurate (Mullennix and Pisoni, 1990; Nygaard et al., 1994). Neuroimaging experiments of speech perception have shown that listening to speech from a consistent speaker results in adaptation (reduced activation) in auditory cortices (Belin and Zatorre, 2003; Wong et al., 2004). In experiment 1, we measured neurophysiological adaptation to speech from a consistent speaker versus multiple different speakers while participants performed a speech perception task (auditory word-to-picture matching). We hypothesized that individuals with dyslexia would exhibit diminished neurophysiological adaptation to phonetic consistency during speech perception compared to controls, following their behavioral impairments in this domain (Perrachione et al., 2011).

We further sought to determine whether neural adaptation deficits in dyslexia are specific to phonetic/phonological processing of speech, or whether they might be observed for repeated stimuli more generally. In four additional experiments (experiments 2a–d), we measured neurophysiological adaptation to the repeated presentation of a single stimulus token versus multiple, different tokens of that stimulus category for (a) spoken words, (b) written words, (c) photographs of objects, and (d) photographs of faces. Different conclusions about the role that adaptation deficits may play in reading impairment can be drawn based on the stimulus types for which diminished adaptation is observed. If adaptation deficits are not observed for any conditions in experiment 2, we can conclude they are related specifically to phonetic/phonological learning. If they are observed for spoken, but not written, words we can conclude adaptation deficits are specific to auditory processing of speech, whereas, if adaptation is diminished for both spoken and written words,

but not objects or faces, we can infer a core dysfunction of linguistic processing in dyslexia. However, if adaptation is also diminished for the nonlinguistic stimulus categories of visual objects and faces, we must consider that dysfunction of rapid neural adaptation during perceptual processing may be a generalized property of the brain in dyslexia. Finally, in experiment 3, we investigated whether diminished neural adaptation was also present in young children with dyslexia. We hypothesized that, if dysfunctional neurophysiological adaptation underlies reading impairment (rather than being a response to the impairment), it should be observed even in early stages of reading development.

RESULTS

Experiment 1

Adaptation to the consistent phonetic-phonological correspondence of speech from a single talker is a hallmark of abstract phonological processing in speech perception (Mullennix and Pisoni, 1990; Nygaard et al., 1994). We measured neurophysiological adaptation to the consistent phonetic features of speech in a block-design, sparse-sampling fMRI paradigm in which listeners heard spoken words and matched them to pictures (Figures 1A and S1). In each block, we varied whether words were spoken by a single voice ("Adapt" condition) versus multiple different voices ("No-Adapt" condition), with the expectation that listeners would show neural adaptation to the consistent voice (Wong et al., 2004). Adults with dyslexia (defined as a lifelong history of reading impairment and current performance in the bottom 25th percentile on two or more subtests of reading speed or accuracy) and control adults participated in this experiment (Tables 1 and S1).

Participants successfully maintained attention to the auditory stimuli throughout the word-to-picture matching task, as indicated by near-ceiling accuracy in both groups (control = 99.2% and dyslexia = 98.8%). A repeated-measures ANOVA for effects of group and condition revealed significantly greater accuracy in controls ($F_{1,33} = 5.14$, $p = 0.03$, $\eta^2 = 0.07$), but no effect of condition ($p = 0.64$) or interaction ($p = 0.81$). The same test for response time revealed a significant effect of condition ($F_{1,33} = 53.62$, $p < 0.0001$, $\eta^2 = 0.18$)—with faster response times in the Adapt condition (502 ms versus 563 ms)—but no effect of group ($p = 0.18$) or interaction ($p = 0.50$).

In the control group, significant neural adaptation (No-Adapt > Adapt contrast) was observed in two bilateral clusters, each extending throughout superior temporal gyrus (STG; including Heschl's gyrus [HG] and planum temporale [PT]) and into posterior middle temporal gyrus (pMTG; Figure 1B). In the dyslexia group, the magnitude and extent of adaptation were markedly reduced, with smaller clusters of significant adaptation encompassing only bilateral HG, PT, and right pMTG (Figure 1C). There was no repetition-related enhancement (Adapt > No-Adapt) in either group. There were no overall group differences in the basic Task > Rest contrast (Figure S1).

Compared to the control group, there was significantly less adaptation in the dyslexia group in clusters encompassing STG, PT, supramarginal gyrus (SMG), and pMTG bilaterally (Figure 1D). There were no clusters in which the dyslexia group

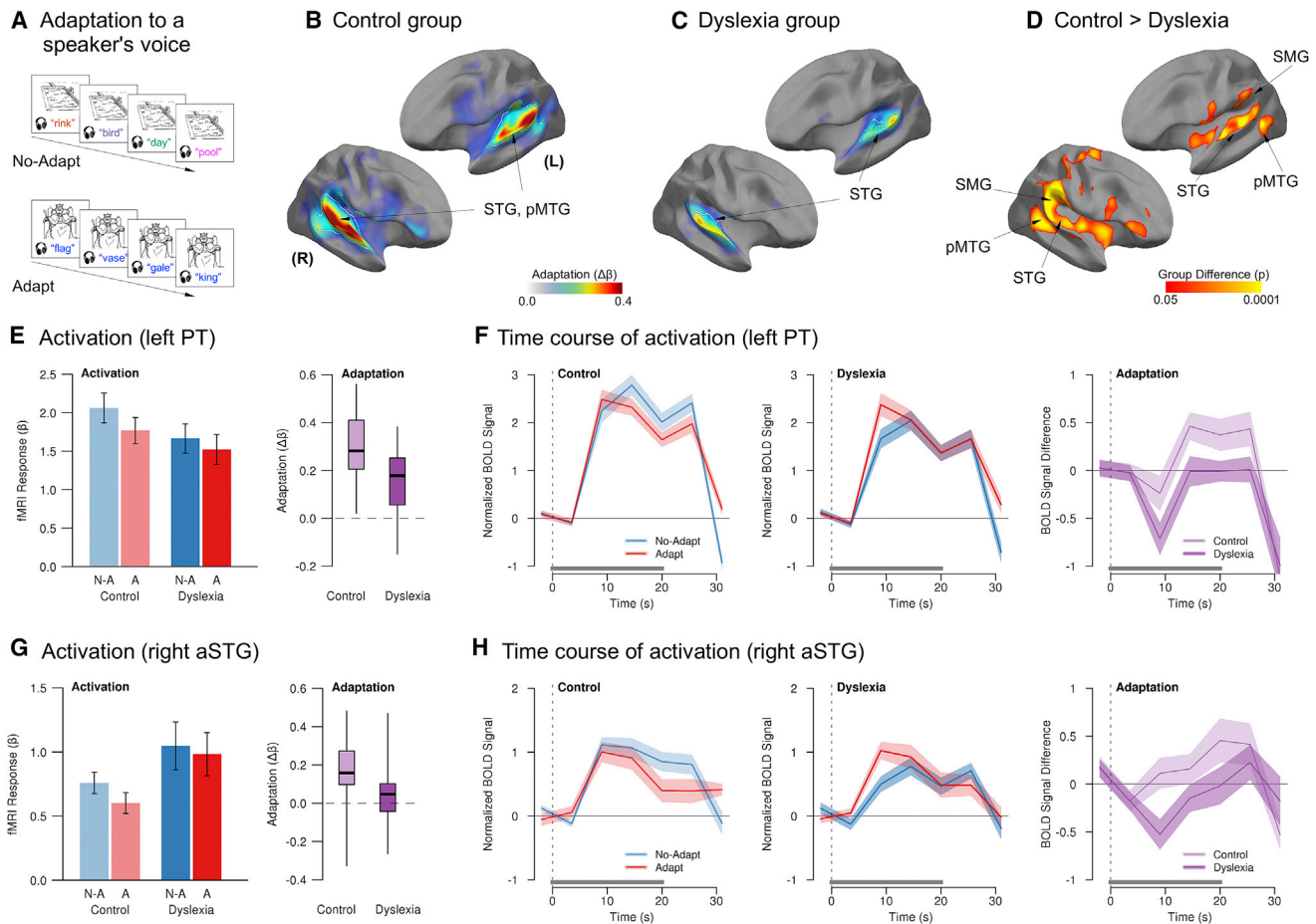


Figure 1. Reduced Neural Adaptation in Dyslexia When Listening to Speech from a Consistent Voice versus Many Voices

(A) Schematic of the stimulation paradigm (detailed design in Figure S1).

(B) Magnitude of neural adaptation (difference in activation for No-Adapt > Adapt conditions) for the control group; areas of significant adaptation are outlined with white contours and labeled. The control group exhibited significant adaptation in bilateral STG and pMTG when listening to speech from a single, consistent voice (Adapt) versus many different voices (No-Adapt).

(C) Magnitude of neural adaptation for the dyslexia group, with significant, though weaker, adaptation in bilateral STG.

(D) Areas of significantly reduced adaptation in the dyslexia group compared to controls. The magnitude of adaptation in the dyslexia group was significantly reduced throughout perisylvian areas for speech processing, including bilateral STG, SMG, and pMTG.

(E–H) These plots explore the nature of the group differences in adaptation.

(E) Barplots: magnitude of neural response (activation) by condition (No-Adapt: “N-A”, blue and Adapt: “A”, red) and group (controls: lighter bars and dyslexia: darker bars) in left PT. The error bars denote SEM. The difference in neurophysiological response between conditions (adaptation) in left PT by group are shown (boxplot). The shaded regions include the middle 50% of the distribution; whiskers extend to the maximum and minimum points; and solid dark lines indicate the median.

(F) Mean time course (solid lines) \pm SEM of BOLD responses to the No-Adapt and Adapt conditions by group, and their difference (adaptation, rightmost image), in left PT. The onset and duration of stimulation are indicated by the vertical dotted line, the solid horizontal bar above the abscissa, respectively. The adaptation effect is evident when the red line (Adapt condition) is beneath the blue line (No-Adapt condition) and reflected in a positive deflection of the difference trace, shown for each group in the rightmost image.

(G and H) (G) Mean neural response by condition (barplots) and adaptation (boxplots), and (H) mean time courses of activation and adaptation in left STG. The control group exhibited greater difference between conditions, with adaptation magnitude increasing across the stimulation period, whereas the dyslexia group showed little difference between conditions, with an increased response to repetition in the short term. (See also Figure S1 and Table S4).

showed more adaptation than controls. The group difference in adaptation was due to an increasing difference between the Adapt and No-Adapt conditions over the course of stimulation in the control group, whereas the dyslexia group showed similar response magnitude to both conditions throughout (Figures 1E–1H; Table S4).

We further explored how the magnitude of auditory adaptation in individuals with dyslexia was related to their reading abilities. Better core reading abilities in the dyslexia group, as measured by efficiency applying phonological and structural rules in decoding novel word forms (Woodcock, 1998), were associated with greater adaptation in both right ($r = 0.56$, $p < 0.02$) and left

Table 1. Summary Behavioral Characterization of Participants

Construct ^a	Control	Dyslexia
Experiment 1 (Adults)		
Nonverbal IQ ^b	119.7 ± 5.6	112.4 ± 12.6
Phonological awareness ^c	111.6 ± 4.5	94.9 ± 11.3
Rapid naming ^d	113.7 ± 3.3	103.1 ± 7.4
Reading ^e	110.4 ± 6.6	86.3 ± 6.6
Working memory ^f	13.4 ± 3.3	8.6 ± 2.3
Experiment 2 (Adults)		
Nonverbal IQ	115.2 ± 9.1	113.6 ± 12.0
Phonological awareness	111.4 ± 5.9	93.6 ± 12.6
Rapid naming	113.7 ± 5.4	100.7 ± 13.5
Reading	108.0 ± 6.7	84.2 ± 6.6
Working memory	12.3 ± 2.8	8.1 ± 1.9
Experiment 3 (Children)		
Nonverbal IQ ^g	119.6 ± 15.9	104.5 ± 13.2
Phonological awareness	117.3 ± 12.9	95.6 ± 10.1
Rapid naming	100.7 ± 9.7	93.4 ± 9.6
Reading	114.2 ± 7.5	81.2 ± 6.5
Working memory ^h	116.3 ± 12.8	95.0 ± 9.8

^aMean ± SD of standard/composite scores are shown.

^bPerformance IQ from the WASI.

^cPhonological awareness composite from the CTOPP.

^dRapid letter naming from the RAN/RAS.

^eMean of Phonological Decoding and Sight Word Efficiency subtests of the TOWRE and Word ID and Word Attack subtests of the WRMT-R/NU.

^fDigit span from the WAIS-IV.

^gNonverbal IQ from the KBIT-2.

^hMemory for digits from the CTOPP. For full behavioral characterization of participants and citations to tests, see Tables S1–S3.

($r = 0.54$, $p < 0.03$) planum temporale, an area known to be involved in phonetic-phonological abstraction in speech-sound processing (Graves et al., 2008; Griffiths and Warren, 2002).

Experiment 2

Following the discovery in experiment 1 of significantly diminished auditory adaptation in dyslexia to the phonetic-phonological correspondence of speech, we conducted four follow-up experiments intended to determine the extent of neurophysiological adaptation differences in dyslexia. We investigated whether adaptation differences would be limited to auditory stimuli or to stimuli with linguistic content, or whether diminished adaptation would be observed for the repetition of stimuli of any kind, indicating dysfunctional adaptation as a generalized feature of information processing in the dyslexic brain. A new sample of adult participants with and without dyslexia was recruited for these experiments, with the same inclusionary criteria as experiment 1 (Tables 1 and S2).

Experiment 2a: Spoken Words

We first investigated whether adaptation in the brains of adults with and without dyslexia would differ to a more obvious repetition of auditory stimuli than the subtle differences between talkers' voices used in experiment 1. In this experiment, we measured neurophysiological adaptation to blocks with the

repeated presentation of a single spoken word (Adapt) versus blocks with multiple different spoken words (No-Adapt) from a single speaker (Figure 2A).

In the control group, hearing multiple repetitions of the same word resulted in significant adaptation (No-Adapt > Adapt) in left anterior STG and dorsal superior temporal sulcus (STS), as well as right aSTG, pMTG, and frontal operculum (FOC) (Figure 2B). As before, the magnitude and extent of adaptation were markedly reduced in the dyslexia group, with smaller clusters of significant adaptation encompassing only left aSTG and right FOC. In both groups, there was a single cluster of repetition-related enhancement (greater BOLD response in the Adapt than No-Adapt condition) in left anterior supramarginal gyrus. There were no overall differences in the groups' task-related activations (Figures S1C and S1D).

The dyslexia group again exhibited significantly reduced adaptation compared to controls throughout perisylvian speech areas, including left STG, pMTG, and ventral premotor cortex, as well as right aSTG, planum polare, ventral premotor cortex, and pMTG. There were no clusters in which the dyslexia group showed more adaptation than controls. Whereas stimulus repetition attenuated neurophysiological response in the control group, individuals with dyslexia showed no such distinction in response magnitude (Figures 2E and 2G). Likewise, whereas the magnitude of adaptation increased over time in controls, even multiple repetitions of a single adapting stimulus did not attenuate the response in dyslexia (Figures 2F and 2H; Table S4).

As in experiment 1, we investigated whether the magnitude of neural adaptation in individuals with dyslexia was related to their reading abilities. We observed a positive correlation between greater adaptation in left PT and better reading skills (Woodcock, 1998) in individuals with dyslexia ($r = 0.42$, $p = 0.05$).

Experiment 2b: Written Words

We next investigated whether the control and dyslexia groups would differ in neural adaptation to the repeated presentation of written words (text), still linguistic, but now visual stimuli. We measured neurophysiological adaptation to text by contrasting blocks of viewing multiple different written words versus blocks with the repeated presentation of a single written word (Figure 3A).

In the control group, significant adaptation to the repeated presentation of a written word was observed in temporal (fusiform gyrus [FusG], inferior temporal gyrus [ITG], pSTG, and pMTG), frontal (inferior frontal gyrus [IFG], FOC, premotor cortex, and presupplementary motor area [SMA]), and visual (pericalcarine) cortices, all in the left hemisphere only (Figure 3B). In dyslexia, the only cluster of significant adaptation to repeated visual words was found in left FOC (Figure 3C). The dyslexia group also showed two clusters of significant enhancement in right pMTG and bilateral precuneus, with both areas also showing task-related deactivations (Figure S2) (Buckner et al., 2008). Although there was a trend toward overall less activation to text stimuli in dyslexia, this Task > Rest group difference was not significant (Figures S2C and S2D).

Compared to the control group, the dyslexia group exhibited significantly attenuated adaptation throughout FusG, pMTG, PT, SMG, and occipital cortex (Figure 3D), left hemisphere areas comprising the core of a network for reading (Dehaene and

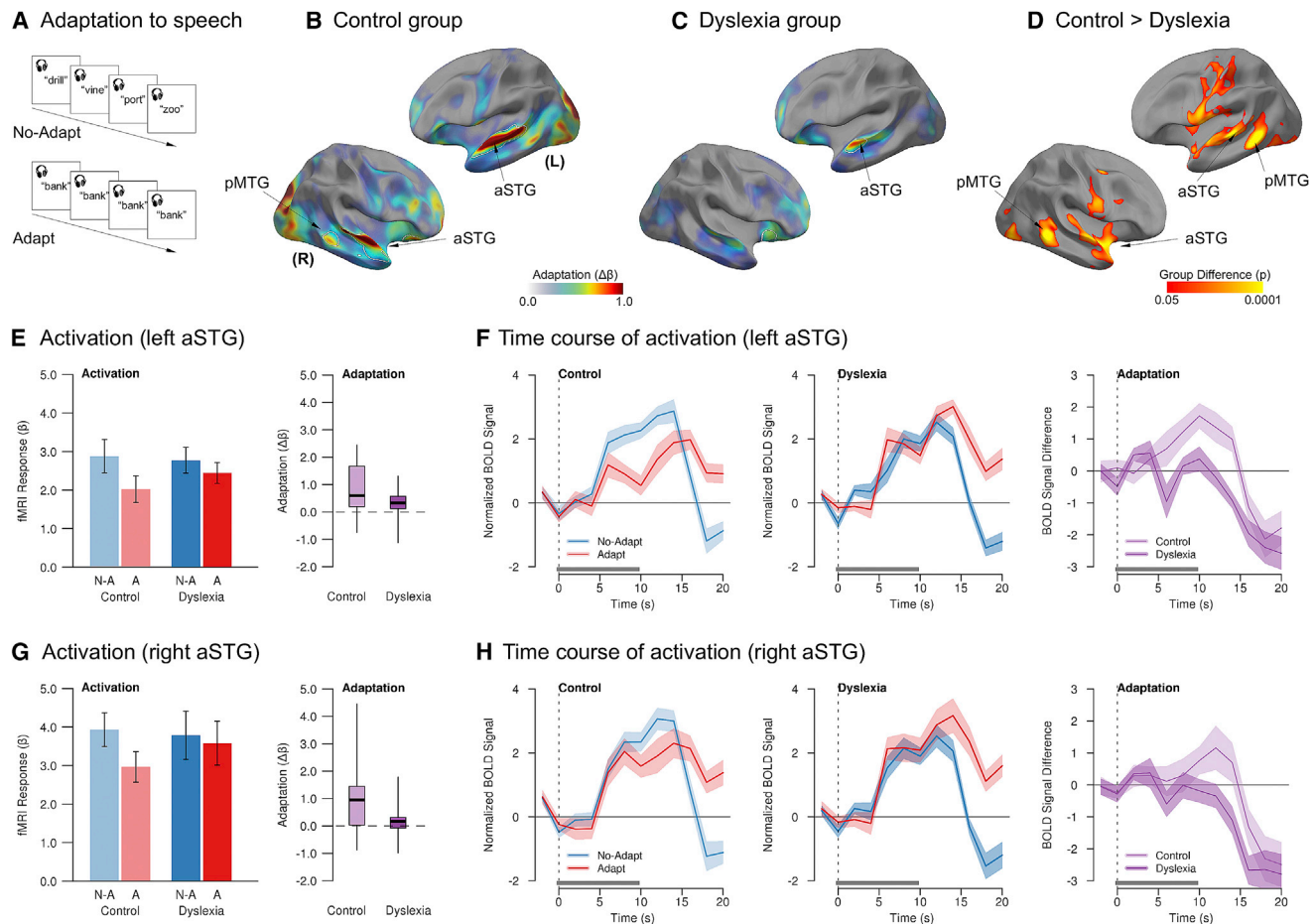


Figure 2. Reduced Neural Adaptation in Dyslexia When Listening to Repeated Speech

(A) Schematic of the stimulation paradigm.

(B) The control group exhibited significant adaptation in bilateral STG and right pMTG.

(C) Adaptation in the dyslexia group was significant, though weaker, in left STG only.

(D) The magnitude of adaptation in the dyslexia group was significantly reduced throughout perisylvian areas for speech processing, including bilateral aSTG and pMTG.

(E–H) (E) In aSTG, the control group exhibited a consistently greater difference between conditions, (F) with the magnitude of adaptation increasing across the stimulation period, whereas the dyslexia group showed little or no difference between conditions across time. The same pattern of (G) mean, and (H) time course differences was also seen in right aSTG. (See Figure 1 for details of plots and plotting conventions). (See also Figures S2A and S2B and Table S4).

Cohen, 2011; McCandliss et al., 2003; Price, 2012; Price and Devlin, 2011). Additional clusters of significantly reduced adaptation were found in right insula, left motor cortex, and right angular gyrus (AG). There were no clusters in which the dyslexia group showed more adaptation than controls. Adaptation differences in FusG were the result of a smaller difference between the No-Adapt and Adapt conditions in the dyslexia group than in controls (Figures 3E and 3F), with increasing group differences over time (Table S4). The group difference in pMTG (an area associated with semantic processing; Hickok and Poeppel, 2007) was qualitatively different: whereas the control group showed modest, but nonsignificant, adaptation in this region, the dyslexia group showed a trend for enhancement, with greater activation the more times a written word was repeated (Figures 3G and 3H; Table S4). Unlike speech stimuli, and unlike experiment 1, we did not observe any correlation between adap-

tation in ventral or lateral temporal areas and reading ability in dyslexia.

Experiment 2c: Objects

In addition to linguistic stimuli in auditory and visual modalities, we also investigated whether reduced adaptation in dyslexia would be observed for nonverbal visual stimuli such as color photographs of objects. We measured neurophysiological adaptation by contrasting blocks of viewing photographs of multiple different objects versus blocks with the repeated presentation of the same photograph of a single object (Figure 4A).

In both control and dyslexia groups, significant adaptation to the repeated presentation of a photograph of an object was observed throughout visual and ventral temporal cortices known to process visual objects (Malach et al., 1995), including ITG, FusG, and lateral occipital cortex (LOC) extending dorsally into

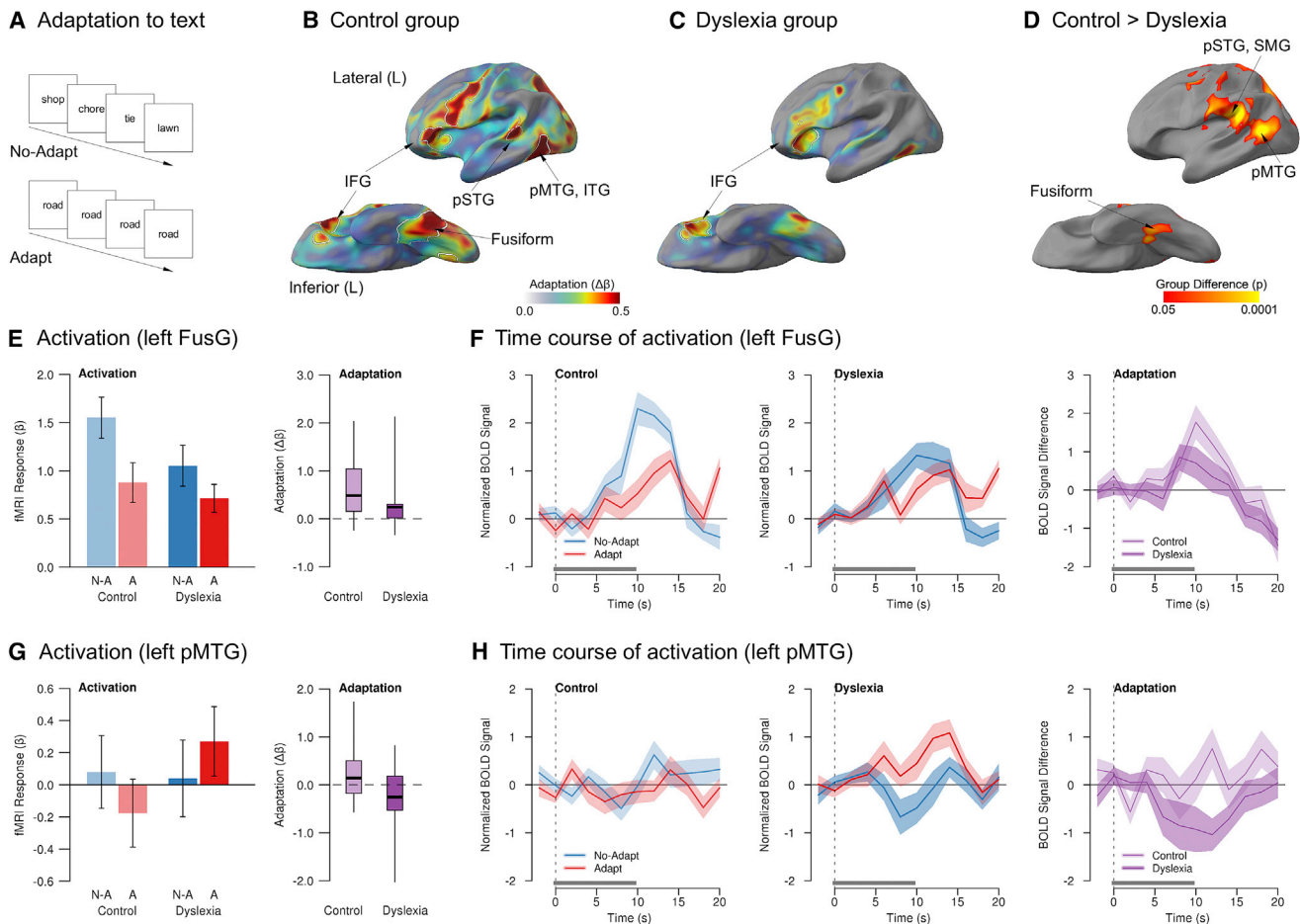


Figure 3. Reduced Neural Adaptation in Dyslexia When Viewing Repeated Text

(A) Schematic of the stimulation paradigm.

(B) The control group exhibited significant adaptation in classical reading areas in the left hemisphere: FusG, pSTG, and IFG.

(C) The dyslexia group showed significant adaptation in IFG only, with weaker and nonsignificant adaptation in FusG.

(D) Adaptation in the dyslexia group was significantly reduced throughout posterior reading areas, including pSTG, SMG, pMTG, and FusG.

(E and F) (E) In FusG, the control group exhibited a consistently greater adaptation than the dyslexia group, (F) with increasing differences across time. Controls also tended to show greater overall response to text, although this difference was not significant (Figures S3C and S3D).

(G and H) (G) The control group showed a modest trend toward adaptation in left pMTG, whereas the dyslexia group showed a greater trend toward enhancement (greater response to the Adapt than No-Adapt condition), (H) with this group difference increasing over time. (See Figure 1 for details of plots and plotting conventions). (See also Figures S2C and S2D and Table S4.)

superior parietal lobule (SPL), as well as in bilateral inferior frontal sulcus (IFS), FOC, and preSMA (Figures 4B and 4C). Both groups also showed significant enhancement in bilateral PT and precuneus (a task-deactivated area), and controls showed enhancement in two other task-deactivated areas: medial prefrontal cortex (MePFC) and superior frontal gyrus (SFG).

The magnitude of adaptation to object repetition in the dyslexia group was significantly less than in the control group throughout occipital and ventral temporal areas, including ITG, FusG, and LOC extending dorsally into SPL (Figure 4D). Stimulus repetition resulted in a greater reduction of the BOLD response over time in the control group than in the dyslexia group (Figures 4E–4H; Table S4). There were no clusters in task-activated cortex in which the dyslexia group showed more adaptation than the control group. Better reading skills in the dyslexia group

were significantly correlated with greater adaptation to repeated visual objects in both left ($r = 0.45$, $p < 0.03$) and right LOC ($r = 0.42$, $p < 0.05$).

Experiment 2d: Faces

Although putatively nonverbal, objects are nameable, and visual processing of objects may nonetheless involve automatic activation of their linguistic labels (Chabal and Marian, 2015), which may be impaired in dyslexia (Norton and Wolf, 2012; Wolf, 1984); therefore, we lastly investigated whether reduced adaptation in dyslexia would be observed for nonnameable visual stimuli, such as photographs of unfamiliar faces. We measured neurophysiological adaptation to faces by contrasting blocks of viewing photographs of multiple different people's faces versus blocks with the repeated presentation of the same photograph of a single person's face (Figure 5A).

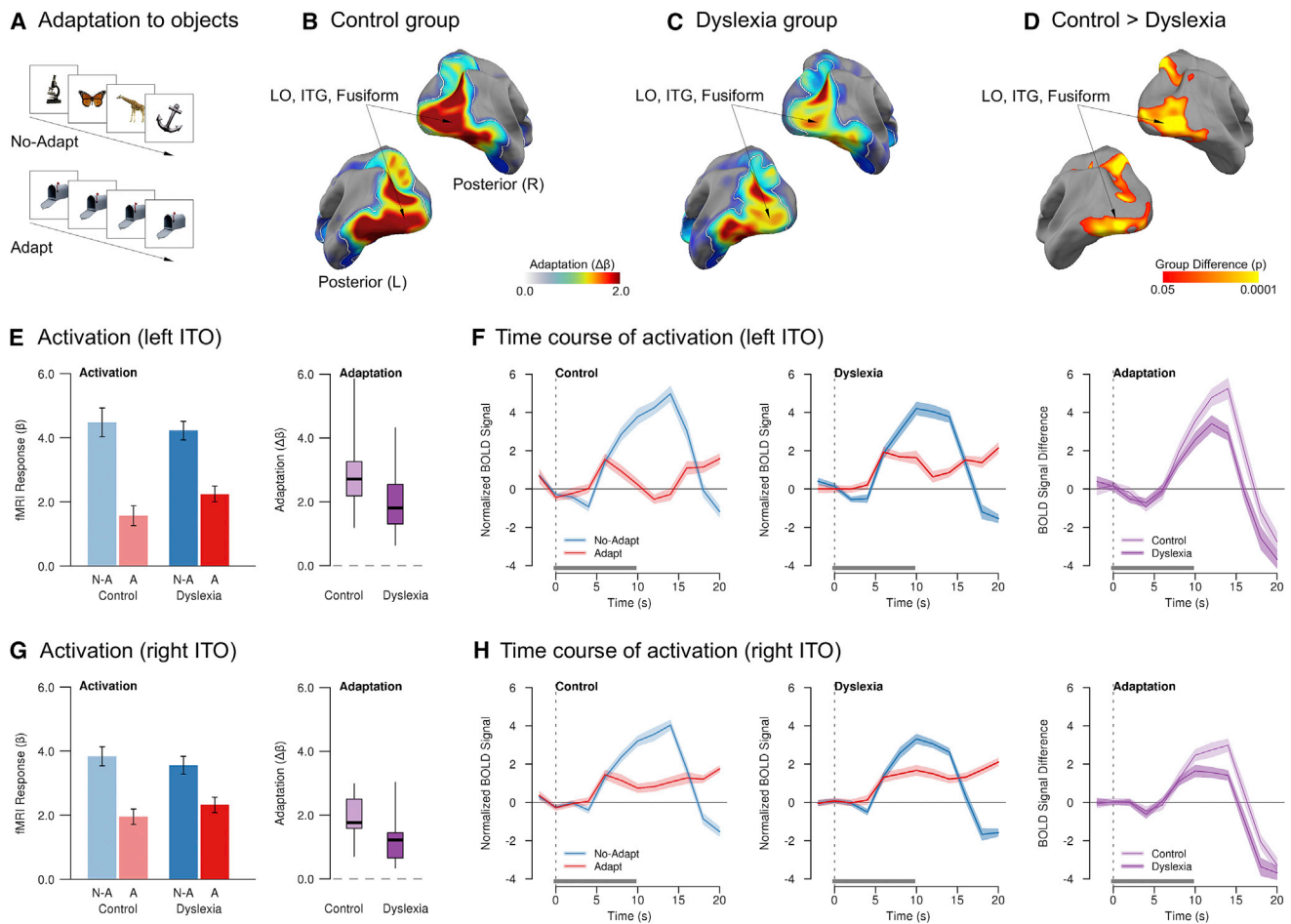


Figure 4. Reduced Neural Adaptation in Dyslexia When Viewing Repeated Objects

(A) Schematic of the stimulation paradigm.

(B) The control group exhibited significant adaptation to repetition of photographs of objects throughout lateral inferior temporal-occipital cortex (ITO).

(C and D) Weaker adaptation was observed in the dyslexia group throughout the same areas, (D) which was significantly reduced compared to controls.

(E–H) (E) The control group exhibited a consistently greater difference between conditions than the dyslexia group in left ITO, (F) with the magnitude of adaptation increasing across the stimulation period. The dyslexia group also showed significant adaptation, albeit at a consistently lower magnitude than controls. The same pattern of mean (G), and time course (H) differences was also seen in right ITO. (See Figure 1 for details of plots and plotting conventions). (See also Figures S2E and S2F and Table S4).

In the control group, repeated presentation of the same picture of a face yielded significant adaptation throughout ventral temporal and visual cortices, including bilateral FusG and LOC, and right amygdala and anterior hippocampus (Figure 5B). In the dyslexia group, significant adaptation was only observed in smaller bilateral FusG clusters (Figure 5C). The dyslexia group exhibited significantly less adaptation than the control group in numerous regions associated with face processing (Kanwisher and Yovel, 2006; Tsao and Livingstone, 2008), including bilateral FusG and LOC; right hippocampus, temporal pole, and amygdala; and left premotor cortex and insula (Figure 5D). As in all other experiments, this group difference was related to a greater reduction of the BOLD response to repeated stimuli in the control group than in the dyslexia group (Figures 5E–5H; Table S4). There were no clusters in which the dyslexia group showed more adaptation than controls, and we did not observe any cor-

relation between adaptation in occipital or ventral temporal areas and reading ability in dyslexia.

To confirm that the group difference in adaptation did not reflect more heterogeneous localization of adaptation effects in the dyslexia group than in the control group, we performed an additional analysis that measured adaptation only in the face-selective clusters of each participant. The fusiform face area (FFA; Kanwisher et al., 1997) was localized in individual participants by contrasting activation to faces versus objects and identifying the anterior-most discrete face-selective cluster in the occipitofusiform region. The FFA was successfully localized in 22 participants in the dyslexia group and 18 participants in the control group (Figure 6A). The probability of localizing an FFA did not differ by group ($\chi^2 = 0.63$, $p = 0.43$), nor was there a group difference in the threshold at which the FFA cluster could be localized (independent-sample $t_{38} = 0.06$, $p = 0.95$) or the volume of

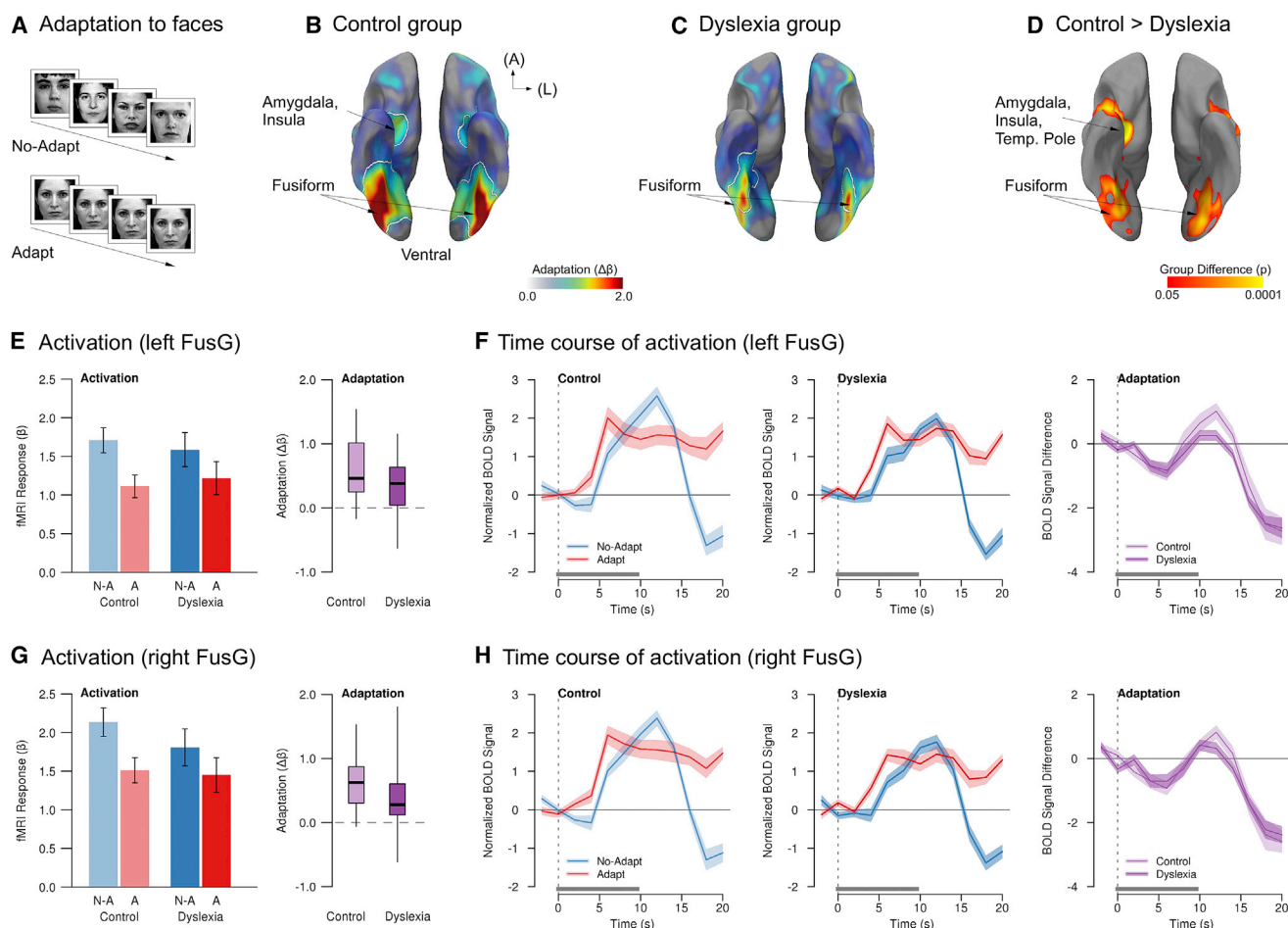


Figure 5. Reduced Neural Adaptation in Dyslexia When Viewing Repeated Faces

(A) Schematic of the stimulation paradigm.
 (B) The control group exhibited significant adaptation to repetition of photographs of faces throughout canonical face-sensitive areas, including FusG, anterior insula, and amygdala.
 (C) The dyslexia group showed weaker adaptation throughout the same areas.
 (D) Adaptation in the dyslexia group was significantly reduced throughout face-sensitive cortex, including prominently in FusG.
 (E–H) (E) The control group exhibited modest, but overall significant adaptation to repetition of faces in left FusG, (F) with the magnitude of adaptation increasing across the stimulation period; the dyslexia group also showed significant adaptation, but at a significantly lower magnitude than controls. The same pattern of mean (G), and time course (H) differences was also seen in right FusG. (See Figure 1 for details of plots and plotting conventions). (See also Figures S2G and S2H and Table S4).

the FFA (independent-sample $t_{38} = 0.65$, $p = 0.52$), indicating no difference in cortical specialization for faces between the two groups. The control group showed significant adaptation in their FFAs to repeated faces (paired $t_{17} = 6.13$, $p < 0.00002$), whereas adaptation in the dyslexia group was not significant (paired $t_{21} = 1.67$, $p = 0.11$). The magnitude of FFA adaptation was significantly less in the dyslexia group than in controls (independent-sample $t_{38} = 3.37$, $p < 0.002$) (Figure 6B). As in the whole-brain analyses, the group difference in adaptation reflected an increasingly smaller response to repeated stimuli in the control group than in dyslexia (Figure 6C; Table S4). (We attempted a similar analysis for the visual word form area [VWFA; McCandliss et al., 2003] in experiment 2b, but were unable to reliably isolate this region in our participants using a Words > Objects contrast.)

Experiment 3

Having seen robust and apparently domain-general neurophysiological adaptation deficits in adults with dyslexia, we further asked whether reading-ability-related adaptation differences were evident in emerging readers (age 6–9 years). We repeated experiment 2a with young children with dyslexia and their age-matched peers with typical reading development. We measured neurophysiological adaptation by contrasting blocks of a single, repeated spoken word versus blocks with multiple, different spoken words from a single speaker (Figure 7A).

Children with and without dyslexia successfully maintained attention to the auditory stimuli throughout in both conditions, as indicated by near-ceiling accuracy in both groups (control = 98.6%; dyslexia = 97.8%). A repeated-measures ANOVA for

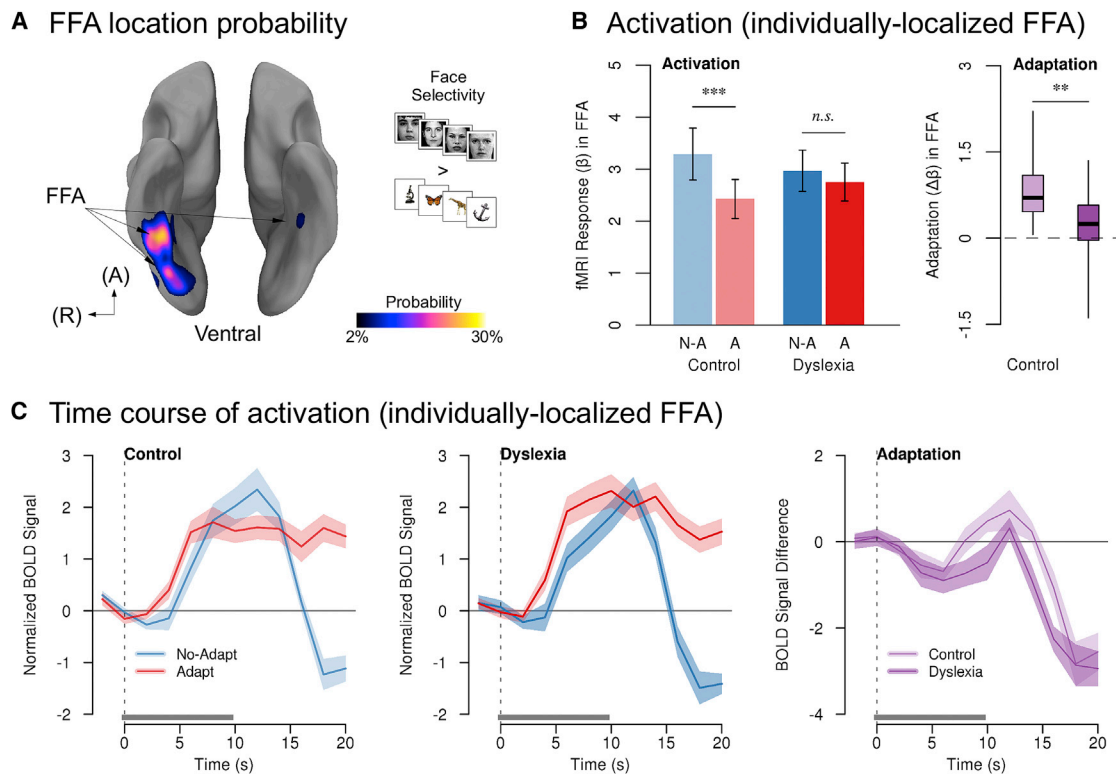


Figure 6. Reduced Neural Adaptation in Dyslexia to Faces in FFA

Individuals with dyslexia exhibited reduced adaptation to repeated versus unrepeat faces, even when adaptation was measured in individually localized face-selective cortex.

(A) Probabilistic location of the FFA across all participants; greater response to faces than objects in ventral temporal cortices was used to localize face-selective clusters in individual participants from experiments 2c and 2d.

(B) Barplots: magnitude of neural response (activation) by condition (No-Adapt: N-A, blue and Adapt: A, red) and group (controls: lighter bars and dyslexia: darker bars) in FFA. The No-Adapt > Adapt contrast was significant in the control group (**p < 0.00002), but not in dyslexia (n.s., p = 0.11). The difference between conditions (adaptation) in FFA by group is shown (boxplot). The difference in adaptation between the two groups was also significant (Group × Condition interaction, **p < 0.002).

(C) Mean time course (solid lines) ± SEM of BOLD responses to the No-Adapt and Adapt conditions by group and their difference (adaptation) in FFA (all plotting conventions as in Figure 1) (see also Figure S3 and Table S4).

effects of group and condition on accuracy revealed no effect of group ($F_{1,43} = 1.64$, $p = 0.21$), no effect of condition ($p = 0.17$), and no interaction ($p = 0.33$). The same test for response time revealed a significant effect of condition ($F_{1,43} = 6.16$, $p < 0.02$, $\eta^2 = 0.03$)—with faster response times in the Adapt condition (977 ms versus 1,044 ms)—but no effect of group ($p = 0.59$) or interaction ($p = 0.56$).

In control children, hearing multiple repetitions of the same word resulted in significant adaptation in bilateral STG, PT, and SPL (Figure 7B). For children with dyslexia, however, there were no areas exhibiting significant adaptation (Figure 7C). There were no clusters of repetition-related enhancement in either group. Adaptation in children with dyslexia was significantly less than that of controls in left PT, STG, and IFG (Figure 7D). This group difference was the result of an increasingly large reduction of response to stimulus repetition over time in the control group than in the dyslexia group, who in turn showed almost no response distinction between the Adapt and No-Adapt conditions (Figures 7E–7H; Table S4). There were no clusters in which the dyslexia group showed more adaptation than controls.

Because the children with dyslexia were in only preliminary stages of reading development, we investigated whether the magnitude of auditory adaptation was related to their phonological awareness, an important preliterate skill (Bradley and Bryant, 1983) that is a better predictor of long-term reading outcomes than early reading abilities (MacDonald and Cornwall, 1995). We observed positive correlations in the children with dyslexia between the magnitude of adaptation in left PT ($r = 0.46$, $p < 0.04$) and left aSTG ($r = 0.50$, $p < 0.025$) and their phonological awareness (Wagner et al., 1999).

DISCUSSION

Across six experiments, we found that rapid neural adaptation, as indexed by repetition-induced reduction of the fMRI BOLD signal (Grill-Spector and Malach, 2001), was diminished in children and adults with dyslexia for every stimulus type assessed, auditory language, visual language, visual objects, and faces. This deficit in adaptation was found selectively in the brain regions known to be critically involved in processing each stimulus

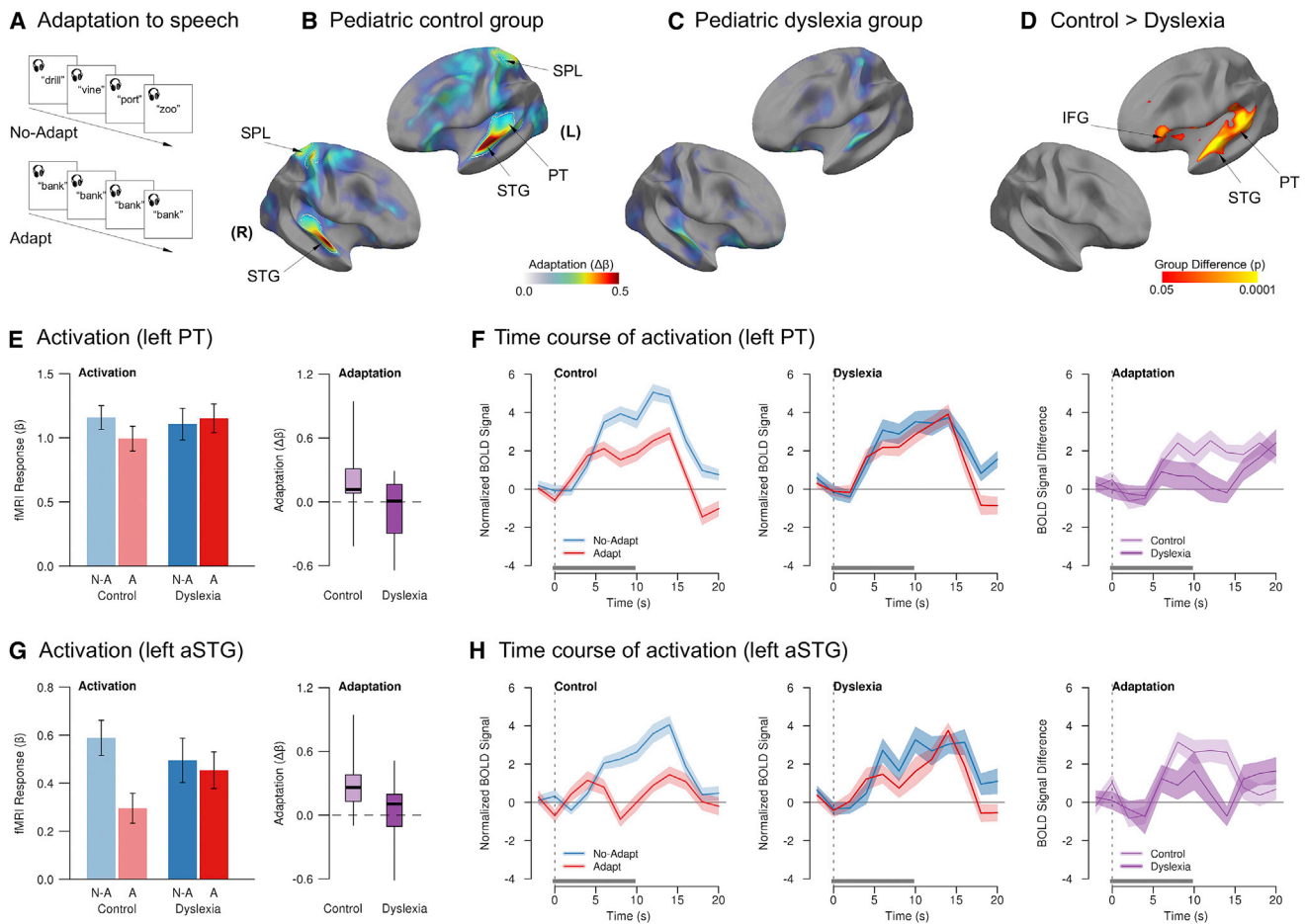


Figure 7. Reduced Neural Adaptation to Speech in Children with Dyslexia

(A) Schematic of the stimulation paradigm.

(B) The control group exhibited significant adaptation in bilateral STG, including left PT.

(C) The dyslexia group showed no significant adaptation.

(D) The magnitude of adaptation in the dyslexia group was significantly reduced in left-hemisphere speech perception areas, including IFG, aSTG, and PT.

(E–H) (E) The control group exhibited a consistently greater difference between conditions in left PT, (F) with the magnitude of adaptation increasing across the stimulation period, whereas the dyslexia group showed little or no difference between conditions across time. The same pattern of mean (G), and time course (H) differences was also seen in left aSTG. (See Figure 1 for details of plots and plotting conventions). (See also Figure S4 and Table S4).

type (Bell et al., 2011; Chandrasekaran et al., 2011; Kanwisher et al., 1997; Malach et al., 1995; McCandliss et al., 2003; Weiner et al., 2010). Correspondingly, the amount of preserved adaptation in these stimulus-specific brain regions was related to the reading skills of adults and preliterate skills of children with dyslexia. The breadth of this deficit—across ages, brain regions, and stimulus types—suggests that dysfunction of neural adaptation may be an important neurophysiological difference in many individuals with dyslexia.

Diminished neural adaptation to linguistic stimuli parallels known behavioral deficits in these domains. Adults with dyslexia exhibited less neural adaptation to the speech of a consistent talker, corresponding to their reduced behavioral ability to learn the specific phonetic-phonological features of individual voices (Perrachione et al., 2011) and impaired implicit learning of auditory categories (Gabay and Holt, 2015). Adaptation deficits in

dyslexia cannot be ascribed to failure to notice the subtle repetition of stimulus features (voices) in experiment 1, because even the highly salient, multiple repetitions of single spoken or written words in experiment 2 resulted in less neural adaptation in dyslexia than controls. Furthermore, these adaptation deficits were found in children with dyslexia early in their literacy development, suggesting that reduced sensitivity to the repetition of language stimuli is present even before reading skills have been extensively trained (Boets, 2014; Goswami, 2015). This parallels the observation that perceptual adaptation is related to preliterate and language skills even before children begin to learn to read (Banai and Yifat, 2012).

Perhaps more surprisingly, we also observed adaptation deficits to repetition of nonlinguistic stimuli such as objects and faces, although strictly perceptual deficits for these stimuli are not generally observed in dyslexia (Rüsseler et al., 2003; cf.

Sigurdardottir et al., 2015). This suggests that, in dyslexia, the general capacity for perceptual processes to establish short-term representations of stimulus consistency may be impaired (Ahissar et al., 2006; Chandrasekaran et al., 2009; Hornickel and Kraus, 2013; Jaffe-Dax et al., 2015; Oganian and Ahissar, 2012).

An impairment in neural adaptation, which reflects the neural processes involved in establishing robust short-term perceptual representations (Alain et al., 2007; Garrido et al., 2009; Jääskeläinen et al., 2007; Khouri and Nelken, 2015) provides a framework for understanding how several other behavioral and neural differences observed in dyslexia may form a constellation of low-level, adaptation-related deficits. First, individuals with dyslexia may have an impairment “anchoring” to consistent stimulus statistics in order to enhance perceptual thresholds (Ahissar et al., 2006; Banai and Ahissar, 2010), a behavioral effect reflected in rapid neural adaptation (Fritz et al., 2003; Garrido et al., 2009). Second, individuals with dyslexia are also frequently observed to have impairments recognizing both auditory and visual stimuli in the presence of noise (Sperling et al., 2005, 2006; Ziegler et al., 2009). Correspondingly, short-term adaptation of auditory and visual cortices to the statistics of noise facilitate perception in animal models (Atiani et al., 2009), and neural adaptation may also support noise exclusion in humans (Parbery-Clark et al., 2011). Third, neural coding deficits in auditory thalamus and brainstem have been found in dyslexia for tasks that use consistent stimulus or noise features (Chandrasekaran et al., 2009; Diaz et al., 2012). Our observation of dysfunction in cortical adaptation suggests these may be systems-level deficits, given corticofugal signaling is responsible for modulating auditory representations in thalamus and brainstem (Chandrasekaran et al., 2014; Suga et al., 2002). Finally, individuals with dyslexia may exhibit differences in gamma-band neural synchronization to auditory stimuli (Lehongre et al., 2011). Synchronous neural activity at these frequencies is induced by neural adaptation (Hansen and Dragoi, 2011), and such neural entrainment to stimulus consistency aids perception (Giraud and Poeppel, 2012; Park et al., 2015). This cluster of adaptation-related impairments may arise from dysfunction in common or related neurobiological mechanisms, namely, ones that constrain the extent to which the dyslexic brain can overcome internal noise and establish the perceptual constancy that underlies short-term perceptual facilitation and supports long-term perceptual learning (Hornickel and Kraus, 2013; Jääskeläinen et al., 2007; Jaffe-Dax et al., 2015).

Could Adaptation Differences Reflect Attentional Differences?

The suggestion that visual-spatial attention deficits may, in some cases, underlie impaired reading (Franceschini et al., 2012; Vidyasagar and Pammer, 2010) warrants considering whether diminished adaptation in dyslexia might have an attentional origin. There are several reasons why it is unlikely that the present results reflect an impairment in voluntary or intentional deployment of top-down attention. First, between-group differences in adaptation were always observed in the cortical areas specifically implicated in processing stimuli of each type, not areas associated with volitional, top-down attention (Hopfinger

et al., 2000; Womelsdorf and Everling, 2015). Second, substantial fMRI adaptation is readily observed in both attentive and passive tasks (Kourtzi and Kanwisher, 2001; Larsson and Smith, 2012; Sawamura et al., 2005). Third, our original observation of adaptation differences (experiment 1) occurred in a speech perception task where the attentional demands of the Adapt and No-Adapt conditions did not differ.

Attention may nonetheless affect adaptation in subtler ways. Stimuli in Adapt conditions were highly repetitive and thus highly predictable. Perceptual expectations influence the magnitude of neural adaptation (Costa-Faidella et al., 2011; Summerfield et al., 2008; Todorovic et al., 2011). Likewise, animal models have shown that rapid changes in neural responses to repeated stimuli require top-down neuromodulatory input (Fritz et al., 2003; Froemke et al., 2007). Diminished adaptation in dyslexia might therefore represent a failure to generate robust, top-down perceptual expectations (Jaffe-Dax et al., 2015): Higher cortical areas may not provide appropriate feedback signals to sensory cortices to facilitate adaptation (Boets et al., 2013; Saygin et al., 2013; Yeatman et al., 2011). Alternatively, there is some evidence for microanatomical abnormalities that disrupt laminar structure in dyslexia (Galaburda et al., 1994), and disruptions to the local organization of laminar circuits may interfere with the local or long-range connections supporting adaptation, which depends on finely tuned neuromodulatory input (Froemke et al., 2007) and lamina-specific synchronization in sensory cortex (Hansen and Dragoi, 2011).

General Neural Dysfunction and Specific Reading Impairment

A widely replicated finding in the neuroscience of dyslexia is the observation of reduced activation to print in the canonical reading network, and particularly in left occipitotemporal cortex (Paulesu et al., 2014; Shaywitz et al., 1998). However, the causal connection between developmental dyslexia and reduced sensitivity to print in this region remains unclear. On the one hand, dysfunction of left occipitotemporal cortex itself could be a pathway to dyslexia. Alternatively, reduced sensitivity to print in this region could result from developmental differences in other processes that are compromised in dyslexia prior to learning to read, such as phonemic awareness in speech (Bradley and Bryant, 1983) or rapid naming of visual stimuli (Norton and Wolf, 2012). Weaknesses in these preliterate skills may encumber the functional integration of occipitotemporal cortex into a robust reading network. Correspondingly, there has been a strong interest in identifying low-level deficits in dyslexia that might serve as neural precursors to explain weaknesses in these preliterate skills.

A challenge for any hypothesis of low-level impairments in dyslexia is to explain how a “general” biological dysfunction gives rise to a “specific” impairment in reading without impacting other complex behaviors. For instance, proponents of various low-level auditory deficits as an explanation for poor reading (Goswami, 2011; Tallal and Piercy, 1973) must offer an account for how these interfere specifically with reading, but do not produce apparent disruptions to complex auditory abilities like perceiving speech and music. Likewise, proponents of core visual deficits (Franceschini et al., 2012; Stein, 2001;

Vidyasagar and Pammer, 2010) must be able to explain how these impairments affect reading, but do not result in correspondingly serious disruptions to other complex visual behaviors like recognizing objects or driving a car.

A dysfunction of neural adaptation differs from other low-level hypotheses in that it does not posit an impairment in processing specific stimulus features that are critical for other auditory or visual abilities. Instead, it suggests that there may be a general impairment in processes that facilitate perception under adverse or challenging conditions (Jääskeläinen et al., 2007), which, at its core, represents an impairment in mechanisms for rapid perceptual learning, including learning the robust speech-sound categories necessary for sound-to-symbol matching in reading (Bradley and Bryant, 1983). Neural adaptation facilitates behaviors such as detecting stimuli in noise (Atiani et al., 2009; Chandrasekaran et al., 2009; Parbery-Clark et al., 2011), discriminating subtle stimulus differences (Edeline et al., 1993; Fritz et al., 2003), and rapid learning of new perceptual categories (Alain et al., 2007; Garrido et al., 2009). Correspondingly, for all of these behaviors facilitated by adaptation, significant deficits have consistently been reported in dyslexia.

Although the brain has evolved to be computationally powerful for solving certain types of problems such as perceiving speech and recognizing objects, learning to read differs in that it is a cultural invention imposing itself upon circuitry that evolved for other purposes (Dehaene et al., 2010; McCandliss et al., 2003). Learning to read depends on the ability to orchestrate, across two perceptual modalities, the complex correspondence between abstract phonological representations of speech sounds and abstract orthographic representations of written symbols, a task that becomes disproportionately more difficult if either type of representation, or access to them, is impaired. Correspondingly, learning to read is one of the most complex examples of human learning, the demands of which are evident from its lengthy and explicit instruction throughout childhood and into adulthood. There is no other human behavior that approaches reading's demands for coordinating multimodal perceptual representations and cognitive processes. In this way, a general neural dysfunction that is subtly detrimental to other behaviors may be substantially detrimental for learning to read.

Extensions and Limitations of the fMRI Adaptation Technique

The specific physiological mechanisms that give rise to adaptation in the BOLD signal are not yet fully understood (Grill-Spector et al., 2006; Krekelberg et al., 2006; Sawamura et al., 2006), and repetition-related fMRI adaptation is likely to reflect a variety of diverse neurophysiological processes depending on variables like the cortical location (Weiner et al., 2010), stimulation paradigm (Müller et al., 2013), and task demands (Jiang et al., 2013) in which it is observed. Interestingly, fMRI adaptation is attenuated for perceptually noisy stimuli (Turk-Browne et al., 2007), paralleling hypotheses that neural representations themselves may be disproportionately noisy in dyslexia (Hornickel and Kraus, 2013; Jaffe-Dax et al., 2015; Ziegler et al., 2009).

Although the coarseness of fMRI signals precludes this tool from resolving the circuit- or cellular-level source of adaptation

impairments in dyslexia by itself, the present observations provide a stronger foundation for the targeted pursuit of neurophysiological differences in dyslexia informed by basic research in animal models. For instance, the necessary role of cholinergic neuromodulation for rapid neural adaptation and consequent behavioral enhancement is well known at the cellular level (Froemke et al., 2007; Suga et al., 2002), with similar effects shown in BOLD imaging (Thiel et al., 2002). Atypical cerebral concentration of neurometabolic precursors to acetylcholine have been found in dyslexia (Bruno et al., 2013; Pugh et al., 2014). Advances in cholinergic radioligands now permit targeted investigation of this neurotransmitter in behavioral adaptation tasks and in dyslexia. Although this example is speculative, our observation of generalized differences in neurophysiological adaptation contributes to a growing literature from which we can begin to develop a systems- (as opposed to cognitive-) neuroscientific framework for investigating dyslexia.

The complexity of reading makes successfully learning this skill vulnerable to a broad range of linguistic, visual, and attentional dysfunctions that may occur in variable mixtures in individual children with dyslexia. Correspondingly, although perceptual adaptation deficits in dyslexia have been observed across a large number of studies and diverse range of tasks, some studies have found deficits on only a subset of tasks employed (Beattie et al., 2011), for only a subset of participants (Willburger and Landerl, 2010) or for none at all (Wijnen et al., 2012). The results from the present study, however, provide multiple converging lines of evidence for a substantive relationship between neural adaptation deficits and reading impairment. We not only observed that the degree of neural adaptation in task-relevant brain regions was significantly correlated with reading abilities in adults with dyslexia and with phonological skills in children with dyslexia, we also observed consistent and significant group differences in neural adaptation for all tasks. Such correlations, combined with reliable group differences, correspond to the two ways that neuroimaging and behavioral studies are able to empirically characterize differences between typical and dyslexic brain function.

Finally, although we observed consistently diminished adaptation in dyslexia, and although the magnitude of that adaptation was related to reading ability in dyslexia, our choice to use high-level, perceptually complex stimuli in our adaptation paradigms meant we could not observe whether the degree of neural adaptation was directly related to perceptual adaptation, as would have been possible with a task designed to evaluate perceptual thresholds (Brida et al., 1984). Nevertheless, two-way relationships between neural and perceptual adaptation (Alain et al., 2007), perceptual adaptation and reading abilities (Ahissar et al., 2006; Banai and Yifat, 2012), and neural adaptation and reading impairment (present work) have now been repeatedly demonstrated, and confirmation of the three-way relationship among these three factors can be made in future studies.

An Emerging Picture of the Dyslexic Brain

Dyslexia is a specific impairment in developing typical reading abilities. Correspondingly, structural and functional disruptions to the network of brain areas known to support reading are

consistently observed in dyslexia (Norton et al., 2015). However, these observations confound cause and consequence, especially since reading is a cultural invention that must make use of existing circuitry evolved for other purposes (Dehaene and Cohen, 2007; Dehaene et al., 2010). In this way, differences between brains that exert more subtle influences on nonreading behaviors are likely to be the culprit in a cascade of perceptual and mnemonic challenges that interfere with the development of typical reading abilities. Recent research has begun to elucidate a cluster of behaviorally distinct, but potentially physiologically related, impairments that are evinced by individuals with reading difficulties and observable in their brains. Through this collection of neural signatures—including unstable neural representations (Hornickel and Kraus, 2013), diminished top-down control (Boets, 2014; Boets et al., 2013; Chandrasekaran et al., 2009), susceptibility to noise (Sperling et al., 2005; Ziegler et al., 2009), and inability to construct robust short-term perceptual representations (Díaz et al., 2012; Jaffe-Dax et al., 2015; Lehongre et al., 2011)—we are beginning to see that reading impairments can arise from general dysfunction in the processes supported by rapid neural adaptation.

EXPERIMENTAL PROCEDURES

Participants

Separate groups of adults completed experiments 1 ($n = 19$ dyslexia, 19 control) and 2 ($n = 24$ dyslexia, 23 control). Children with dyslexia ($n = 26$) and with typical reading development ($n = 25$) completed experiment 3. See Tables S1–S3 for participant assessment and characterization. This study was approved by the Committee on the Use of Humans as Experimental Subjects (COUHES) at MIT.

Task and Stimuli

In experiment 1, participants matched auditory words to pictures during a 42 min, sparse-sampling, block-design fMRI task. In the No-Adapt condition, words were spoken by four different voices; in the Adapt condition, words were spoken by one consistent voice.

In experiments 2 and 3, participants passively attended speech, text, objects, or faces during separate 10 min, continuous-sampling, and block-design fMRI tasks. There were eight unique stimuli that were presented in No-Adapt blocks; a single stimulus was repeated eight times in Adapt blocks. Children underwent only the speech task.

fMRI Analysis

Functional data were preprocessed and modeled in SPM8, Freesurfer, and Nipype. Model and contrast estimation were conducted in EPI space, contrast images were coregistered to participants' anatomy, and then normalized to MNI space. Group-level mixed-effects models assessed adaptation within and between groups.

For full methods details, see Supplemental Experimental Procedures.

SUPPLEMENTAL INFORMATION

Supplemental Information includes Supplemental Experimental Procedures, four figures, and five tables and can be found with this article online at <http://dx.doi.org/10.1016/j.neuron.2016.11.020>.

AUTHOR CONTRIBUTIONS

T.K.P. and J.D.E.G. designed the study. S.N.D. and R.W. conducted behavioral assessments and characterization of participants in experiments 1 and 2 and P.C., A.C., K.H., and J.A.C. did so for participants in experiment 3. T.K.P., S.N.D., and R.W. collected fMRI data in experiments 1 and 2 and

T.K.P., J.M., A.C., and J.A.C. did so for experiment 3. T.K.P. and S.S.G. analyzed the data. T.K.P. and J.D.E.G. wrote the manuscript. All authors read and approved the manuscript.

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Supplemental Information

Dysfunction of Rapid Neural Adaptation in Dyslexia

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SUPPLEMENTAL INFORMATION

Table S1. Cognitive, behavioral, and demographic assessment of participants in Experiment 1. (See also Table 1)

Values are mean \pm standard deviation. Also shown are the effect size of the group difference in standard scores (Cohen's d), the reliability of this difference (t -statistic), and the two-tailed probability this difference arose by chance (p -value). Asterisks (*) indicate group differences probable with Bonferroni-corrected $\alpha = 0.0025$. Diamonds (\diamond) denote tests used as inclusionary/exclusionary criteria for group membership. *Abbreviations:* WASI: *Wechsler Abbreviated Scale of Intelligence*, (Wechsler, 1999); CTOPP: *Comprehensive Test of Phonological Processing* (Wagner, Torgesen, & Rashotte, 1999); RAN: *Rapid Automatized Naming* (Wolf & Denckla, 2005); WRMT-R/NU: *Woodcock Reading Mastery Test – Revised/Normative Update* (Woodcock, 1998); TOWRE: *Test of Word Reading Efficiency* (Torgesen, Wagner, & Rashotte, 1999); WJ-III: *Woodcock-Johnson Test of Cognitive Abilities III* (Woodcock, McGrew, & Mather, 2001); WAIS-IV: *Wechsler Adult Intelligence Scale* (Wechsler, 2008); M: male; F: female.

Test	Subtest	Control (N = 19)		Dyslexia (N = 19)		Group difference		
		Raw Score	Standard Score	Raw Score	Standard Score	$d =$	$t =$	$p =$
WASI	Block Design	62.1 \pm 5.9	62.4 \pm 4.0	52.3 \pm 14.0	56.4 \pm 9.2	0.860	2.351	0.025
	Matrix Reasoning	30.9 \pm 1.7	60.7 \pm 3.4	29.3 \pm 3.3	58.1 \pm 7.3	0.453	1.239	0.225
	Performance IQ	123.1 \pm 5.5	119.7 \pm 5.6	114.5 \pm 13.8	112.4 \pm 12.6	0.766	2.094	0.045
CTOPP	Elision	19.5 \pm 0.7	11.5 \pm 0.7	16.1 \pm 2.8	8.5 \pm 1.9	2.061	5.634	0.000 *
	Blending Words	18.0 \pm 1.1	12.0 \pm 1.1	14.6 \pm 4.1	9.5 \pm 3.0	1.091	2.981	0.006
	Non-word Repetition	15.3 \pm 1.6	11.3 \pm 1.6	10.0 \pm 1.6	6.9 \pm 1.0	3.397	9.286	0.000 *
RAN	Numbers	15.7 \pm 1.6	113.7 \pm 3.3	23.4 \pm 5.3	103.1 \pm 7.4	1.887	5.079	0.000 *
	Letters	15.7 \pm 1.6	113.7 \pm 3.3	23.4 \pm 5.3	103.1 \pm 7.4	1.887	5.079	0.000 *
	Numbers & Letters	15.7 \pm 1.7	112.1 \pm 3.0	23.6 \pm 6.3	99.9 \pm 9.3	1.781	4.793	0.000 *
WRMT-R/NU	\diamond Word ID	101.4 \pm 3.6	113.0 \pm 11.5	89.7 \pm 7.5	91.1 \pm 10.5	2.064	5.642	0.000 *
	\diamond Word Attack	40.7 \pm 2.6	112.9 \pm 12.5	31.8 \pm 3.6	91.6 \pm 6.9	2.217	6.061	0.000 *
	Passage Comprehension	17.0 \pm 1.6	116.4 \pm 4.2	27.8 \pm 8.7	99.7 \pm 10.5	2.134	5.743	0.000 *
TOWRE	\diamond Sight Word Reading	100.5 \pm 4.7	107.1 \pm 7.9	80.0 \pm 9.0	83.4 \pm 7.1	3.288	8.986	0.000 *
	\diamond Decoding	56.7 \pm 5.7	108.5 \pm 10.5	34.8 \pm 10.4	79.2 \pm 9.4	3.040	8.310	0.000 *
	Total	204.0 \pm 40.5	109.3 \pm 7.2	162.6 \pm 15.2	77.5 \pm 9.0	4.003	10.942	0.000 *
WJ-III	Fluency	103.6 \pm 19.1	120.9 \pm 13.2	64.7 \pm 15.3	94.0 \pm 10.8	2.318	6.132	0.000 *
WAIS-IV	Digit Span Total	34.4 \pm 6.0	13.4 \pm 3.3	25.8 \pm 4.7	8.6 \pm 2.3	1.733	4.501	0.000 *
Age (years)		22.1 \pm 3.7		24.5 \pm 5.9		0.494	1.349	0.187
Education (years)		15.3 \pm 1.6		14.9 \pm 2.3		0.184	0.495	0.624
Sex (M / F)		9 / 10		7 / 12		0.053 (ϕ)	0.108 (χ^2)	0.740

Table S2. Cognitive, behavioral, and demographic assessment of participants in Experiment 2. (See also Table 1)

Conventions and abbreviations as in Table S1.

Test	Subtest	Control (N = 24)		Dyslexia (N = 23)		Group Difference		
		Raw Score	Standard Score	Raw Score	Standard Score	d =	t =	p =
WASI	Block Design	59.4 ± 8.5	60.5 ± 5.7	54.3 ± 14.8	57.4 ± 9.7	0.399	1.231	0.226
	Matrix Reasoning	31.0 ± 4.9	63.0 ± 17.4	30.9 ± 4.4	61.0 ± 14.7	0.121	0.387	0.701
	Performance IQ	118.0 ± 9.5	115.2 ± 9.1	115.7 ± 13.3	113.6 ± 12.0	0.160	0.511	0.612
CTOPP	Elision	19.3 ± 0.9	11.3 ± 0.9	16.3 ± 3.1	8.7 ± 2.1	1.703	5.709	0.000 *
	Blending Words	18.3 ± 1.1	12.1 ± 1.4	14.4 ± 3.5	9.0 ± 2.7	1.452	4.870	0.000 *
	Non-word Repetition	14.3 ± 1.9	10.4 ± 1.8	10.8 ± 2.5	7.3 ± 1.2	2.105	7.060	0.000 *
RAN	Numbers	16.1 ± 3.2	113.7 ± 5.4	23.9 ± 11.4	100.7 ± 13.5	1.297	4.300	0.000 *
	Letters	16.1 ± 3.2	113.7 ± 5.4	23.9 ± 11.4	100.7 ± 13.5	1.297	4.300	0.000 *
	Numbers & Letters	16.3 ± 3.1	110.6 ± 4.8	23.3 ± 6.9	100.6 ± 11.0	1.216	4.032	0.000 *
WRMT-R/NU	◊ Word ID	100.2 ± 3.3	109.0 ± 9.1	88.1 ± 7.3	89.7 ± 8.6	2.231	7.481	0.000 *
	◊ Word Attack	39.0 ± 3.2	107.3 ± 13.7	29.5 ± 4.8	87.0 ± 6.0	1.940	6.506	0.000 *
	Passage Comprehension	18.1 ± 4.1	115.3 ± 8.3	26.2 ± 7.7	101.4 ± 10.6	1.513	4.966	0.000 *
TOWRE	◊ Sight Word Reading	100.6 ± 5.0	107.2 ± 8.4	77.2 ± 16.0	84.0 ± 10.9	2.456	8.140	0.000 *
	◊ Decoding	58.5 ± 2.8	108.3 ± 8.2	32.7 ± 10.9	76.7 ± 10.6	3.419	11.465	0.000 *
	Total	215.5 ± 12.1	109.3 ± 7.3	159.5 ± 19.8	75.7 ± 11.8	3.524	11.818	0.000 *
WJ-III	Fluency	103.7 ± 22.1	122.5 ± 17.5	70.9 ± 16.4	98.0 ± 11.9	1.646	5.233	0.000 *
WAIS-IV	Digit Span Total	32.7 ± 5.2	12.3 ± 2.8	24.6 ± 3.8	8.1 ± 1.9	1.786	5.622	0.000 *
Age (years)		22.2 ± 3.4		22.3 ± 4.4		0.025	0.083	0.935
Education (years)		15.4 ± 1.7		14.9 ± 1.9		0.266	0.881	0.383
Sex (M / F)		12 / 12		4 / 19		0.299 (φ)	4.204 (χ ²)	0.040

Table S3. Cognitive, behavioral, and demographic assessment of participants in Experiment 3.

(See also Table 1)

Abbreviations: KBIT-2: *Kaufman Brief Intelligence Test 2* (Kaufman & Kaufman, 2004); WISC-IV: *Wechsler Intelligence Scale for Children IV* (Wechsler, 2004). Other conventions and abbreviations as in Table S1.

Test	Subtest	Control (N = 25)		Dyslexia (N = 26)		Group Difference		
		Raw Score	Standard Score	Raw Score	Standard Score	d =	t =	p =
KBIT-2								
	Nonverbal IQ	31.3 ± 6.7	119.6 ± 15.9	25.7 ± 5.3	104.5 ± 13.2	1.056	3.696	0.001 *
CTOPP								
	Elision	15.8 ± 4.2	13.3 ± 2.4	6.9 ± 2.1	7.9 ± 1.4	2.765	9.368	0.000 *
	Blending Words	14.7 ± 3.8	12.2 ± 2.8	12.4 ± 3.4	10.4 ± 2.4	0.684	2.368	0.022
	Phonological Awareness Composite		10.8 ± 2.6		7.8 ± 1.6	1.360	4.553	0.000 *
	Non-word Repetition	11.0 ± 2.8	12.5 ± 2.4	7.5 ± 2.0	9.4 ± 2.2	1.378	4.774	0.000 *
	Memory for Digits	15.0 ± 2.4	116.3 ± 12.8	11.8 ± 2.2	95.0 ± 9.8	1.899	6.357	0.000 *
	Phonological Memory Composite		109.8 ± 11.1		92.1 ± 10.6	1.667	5.508	0.000 *
RAN								
	Letters	32.7 ± 6.7	100.7 ± 9.7	39.0 ± 12.3	93.4 ± 9.6	0.779	2.639	0.011
	Objects	51.1 ± 9.6	98.4 ± 13.0	57.7 ± 9.8	89.1 ± 11.2	0.788	2.701	0.010
	Numbers & Letters	36.2 ± 9.3	109.0 ± 12.9	45.9 ± 14.1	95.7 ± 11.8	1.102	3.814	0.000 *
WRMT-III								
	◊ Word ID	28.4 ± 3.1	118.3 ± 9.3	13.8 ± 4.7	81.7 ± 9.0	4.081	14.28	0.000 *
	◊ Word Attack	17.4 ± 4.1	113.6 ± 9.4	6.1 ± 3.2	84.8 ± 9.3	3.142	10.994	0.000 *
	Passage Comprehension	21.2 ± 6.3	122.1 ± 15.1	10.3 ± 2.8	89.0 ± 7.5	2.848	9.967	0.000 *
TOWRE								
	◊ Sight Word Reading	64.0 ± 8.0	113.4 ± 7.7	31.1 ± 11.4	80.3 ± 9.6	3.869	13.391	0.000 *
	◊ Decoding	34.8 ± 9.1	112.2 ± 8.7	9.3 ± 4.9	78.1 ± 7.1	4.374	14.989	0.000 *
	Total	225.7 ± 15.2	113.7 ± 8.0	157.6 ± 14.0	77.7 ± 7.4	4.758	16.135	0.000 *
WISC-IV								
	Coding	39.7 ± 12.1	9.8 ± 3.0	37.3 ± 11.1	8.7 ± 2.7	0.423	1.433	0.159
	Symbol Search	21.2 ± 8.3	10.2 ± 3.2	22.0 ± 6.3	10.0 ± 1.8	0.063	0.213	0.832
Age (years)		8.0 ± 0.7		7.9 ± 0.6		0.056	0.195	0.846
Grade (1 / 2 / 3)		7 / 13 / 5		12 / 14 / 0		0.147 (φ)	1.104 (χ²)	0.293
Sex (M / F)		16 / 9		19 / 7		0.055 (φ)	0.157 (χ²)	0.692

Table S4. Group by condition by time differences in the BOLD response. (See also Figures 1-7)

Region of Interest	Figure	Group × Condition × Time	
		<i>t</i> =	<i>p</i> =
Experiment 1 (Voices)			
left PT	Fig. 1F	2.755	0.004
right aSTG	Fig. 1H	2.178	0.018
Experiment 2a (Speech)			
left STG	Fig. 2F	4.650	2×10 ⁻⁵
right STG	Fig. 2H	4.080	1×10 ⁻⁴
Experiment 2b (Text)			
left FusG	Fig. 3F	2.194	0.017
left pMTG	Fig. 3H	3.798	2×10 ⁻⁴
Experiment 2c (Objects)			
left ITO	Fig. 4F	6.422	3×10 ⁻⁸
right ITO	Fig. 4H	5.987	2×10 ⁻⁷
Experiment 2d (Faces)			
left FusG	Fig. 5F	3.210	0.001
right FusG	Fig. 5H	2.716	0.005
FFA	Fig. 6C	2.942	0.003
Experiment 3 (Speech) (Children)			
left PT	Fig. 7F	3.478	5×10 ⁻⁴
left aSTG	Fig. 7H	3.409	6×10 ⁻⁴

Temporal analysis of adaptation effects

Statistical Analysis

We investigated how neural adaptation to stimulus repetition unfolded across time. The time course of the BOLD response to each stimulation block in each experiment was extracted from target ROIs and normalized to the onset of that block (see *Experimental Procedures: MRI Data Analysis: Time course analysis* for details). These time courses were analyzed in a series of linear mixed effects models, with fixed factors of condition (No-Adapt vs. Adapt), group (Control vs. Dyslexia), and time; random factors included by-subject intercepts, by-subject slopes for the condition term, and by-item intercepts (stimulation blocks), such that the model took the following form (Barr et al., 2013):

$$Y_{\text{BOLD}} \sim X_{\text{time}} * X_{\text{group}} * X_{\text{condition}} + (1 + \text{condition} | \text{subject}) + (1 | \text{block}) \quad (1)$$

In Experiment 1, we analyzed five volumes (27.5s) of activation following the onset of neurophysiological response; in Experiments 2 and 3 we likewise analyzed seven volumes (14s) of activation. These epochs were chosen to correspond to the rise (and plateau) of the hemodynamic response resulting from stimulation during the block.

The model term of interest was the three-way interaction between condition, time, and group. This term tests for whether there is a difference between groups in how their responses to the two conditions unfolded over time. To determine the significance of model terms, we conservatively assumed a *t*-distribution with reduced degrees of freedom equal to the number of participants – rather than the number of observations in the model – and a criterion of $\alpha = 0.05$.

Results

In all experiments, in all ROIs, there was a significant three-way interaction between group, condition, and time. The associated model terms were always positive, indicating that the change in the difference between the No-Adapt and Adapt conditions was greater (became more positive) over time for the control group than the dyslexia group. This result suggests that, for the control group, neurophysiological response magnitude increased throughout the no-adapt blocks as new stimuli were presented, whereas the response magnitude was lower, and may even have decreased over time, following multiple repetitions of a single stimulus. Conversely, for the dyslexia group, the magnitude of the difference between the No-Adapt and Adapt conditions did not increase as new stimuli were presented compared to repetition of the same stimulus.

As shown in the figures indicated in Table S4, this pattern of difference is true for all ROIs in all experiments. The qualitative exception to this pattern is the response of left pMTG to repeated text. In that region (Fig. 3H), there was only a small adaptation effect in the control group, whereas the dyslexia group tended to show an “enhancement” effect – i.e., increased response following multiple repetitions of the same stimulus.

Table S5. Regions of significant adaptation in each experiment. (See also Figures 1-5 & 7)

The region containing or closest to the peak voxel is indicated in bold text. *Abbreviations:* anterior (a); posterior (p); medial (m); dorsal (d); middle (mid); ventral (v); angular gyrus (AG); cingulate gyrus (CG); central operculum (CO); frontal medial cortex (FMC); frontal operculum (FO); frontal orbital cortex (FOC); frontal pole (FP); Heschl's gyrus (H); inferior frontal gyrus pars opercularis (IFo); inferior frontal sulcus (IFs); inferior frontal gyrus pars triangularis (IFt); insula (INS); inferior temporal gyrus (ITg); inferior temporal occipital gyrus (ITO); lingual gyrus (LG); motor cortex (MC); middle frontal gyrus (MFg); middle temporal gyrus (MTg); middle temporal occipital gyrus (MTO); occipital cortex (OC); precuneus (PCN); parahippocampal gyrus (PH); premotor cortex (PMC); parietal operculum (PO); planum polare (PP); planum temporale (PT); pre-supplementary motor area (preSMA); somatosensory cortex (SC); subcallosal cortex (SCC); superior frontal gyrus (SFg); supplementary motor area (SMA); supramarginal gyrus (SMg); superior parietal lobule (SPL); superior temporal gyrus (STg); superior temporal sulcus (STs); temporal fusiform gyrus (TF); temporal occipital fusiform gyrus (TOF); temporal pole (TP).

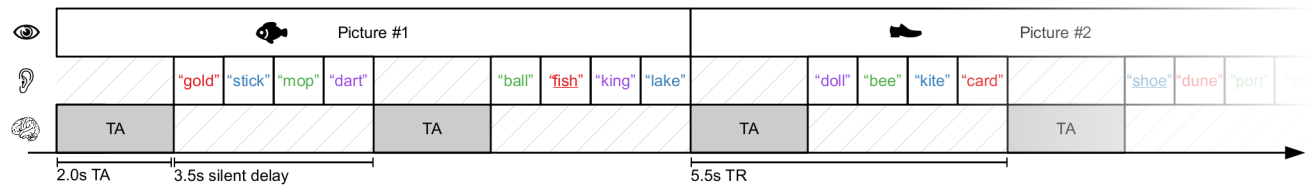
Region names (% of region inside cluster)	Peak voxel	t-value	Cluster
	MNI coordinates		Volume (cc)
Experiment 1 (Voices)			
<i>Control</i>			
Right: pdSTs (86%), pSTg (83%), PT (79%), H (66%), PP (38%), pvSTs (24%), aSTg (22%), MTO (15%), PO (12%), pCO (11%), pINS (3%), aSMg (3%), vSC (2%), pSMg (1%),	[64, -26, 10]	10.6	25.4
Left: PT (73%), H (71%), pSTg (59%), pdSTs (54%), PO (40%), PP (17%), pCO (15%), MTO (9%), pINS (2%), aSTg (2%), adSTs (2%), pSMg (1%),	[-62, -34, 13]	10.3	20.6
<i>Dyslexia</i>			
Right: pSTg (18%), PT (14%), pdSTs (13%), H (5%)	[64, -21, 5]	6.65	4.6
Left: pSTg (10%), pdSTs (8%), PT (7%)	[-63, -37, 12]	7.08	1.6
Left: PT (13%), H (8%), pdSTs (1%)	[-57, -13, 1]	5.84	1.6
<i>Control > Dyslexia</i>			
Left: midCG (41%), pCG (17%), preSMA (16%), pdPMC (12%), SMA (10%), dMC (4%), aCG (1%)	[63, -30, 31]	5.14	99.5
Right: PT (85%), PO (78%), PP (65%), pINS (62%), pSMg (60%), IFt (56%), aSMg (53%), aINS (51%), pSTg (50%), MTO (48%), H (46%), pdSTs (40%), SMA (35%), midCG (34%), dSC (33%), pdPMC (31%), midMC (31%), IFo (30%), dMC (29%), pvSTs (20%), pIFs (20%), vSC (19%), pTF (18%), pFO (18%), pCO (18%), mdPMC (18%), aCO (18%), pCG (16%), vPMC (15%), aIFs (14%), AG (14%), aMFg (11%), midPMC (9%), SPL (7%), aFO (6%), preSMA (5%), aSTg (5%), PCN (3%), Amygdala (3%), Putamen (2%), vMC (1%), ITO (1%), FP (1%), FOC (1%)			
Left: PT (75%), H (55%), PO (54%), pCO (54%), MTO (54%), pSTg (51%), pINS (44%), PP (34%), vMC (23%), vSC (18%), pSMg (18%), aINS (16%), aSMg (15%), pdSTs (12%), ITO (10%), aCO (10%), aSTg (6%), vPMC (5%), OC (2%), Putamen (1%)	[-63, -13, 4]	3.96	38.1
Experiment 2a (Speech)			
<i>Control</i>			
Left: pdSTs (56%), pSTg (47%), pvSTs (43%), aSTg (33%), adSTs (33%), avSTs (14%), pMTg (13%), MTO (11%), PT (8%), PP (1%)	[-58, -32, 4]	6.93	13.0
Right: aSTg (41%), pdSTs (30%), adSTs (23%), avSTs (22%), pvSTs (19%), pSTg (11%), pMTg (2%), aTF (1%)	[60, -7, -5]	6.28	7.2
Left: TOF (28%), pTF (24%), LG (2%), ITO (2%)	[-38, -49, -15]	4.75	5.8
Right: TOF (11%), pTF (8%), pPH (7%)	[34, -47, -22]	4.43	2.7
Right: pvSTs (11%), MTO (5%), pMTg (3%), pdSTs (3%)	[64, -33, 0]	4.84	2.2
Right: FOC (7%)	[35, 25, -14]	4.19	1.6
<i>Dyslexia</i>			
Left: SFg (13%), aCG (4%),	[12, 42, 22]	4.45	5.7
Right: aCG (13%), SFg (8%), preSMA (2%), midCG (1%)			
Right: FOC (8%), aINS (3%), FP (2%)	[29, 26, -12]	4.32	3.5
Left: pSTg (13%), pvSTs (12%), pdSTs (12%), adSTs (8%), pMTg (4%), aSTg (1%)	[-58, -11, -7]	5.69	2.6
<i>Control > Dyslexia</i>			
Left: MTO (84%), vMC (51%), pCO (48%), aSTg (43%), TOF (41%), PT (41%), H (41%), pSTg (40%), pdSTs (39%), adSTs (37%), PO (36%), Putamen (33%), vSC (29%), midMC (27%), PP (25%), pvSTs (22%), pTF (19%), ITO (17%), dSC (16%), pMTg (15%), TP (14%), avSTs (14%), OC (13%), pINS (11%), dMC (11%), aCO (10%), LG (9%), Hippocampus (8%), Pallidum (6%), pdPMC (4%), aPH (4%), vPMC (3%), pPH (3%), IFo (2%), Amygdala (2%), aMTg (2%), aINS (2%), pMFg (1%), midPMC (1%), FOC (1%), Cerebellum (1%), aSMg (1%)	[-60, -57, 7]	4.67	80.4
Right: aSTg (81%), avSTs (69%), adSTs (68%), PP (67%), vMC (53%), H (52%), TP	[25, 11, -27]	4.14	70.4

Region names (% of region inside cluster)	Peak voxel	Cluster	
	MNI coordinates	t-value	Volume (cc)
(47%), MTO (38%), pSTg (36%), PT (35%), Amygdala (32%), pINS (30%), aPH (28%), Putamen (26%), aINS (26%), pvSTs (24%), pdSTs (23%), vSC (19%), pTF (17%), pMTg (16%), midMC (16%), TOF (14%), aMTg (13%), OC (12%), aCO (11%), FOC (9%), aTF (9%), pFO (8%), PO (7%), pCO (7%), ITO (6%), alTg (6%), pIFs (5%), pdPMC (5%), Pallidum (4%), pPH (3%), pMFg (3%), IFt (3%), Hippocampus (3%), vPMC (2%), midPMC (2%), LG (2%), Caudate (2%), aSMg (2%), Thalamus-Proper (1%), pITg (1%), Cerebellum (1%)			
Experiment 2b (Text)			
<i>Control</i>			
Left: IFt (41%), aFO (41%), Putamen (37%), aSTg (18%), Caudate (14%), Pallidum (9%), IFo (8%), FOC (7%), aINS (5%), alFs (1%)	[-21, 7, 0]	5.32	12.8
Left: pTF (47%), ITO (36%), TOF (30%), pPH (7%), pITg (2%), Hippocampus (1%), Cerebellum (1%)	[-38, -41, -19]	6.84	11.9
Left: midPMC (51%), pIFs (44%), vPMC (29%), midMC (29%), IFo (25%), pdPMC (4%), vSC (3%), pMFg (2%)	[-39, 11, 26]	6.10	9.9
Left: OC (1%)	[-17, -76, 12]	4.21	2.4
Left: preSMA (29%), SMA (13%)	[-6, 10, 52]	5.89	2.2
Right: Putamen (14%), FOC (2%), aINS (2%)	[22, 12, -1]	4.32	2.2
Left: pdSTs (25%)	[-56, -39, 6]	4.43	1.8
<i>Dyslexia</i>			
Left: aFO (56%), pFO (10%), FOC (10%), aINS (7%), IFt (4%), IFo (1%)	[-36, 30, -10]	4.83	5.5
<i>Control > Dyslexia</i>			
Left: PCN (51%), PT (45%), aSMg (45%), PO (44%), SPL (37%), vSC (35%), MTO (35%), pdPMC (32%), midPMC (31%), pCO (29%), mdPMC (25%), OC (24%), pTF (22%), pSTg (21%), SMA (17%), pCG (17%), dSC (17%), dMC (17%), pPH (16%), aCO (16%), midMC (15%), AG (14%), midCG (13%), pvSTs (12%), preSMA (12%), pSMg (11%), pdSTs (10%), Cerebellum (10%), ITO (9%), pINS (8%), TOF (5%), pMFg (2%), Hippocampus (2%), aINS (2%), adPMC (1%)	[-50, -42, 24]	4.10	195.6
Right: PCN (54%), pCG (37%), dSC (34%), PO (33%), pCO (30%), pINS (26%), pdPMC (25%), aSMg (24%), AG (23%), mdPMC (19%), aCO (19%), SPL (16%), OC (14%), Putamen (13%), dMC (13%), H (11%), aINS (10%), SMA (8%), midCG (8%), pSMg (7%), ITO (6%), Cerebellum (5%), PT (3%), MTO (3%), pMFg (2%), pvSTs (1%), Caudate (1%)			
Experiment 2c (Objects)			
<i>Control</i>			
Left: TOF (99%), pIFs (97%), ITO (91%), pTF (83%), Hippocampus (76%), LG (60%), alFs (59%), pPH (58%), OC (53%), FOC (53%), aFO (39%), vPMC (38%), SPL (36%), aINS (36%), midPMC (32%), IFo (29%), aPH (29%), Amygdala (22%), MTO (21%), IFt (21%), aTF (17%), AG (17%), Thalamus (16%), pMFg (14%), Cerebellum (14%), TP (13%), pFO (11%), pITg (8%), Putamen (7%), PCN (7%), pCG (6%), aSTg (6%), aMFg (6%), pSMg (4%), SCC (2%), Pallidum (2%), FP (2%), alTg (2%), PP (1%)	[40, -89, 3]	14.60	275.6
Right: TOF (95%), pTF (73%), pPH (69%), ITO (63%), Hippocampus (56%), LG (52%), OC (48%), SPL (37%), aTF (28%), Amygdala (26%), aPH (23%), Cerebellum (16%), Thalamus (11%), TP (5%), pITg (5%), AG (5%), MTO (3%), PCN (2%), pCG (2%), FOC (2%), Putamen (1%), alTg (1%)			
Left: preSMA (56%), SFg (20%), aCG (13%), adPMC (10%)	[-3, 21, 55]	7.44	15.0
Right: preSMA (46%), aCG (14%), midCG (8%), SFg (6%)			
Right: aINS (30%), FOC (25%), aFO (14%), Putamen (9%), FP (3%), TP (1%)	[27, 35, -10]	8.59	12.5
Right: alFs (63%), IFt (43%), pIFs (33%), IFo (21%), vPMC (20%), aMFg (14%), midPMC (5%)	[41, 9, 25]	7.68	10.0
<i>Dyslexia</i>			
Left: pIFs (100%), TOF (99%), pTF (90%), ITO (79%), Hippocampus (76%), LG (70%), aFO (68%), FOC (65%), Amygdala (62%), pPH (58%), OC (50%), IFt (49%), alFs (49%), IFo (37%), aINS (37%), aPH (28%), vPMC (26%), aTF (25%), pFO (24%), PCN (15%), AG (14%), Pallidum (13%), Thalamus (12%), SPL (12%), pMFg (12%), MTO (11%), pITg (9%), pCG (9%), FP (8%), Cerebellum (8%), Putamen (7%), SCC (6%), TP (5%), midPMC (5%), alTg (4%), aMFg (2%)	[-34, -39, -17]	11.10	254.6
Right: TOF (98%), pTF (77%), Hippocampus (69%), pPH (60%), LG (59%), ITO (58%), OC (48%), aTF (45%), Amygdala (29%), aPH (25%), Thalamus (12%), SPL (11%), pCG (9%), pITg (8%), Putamen (7%), Cerebellum (7%), PCN (6%), Pallidum (6%), TP (5%), FOC (5%), MTO (3%), AG (3%), alTg (1%)			
Left: FMC (14%), SCC (7%)	[25, 32, -9]	7.21	19.2

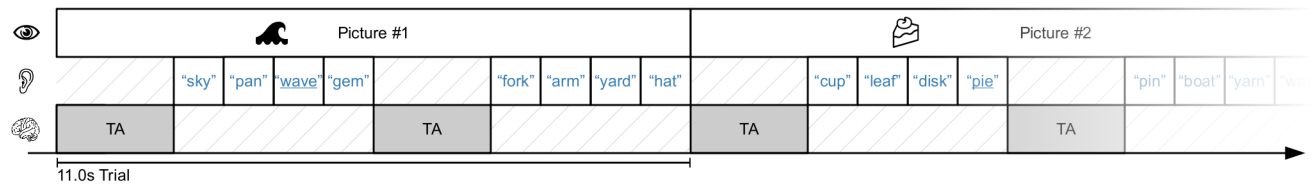
Region names (% of region inside cluster)	Peak voxel	Cluster	
	MNI coordinates	t-value	Volume (cc)
Right: aIFs (61%), pIFs (36%), FOC (35%), IFt (20%), aFO (19%), SCC (13%), FMC (12%), IFo (11%), aINS (8%), vPMC (7%), pMFg (5%), aMFg (4%), FP (3%), midPMC (2%)			
Left: preSMA (26%), SFg (25%), aCG (12%), adPMC (2%)	[-5, 31, 57]	4.80	6.9
Left: Cerebellum (1%), Right: Cerebellum (2%)	[2, -74, -23]	5.47	4.1
Left: FP (5%), SFg (4%)	[-4, 63, 19]	5.22	2.9
Control > Dyslexia			
Left: OC (23%), SPL (20%), TOF (16%), AG (14%), ITO (7%), Cerebellum (6%), PCN (5%), pSMg (3%)	[-16, -67, 37]	4.79	50.1
Right: SPL (11%), PCN (6%), AG (2%), OC (1%)			
Right: OC (17%), ITO (12%), TOF (7%), Cerebellum (5%)	[39, -90, 3]	5.41	26.2
Experiment 2d (Faces)			
Control			
Right: TOF (85%), OC (40%), pTF (37%), ITO (32%), LG (28%), SPL (1%), Cerebellum (1%)	[38, -49, -16]	7.99	58.0
Left: TOF (82%), LG (32%), OC (26%), pTF (23%), ITO (15%), Cerebellum (2%), AG (1%)	[-36, -62, -16]	7.58	36.2
Right: Amygdala (57%), Putamen (8%), Hippocampus (5%), Pallidum (4%), FOC (4%), aPH (3%)	[25, -5, -13]	6.62	4.7
Left: Amygdala (7%), Putamen (4%), Hippocampus (1%)	[-24, -14, -12]	4.25	1.5
Dyslexia			
Right: pTF (36%), TOF (35%), pPH (6%), ITO (2%),	[38, -44, -23]	4.82	6.3
Left: TOF (25%), ITO (5%), pTF (4%)	[-42, -56, -21]	5.18	3.3
Control > Dyslexia			
Left: TOF (47%), OC (23%), LG (21%), pTF (7%), ITO (3%), Cerebellum (1%), AG (1%)	[23, -95, 21]	5.06	90.1
Right: TOF (44%), OC (33%), ITO (19%), pdSTs (18%), pTF (6%), LG (6%), SPL (4%), pvSTs (3%), Cerebellum (2%), MTO (1%)			
Right: pFO (65%), aINS (63%), Putamen (52%), Amygdala (49%), Pallidum (47%), TP (37%), PP (28%), pINS (27%), aSTg (22%), aCO (21%), Hippocampus (19%), adSTs (7%), Thalamus (6%), aITg (5%), FOC (3%), aFO (3%), pdPMC (2%), vPMC (1%), IFo (1%), H (1%), Caudate (1%), avSTs (1%), aMTg (1%)	[25, -6, -12]	4.66	41.5
Left: pFO (54%), PP (42%), aCO (42%), midMC (40%), vMC (37%), aINS (35%), aSTg (28%), pINS (18%), adSTs (18%), vSC (14%), Putamen (13%), preSMA (13%), pCO (12%), Pallidum (12%), pSTg (11%), midPMC (8%), vPMC (7%), midCG (7%), Hippocampus (7%), H (5%), SMA (4%), IFo (4%), Thalamus (3%), PT (3%), aFO (3%), Caudate (2%), avSTs (2%), Amygdala (2%), pMTg (1%), pIFs (1%)	[-31, -13, 29]	3.74	38.3
Experiment 3 (Speech) (Children)			
Control			
Left: pdSTs (55%), H (42%), aSTg (30%), adSTs (29%), pSTg (25%), PT (23%), avSTs (10%), pvSTs (9%), pMTg (2%), PP (1%)	[-60, -10, -4]	9.37	11.3
Left: SPL (10%), dSC (6%)	[-16, -58, 60]	4.60	4.6
Right: dSC (11%), SPL (7%)	[22, -46, 68]	4.64	4.6
Right: pdSTs (26%), aSTg (20%), adSTs (9%), pSTg (8%), PT (4%), H (4%)	[58, -4, -6]	5.76	4.5
Dyslexia			
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Control > Dyslexia			
Left: aSTg (76%), PT (69%), pdSTs (65%), PO (59%), aCO (56%), adSTs (55%), aFO (51%), H (44%), pFO (40%), pvSTs (31%), pSTg (31%), pCO (29%), PP (26%), avSTs (25%), preSMA (22%), SMA (21%), aSMg (18%), IFt (15%), aINS (13%), vSC (11%), midCG (11%), pTF (10%), pMTg (9%), ITO (8%), TOF (7%), IFo (7%), vPMC (4%), vMC (4%), pINS (4%), pSMg (3%), FOC (3%), Cerebellum (3%), aMFg (3%), Hippocampus (2%), aMTg (2%), pITg (1%)	[-58, -4, -4]	4.11	54.2

Experiment 1: Task Design

A. No-Adapt Condition

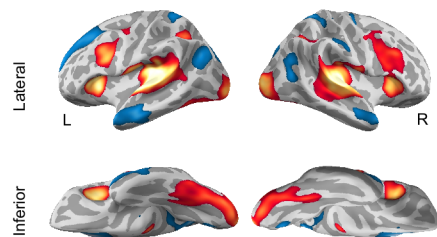


B. Adapt Condition



Experiment 1: Task vs. Resting Baseline

C. Control group



D. Dyslexia group

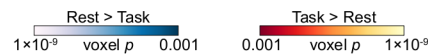
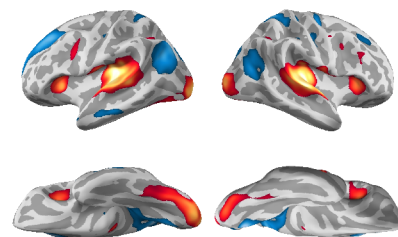


Figure S1. Detailed design of sparse-sampling paradigm and no difference in task-evoked activation between groups in Experiment 1. (See also Figure 1)

For each condition, the panels depict what participants saw (designated with the eye icon), what they heard (designated with the ear icon), and what the scanner acquired (designated with the brain icon). The scanner first acquired a whole-brain functional volume ("TA," acquisition time) in 2.0s, followed by a 3.5s delay during which no MRI data were acquired and auditory stimuli were presented in silence (2.0s TA + 3.5s delay = 5.5s TR). Participants heard four words during the silent delay, with the task of indicating when the picture they were seeing matched the word they heard (indicated here by underlines). **(A)** In the "No-Adapt" condition, the words were spoken by four different talkers (indicated here by different colored text) in random order. **(B)** In the "Adapt" condition, the words were spoken by a single talker. Each picture was on the screen for 11s, and each trial was comprised of one picture and eight spoken words, only one of which was the target. Each block comprised two trials (2 pictures, 16 words) and lasted 22s. The order of the blocks were pseudorandomized and interspersed with an equal proportion of rest blocks (22s; not shown) during which no pictures or words were presented. Task-evoked activation while matching spoken words to pictures is shown for **(C)** control adults and **(D)** adults with dyslexia. The lateral and inferior (ventral) surfaces are shown for both hemispheres. Data are shown thresholded at voxel level $p < 0.001$, corrected for multiple comparisons by controlling cluster-level $p_{FDR} < 0.001$. Both groups showed significant task-evoked activation in bilateral STG, IFG, and FusG. There were no significant differences between groups in task-evoked activation or deactivation (voxel-level $p < 0.01$, cluster-level $p_{FDR} < 0.05$).

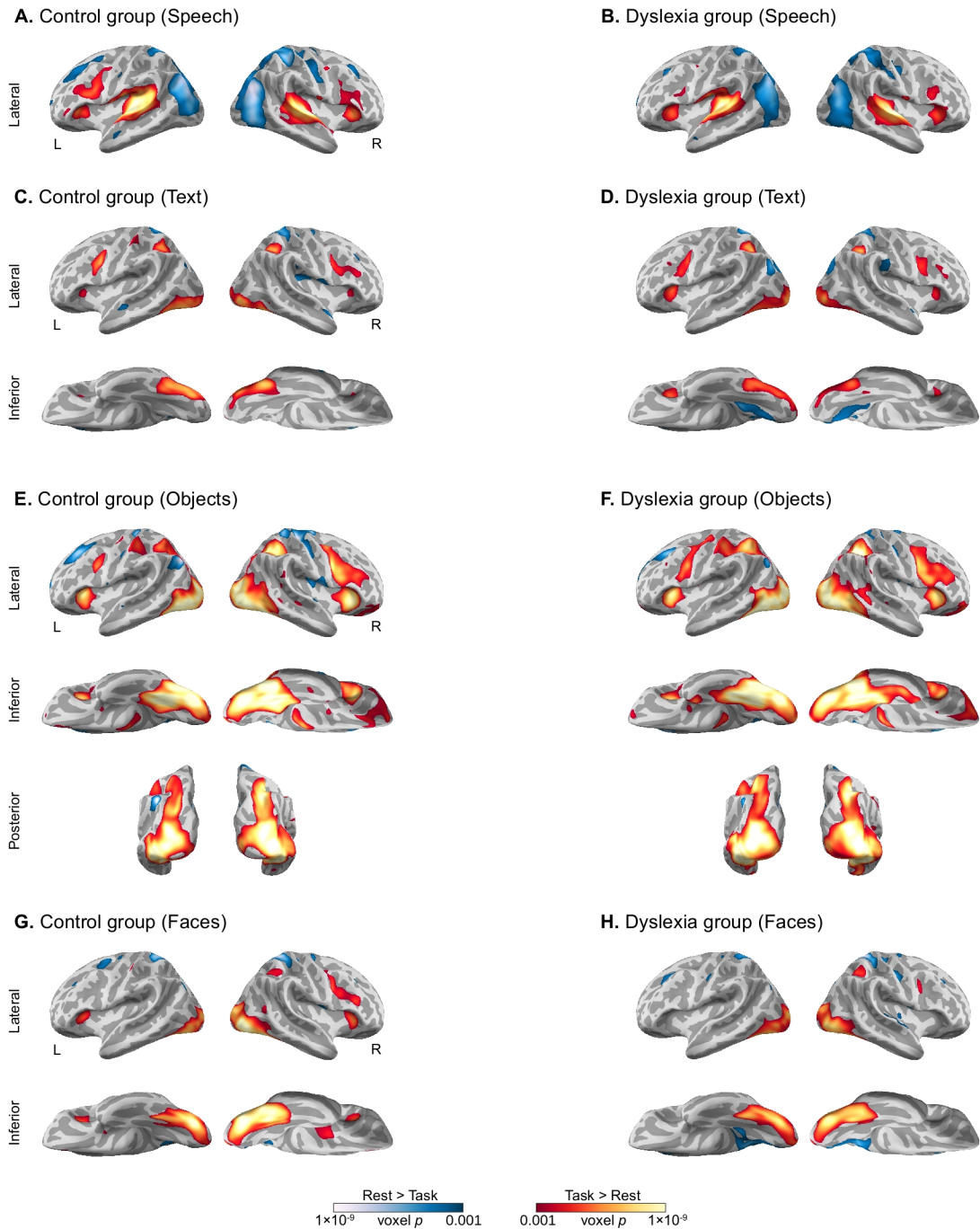


Figure S2. No difference in task-evoked activation between groups in Experiment 2. (See also Figures 2-5) (A) Activation while listening to speech in control adults and (B) adults with dyslexia. Lateral surfaces are shown for both hemispheres. Both groups showed significant task-evoked activation in bilateral STG, IFG, and anterior insula. (C) Activation while viewing written words in control adults and (D) adults with dyslexia. Lateral and inferior surfaces are shown for both hemispheres. Both groups showed significant task-evoked activation in bilateral IFG, anterior insula, intraparietal sulcus (IPS), and FusG. (E) Activation while viewing objects in control adults and (F) adults with dyslexia. Lateral, inferior, and posterior surfaces are shown for both hemispheres. Both groups showed significant task-evoked activation in bilateral FusG, LOC, IPS, anterior insula, and IFG. (G) Activation while viewing faces in control adults and (H) adults with dyslexia. Lateral and inferior surfaces are shown for both hemispheres. Both groups showed significant task-evoked activation in bilateral anterior insula and FusG, as well as right IPS and IFG. In all panels (A-H), data are shown at voxel-level $p < 0.001$, corrected for multiple comparisons by controlling cluster-level $p_{FDR} < 0.001$. In all conditions (speech, text, objects, faces), there was no significant difference between groups in task-evoked activation or deactivation (voxel-level $p < 0.01$, cluster-level $p_{FDR} < 0.05$).

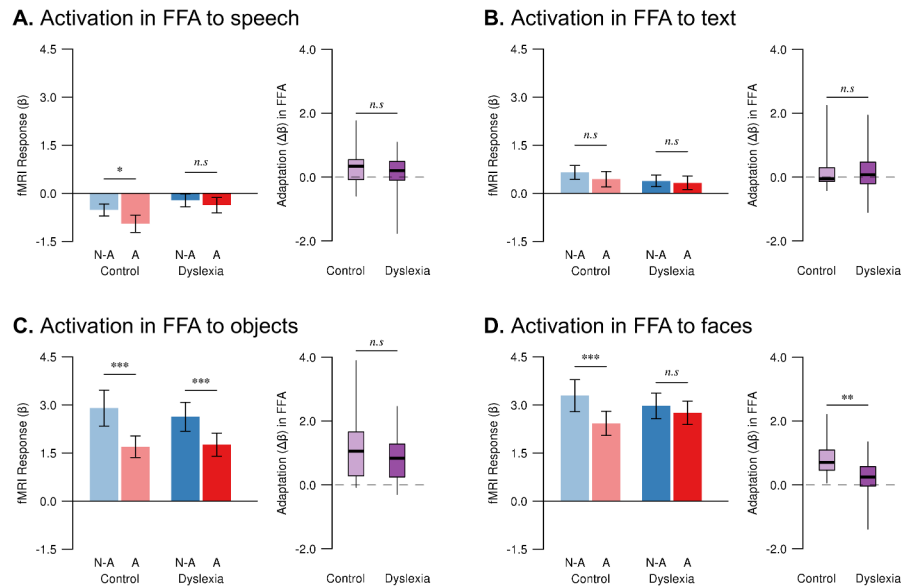


Figure S3. Patterns of activation and adaptation in FFA by experiment and group. (See also Figure 6)

In each panel, activation in the control and dyslexia groups to the No-Adapt (“N-A”, blue) and Adapt (“A”, red) conditions are shown in the barplots; boxplots show the distribution of adaptation magnitudes (N-A > A). The FFA was localized based on the Faces > Objects contrast, and the average location of this cluster is presented in Fig. 3B. **(A)** The FFA responded only weakly to Speech and **(B)** Text, with no significant group difference in adaptation observed in these conditions. **(C)** The FFA responded more strongly to Objects, including with significant adaptation in both groups, but the group difference in adaptation was not significant. **(D)** The FFA responds (by definition) most strongly to Faces, with significant adaptation here for the control group, but not dyslexia group, and a significant difference between groups in the magnitude of adaptation. Asterisks are based on paired (barplots) or independent sample (boxplots) t-tests; *n.s.* not significant, * $p < 0.05$, ** $p < 0.005$, *** $p < 0.0005$; all two-tailed, $\alpha = 0.05$ tests.

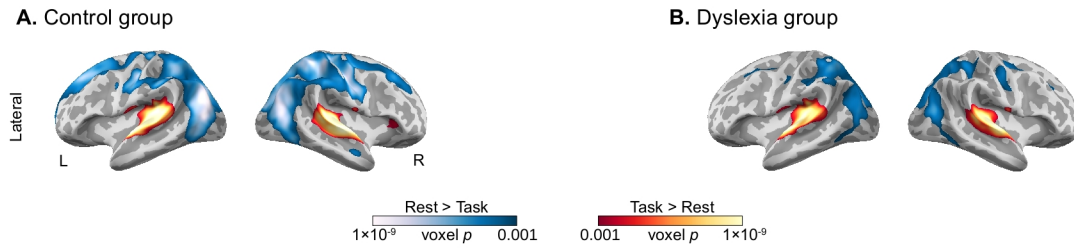


Figure S4. No difference in task-evoked activation between pediatric groups in Experiment 3. (See also Figure 7)

Task-evoked activation while listening to speech is shown for (A) control children and (B) children with dyslexia. Lateral surfaces are shown for both hemispheres. Data are shown thresholded at voxel level $p < 0.001$, corrected for multiple comparisons by controlling cluster-level $p_{FDR} < 0.05$. Both groups showed significant task-evoked activation in bilateral STG and significant task-related deactivation in parietal, occipital, and superior frontal lobes. There were no significant differences between groups in task-evoked activation or deactivation (voxel-level $p < 0.01$, cluster-level $p_{FDR} < 0.05$).

EXPERIMENTAL PROCEDURES

Participants

Experiments 1 and 2

Two groups of adult participants were recruited for Experiments 1 and 2: (i) individuals with a prior dyslexia diagnosis or lifelong history of reading difficulties, and (ii) controls, who had a self-reported history free from reading difficulty. All adult participants were native speakers of American English and had a self-reported history free from additional language, speech, or peripheral hearing disorders, and reported no other known psychological or neurological disorders. Experiment 1 (N = 19 control, 19 dyslexia) and Experiment 2 (N = 24 control, 23 dyslexia) were comprised of unique participant samples, with the exception of three controls and five individuals with dyslexia who participated in both. Analyses of some fMRI runs in Experiment 2 were rejected due to excessive participant motion or other artifacts, such that in Experiment 2a: N = 21 control, 21 dyslexia; Experiment 2b: N = 23 control, 23 dyslexia; Experiment 2c: N = 23 control, 23 dyslexia; Experiment 2d: N = 22 control, 22 dyslexia.

To confirm adult participants' status as typical or impaired readers, their performance on a battery of standardized intelligence, memory, reading, and phonological measures was assessed. Performance at or below the 25th percentile on two or more subtests of timed or untimed word or nonword reading comprised inclusionary criteria for the dyslexia group. Performance at or below the 25th percentile on any one such subtest comprised exclusionary criteria from the control group. Enumeration of the specific assessments used, as well as group average performance on these measures and basic demographics, are reported in Supplemental Table 1 (Experiment 1) and Supplemental Table 2 (Experiment 2).

Experiment 3

Two groups of pediatric participants (age 6;9-9;3, M = 7;10) were recruited for Experiment 3: (i) children with dyslexia (N = 26) and (ii) age-matched controls (N = 25), who had a self-reported history free from reading difficulty. Children with dyslexia were recruited as part of a larger study of intensive summer reading intervention (Christodoulou et al., 2015) and completed both the behavioral assessment and MRI scanning prior to undergoing the intervention.

To confirm pediatric participants' status as typical or impaired readers, their performance on a battery of standardized intelligence, memory, reading, and phonological measures was assessed. Performance at or below the 16th percentile on two or more subtests of timed or untimed word or nonword reading comprised inclusionary criteria for the dyslexia group. Performance at or below the 25th percentile on any one such subtest comprised exclusionary criteria from the control group. All participants were required to demonstrate nonverbal cognitive performance at or above the 16th percentile (Kaufman and Kaufman, 2004). Enumeration of the specific assessments used, as well as group average performance on these measures and basic demographics, are reported in Supplemental Table 3.

Stimuli

Experiment 1: Speech Perception

Audio stimuli consisted of 288 monosyllabic nouns read in isolation by five adult female native English speakers. Recordings of words were 204-1180ms in duration (M = 531ms, SD = 149ms). Of the 288 words, 36 were selected as targets, for which corresponding images were selected from a standard set (Snodgrass and Vanderwart, 1980). Images consisted of black line figures on white backgrounds, 300×300 pixels.

Experiment 2a: Spoken Words

Audio stimuli consisted of 180 monosyllabic nouns read in isolation by one adult female native English speaker. Recordings of words were 234-591ms in duration (M = 425ms, SD = 66ms). 160 words were assigned to the "No-Adaptation" condition, and 20 were assigned to the "Adaptation" condition. Target stimuli consisted of 20 items from each condition whose recordings were time-reversed using Praat (Boersma, 2002) (<http://www.fon.hum.uva.nl/praat/>).

All audio stimuli in Experiments 1 and 2a were recorded in a sound-attenuated chamber via a SHURE SM58 microphone. Stimuli were sampled at 44.1 kHz using an Edirol UA-25EX sound card, and normalized for RMS amplitude to 70 dB SPL using Praat. Normalized stimuli were spectrally filtered to attain frequency response equalization for binaural presentation via a pair of Sensimetrics (Malden, MA) S-14 MRI-compatible insert earphones.

Experiment 2b: Written Words

Orthographic stimuli consisted of 180 monosyllabic nouns, written in bold 18 pt Arial font on a white background of 256×256 pixels. Words were 3-5 letters in length (mode = 4). 160 words were assigned to the No-Adaptation condition, and 20 were assigned to the Adaptation condition. Target stimuli consisted of 20 trials in each condition in which the images were vertically inverted.

Experiment 2c: Objects

Visual object stimuli consisted of 180 color photographs of objects in isolation on a white background, 256×256 pixels. Only objects with unambiguous vertical orientations were selected (e.g., a car or tree, not a pencil or grapefruit). 160 objects were assigned to the No-Adaptation condition, and 20 were assigned to the Adaptation condition. Target stimuli consisted of 20 trials in each condition in which the images were vertically inverted.

Experiment 2d: Faces

Face stimuli consisted of 180 greyscale photographs of individuals, cropped close to the face without excessive hair or backgrounds, and were 256×256 pixels. 160 faces were assigned to the No-Adaptation condition, and 20 were assigned to the

Adaptation condition. Target stimuli consisted of 20 trials in each condition in which the images were vertically inverted.

Experiment 3

Audio stimuli consisted of 180 one and two syllable nouns read in isolation by an adult female native English speaker. All words were selected to be highly familiar to children, with an age of acquisition prior to kindergarten (Gilhooly and Logie, 1980; Morrison et al., 1997), and to have high lexical frequency and contextual diversity (Brysbaert and New, 2009).

Recordings of words were 442-846ms in duration ($M = 633\text{ms}$, $SD = 82\text{ms}$). 160 words were assigned to the No-Adaptation condition, and 20 were assigned to the Adaptation condition. Target stimuli consisted of 20 items from each condition whose recordings were time-reversed using Praat. Recording parameters for these audio stimuli were the same as in Experiments 1 and 2a.

Procedure

Experiment 1: Speech Perception

Participants lay supine in the MRI scanner and undertook a auditory-word to visual-picture matching task during sparse-sampling fMRI. In the task, participants saw target images presented on the screen while listening to spoken words presented binaurally via insert earphones. Participants' task was to press a button indicating when the word they heard matched the picture they saw. This task was performed alternately under two conditions: (1) an Adaptation condition, in which the auditory stimuli were produced by a single, consistent talker; and (2) a No-Adaptation condition, in which the auditory stimuli were produced by four different, inconsistent talkers. Note that this task requires participants to attend to the content of the speech, not the identity of the talker, so the adaptation manipulation is orthogonal to the task demands. Participants underwent four runs of this task, each of which consisted of nine blocks per condition and nine blocks of rest. The order of the conditions and rest blocks was pseudorandomized such that the same condition or rest did not occur in two immediately sequential blocks. Each task block (22s, four TRs) consisted of 2 target images shown in succession for 11s each. During the presentation of each target image, participants heard eight different spoken words (750ms ISI, four words per TR delay), one of which matched the visual image and to which the participant responded by pushing the button. No audio stimuli were played during volume acquisition, but the target image remained on the screen. There was a 500ms delay between the end of the acoustic scanner noise resulting from volume acquisition and the onset of auditory stimulation. Rest blocks were also 22s (four TRs), during which participants maintained fixation on a white "+" symbol in the center of the screen. The projector background remained at 31.25% luminance throughout the experiment. Across the four runs, auditory words and visual pictures occurred equally in the Adaptation and No-Adaptation conditions, and each of the No-Adaptation talkers was equally likely to produce the target words. The talkers assigned to the Adaptation and No-Adaptation conditions respectively were permuted across participants.

Experiment 2a: Spoken Words

Participants lay supine in the scanner and passively listened to spoken words while undergoing continuously-sampled fMRI. This task comprised two runs, each of which consisted of 10 blocks of the Adaptation condition, in which the same word was presented 8 times in succession; 10 blocks of the No-Adaptation condition, in which 8 different words were presented; and 10 blocks of rest. During the task, participants were asked to fixate on a white "+" symbol in the center of the screen, which dimmed slightly during rest blocks to indicate no auditory stimuli were to be expected. The projector background remained at 31.25% luminance throughout the experiment. Auditory stimuli were presented binaurally in blocks of 8 with a duration of 1200ms between the onset of subsequent stimuli. One stimulus in each block was time-reversed; participants maintained attention during the task by indicating their detection of these deviant stimuli by button press.

Experiment 2b-d: Written Words, Objects, and Faces

Participants completed two runs each of the three visual stimulus categories. For each of these tasks, participants lay supine in the scanner and passively viewed stimuli while undergoing continuous-sampling fMRI. Each run consisted of 10 blocks of the Adaptation condition, in which the same visual stimulus was presented 8 times in succession; 10 blocks of the No-Adaptation condition, in which 8 different stimuli were presented; and 10 blocks of rest. Each stimulus remained on the screen for 700ms, with a 500ms inter-trial interval. One stimulus in each block was presented upside-down, and participants maintained attention during the tasks by indicating detection of these deviant stimuli by button press. During rest, participants were asked to fixate on a white "+" symbol in the center of the screen and wait for the images to begin again. The projector background remained at 31.25% luminance throughout the experiment.

Experiment 3

This experiment was identical to Experiment 2a, with the following exceptions: Instead of two runs, pediatric participants completed only one run (10 Adaptation blocks and 10 No-Adaptation blocks). Instead of a fixation cross, children saw a small headphones icon to remind them they should be listening to the audio stimuli. Stimuli were divided between two versions of the experiment; half the participants in each group completed each version of the experiment.

MRI Data Acquisition

Data were acquired on a Siemens Trio 3T scanner with a 32-channel phased array head coil. A whole-head, high-resolution T1-weighted multi-echo MPRAGE anatomical volume (acquisition parameters: $TR = 2530\text{ms}$, $TE = 1.64\text{ms}$, $TI = 1400\text{ms}$, flip angle = 7° , $FOV = 256\text{mm}^2$ (adults) or 220mm^2 (children), 176 slices, voxel resolution = 1.0mm^3) was acquired at the beginning of each session.

Experiment 1

Four functional runs containing 110 volumes each were collected using sparse-sampled T2*-weighted EPI scans (acquisition parameters: TR = 5500ms, TA (acquisition time) = 2000ms, TE = 30ms, flip angle = 90°, voxel resolution = 3.125 × 3.125 × 4.0mm, FOV = 200mm², 32 transverse slices providing whole-brain coverage). Each run was preceded by the four additional TRs in which no data were recorded to allow for stabilization of longitudinal magnetization. Sparse-sampling was used to allow auditory stimuli to be presented in silence (Hall et al., 1999), both to avoid compression of BOLD signal dynamic range in auditory cortex due to acoustic noise in the MR environment, as well as to avoid noise-related perceptual difficulties, which often accompany dyslexia (Ziegler et al., 2009).

Experiments 2 & 3

Two functional runs containing 146 volumes each were collected for each of the four stimulus types (speech, text, objects, and faces) using continuously-sampled T2*-weighted EPI scans (acquisition parameters: TR = 2000ms, TE = 30ms, flip angle = 90°, voxel resolution = 3.0mm³, FOV = 192mm², 32 transverse slices providing whole-brain coverage). Each run was preceded by the five additional TRs from which no data were recorded to allow for stabilization of longitudinal magnetization. (In Experiment 3, pediatric participants completed only one run (146 volumes), instead of two).

MRI Data Analysis (All Experiments)

Preprocessing

Cortical reconstruction and parcellation of anatomical images were performed using the default processing stream Freesurfer v5.0.0 (<http://surfer.nmr.mgh.harvard.edu/>) (Dale, 1999). Functional data were analyzed in SPM8 (<http://www.fil.ion.ucl.ac.uk/spm/software/spm8/>) using workflows in Nipype v0.4 (<http://nipy.org/nipype>) (Gorgolewski et al., 2011). Image preprocessing consisted of motion correction (rigid-body realignment to the mean EPI image from the first functional run) and spatial smoothing (6mm isotropic FWHM 3D Gaussian kernel). Motion and intensity outliers (functional volumes exceeding 1mm in differential motion (1.5mm for the pediatric groups in Experiment 3) or differing from the mean image intensity by > 3 SD) were identified using ART (http://www.nitrc.org/projects/artifact_detect/) and regressed out of the hypothesized timeseries (Siegel et al., 2014).

In Experiment 1, motion and intensity outliers comprised 0.15% of the collected data overall; the number of outliers did not differ between groups ($F_{1,36} = 0.022$, $p = 0.88$). Mean framewise differential motion was 0.23 ± 0.10 mm. In Experiment 2, outliers comprised 0.25% of the collected data and did not differ between groups ($F_{1,49} = 0.292$, $p = 0.59$); mean framewise differential motion was 0.22 ± 0.11 mm. In Experiment 3, the pediatric groups did not differ in number of outliers ($F_{1,49} = 0.258$, $p = 0.61$), which comprised 0.5% of the collected data. Mean framewise differential motion in the pediatric sample was 0.51 ± 0.36 mm.

Model design and estimation

Model design was implemented using the *modelgen* algorithm in Nipype, and included two task regressors (for the No-Adaptation and Adaptation conditions, respectively), six motion parameters, individual regressors for any outlier volumes, Legendre polynomial terms to account for low-frequency components of the MR-signal including scanner drift (Experiment 1: five polynomials; Experiments 2 & 3: three polynomials), and a constant term. To account for timeseries discontinuities due to sparse sampling in Experiment 1, vectors for task regressors were determined by convolving a vector of event onset times with their durations, convolving the resulting vector with a canonical HRF (gamma difference), and resampling the resulting time series to include only timepoints when scanner data were actually acquired (Perrachione and Ghosh, 2013). Within-subject estimation of the general linear model and contrasts were conducted in participants' native EPI space.

Coregistration, normalization, and group analyses

Coregistration transformations between participants' high-resolution anatomical volumes and the mean functional volumes were calculated using six degrees of freedom rigid-body alignment via boundary-based optimization implemented in FreeSurfer program *BBRegister* (Greve and Fischl, 2009). These transforms were applied to the contrast images from each participant's first-level analysis to insure accurate coregistration between functional data and high-resolution anatomy. Participants' high-resolution structural images were aligned to a common space (the MNI152 template from FSL v4.1.6, <http://www.fmrib.ox.ac.uk/fsl/>) (Smith et al., 2004) via nonlinear symmetric diffeomorphic mapping implemented in ANTS v1.5 (<http://www.picsl.upenn.edu/ANTS/>) (Avants et al., 2008). The transformation matrix from this spatial normalization was applied to each participant's coregistered first-level contrast images to align them to the common space. Second-level group comparisons were performed using SPM8 via Nipype workflows. Group-level statistics were thresholded at $p < 0.001$ (within groups) or $p < 0.05$ (between groups) and corrected for multiple comparisons via controlling the cluster-level false-discovery rate (FDR) at $p = 0.05$.

Region of interest analyses

Data for region of interest (ROI) analyses, including brain-behavior correlations, were obtained by sampling the mean BOLD response for a condition (or mean response difference between conditions) over independently-derived anatomical parcels defined individually in each participant using a cortical parcellation optimized for studies of speech and language (Tourville and Guenther, 2003, 2012). This same parcellation scheme was used to identify and describe the anatomical locations of functional effects.

Time course analysis

To identify the temporal features of the adaptation response (i.e., how the response to the No-Adaptation and Adaptation

conditions differed over time and between groups) we repeated the within-subject model design and estimation steps described above, leaving out all task regressors and including only the nuisance regressors (motion, polynomials, outliers). Spatially averaged vectors of temporal residuals were extracted from the various regions of interest for each subject. These vectors were sampled beginning at the timepoint preceding the onset of each stimulation block and were normalized to the mean BOLD signal in the 6s preceding the canonical onset of the hemodynamic response (2s after the onset of stimulation). For each condition, the resulting activation time courses were aggregated over runs, subjects, and groups to determine the mean activation time-course and its variance. Regions of interest were determined as described above.

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