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# Auditory gating in adults with dyslexia: An ERP account of diminished rapid neural adaptation

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HIGHLIGHTS

- Dyslexia is associated with reduced neural adaptation.
- P2 auditory gating was preserved in dyslexia.
- Reduced N1 gating in individuals with dyslexia was linked to their poor word representation.

ABSTRACT

*Objective:* A recent functional magnetic resonance imaging (fMRI) study of adults with dyslexia showed a general deficit in suppressing responses to various types of repetitive stimuli. This diminished neural adaptation may interfere with implicit learning and forming stable word representations. With fMRI, spatial but not temporal characteristics of the adaptation response could be identified. We address this knowledge gap using event-related potentials.
*Methods:* Fourteen adults with dyslexia and 14 controls participated in an auditory gating paradigm using tone pairs. Response amplitudes and latencies for N1 and P2 were measured. Participants also compared word pairs consisting of identical or subtly different words, a task requiring stable word representations.
*Results:* Only the controls showed a robust gating effect in an attenuated N1 response to the second tone relative to the first. The dyslexia group was less accurate than the controls in detecting word differences. The N1 gating magnitude was associated with this detection accuracy.
*Conclusions:* Neural adaptation occurs by approximately 100 ms after stimulus presentation and is diminished in adults with dyslexia. This complements fMRI findings of relevant brain regions by implying a time window representing sensory and pre-attentive auditory processes.
*Significance:* The association between gating magnitude and word discrimination contributes to a neurophysiological account of underspecified word representations.


## 1. Introduction

English is an alphabetic language with a complex and opaque orthography. Reading words requires several cognitive, linguistic, and motoric substrates. These include understanding that words are made up of sequences of individual letters that represent speech sounds called phonemes, but not necessarily on a 1:1 basis, e.g., "ten" consists of three letters representing three corresponding phonemes, /tɛn/, whereas "six" consists of three letters representing four phonemes, /sɪks /, and "three" consists of five letters but only three phonemes, /θri/, because "x" represents two phonemes but "th" and "ee" only one each. Reading words also requires knowing basic orthographic rules such as "The silent 'e' makes the vowel say its name," e.g. "five"; moving the eye gaze sequentially from left to right when decoding (i.e., sounding out) rare but orthographically consistent words, e.g., "numberable"; and recognizing whole words whose letter sequences do not follow orthographic rules and thus cannot be decoded (e.g., "one," "eight"). Writing words requires having stored the letter sequences

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in long-term memory, retrieving them, and writing them sequentially from left to right. Given the large number of homophones (e.g., "write," "right," "rite") and homographs (e.g., "read" /rid/ or /rɛd/), letter sequences and word meanings must be memorized. Efficient reading and writing requires the various subroutines to be automatized and rapidly executed. The complexity of English orthography makes English an ideal language for studies of reading disorders.

According to the International Dyslexia Association, dyslexia is a disability affecting the acquisition of written language at the word level, characterized by deficits in accurate and/or fluent word recognition, decoding, and spelling in the presence of generally normal oral language skills (Lyon et al., 2003, Shaywitz and Shaywitz, 2003). Dyslexia does not result from intellectual disability or lack of reading instruction; rather, it is thought to have neurobiological origins. Dyslexia prevalence estimates range from 5% (Francks et al., 2002) to 9% (Pennington and Bishop, 2009, Peterson et al., 2007) in school-age children, higher in males than females (Shaywitz et al., 1990). Despite intense and costly treatment, many aspects of dyslexia persist into adulthood, including poor spelling and writing abilities (Berninger et al., 2001, Bruck, 1990, 1992, 1993, Felton et al., 1990, Hatcher et al., 2002, Pennington et al., 1990, Ramus et al., 2003, Shaywitz et al., 1990, Wilson and Lesaux, 2001).

Of particular interest for the present study is the dual route model for word reading (Coltheart et al., 2001, Stanovich, 1991). In this model, words are either recognized rapidly as whole chunks based on their shape and context, a process called lexical route, or they are decoded by translating the letters into their phonological counterparts to arrive at the word's meaning, a process called sublexical route. Whereas all readers rely on the sublexical route for novel or artificial words, proficient readers rely mostly on the lexical route when the words are common and familiar, whereas many readers with dyslexia process these words more using the sublexical route (Hawelka et al., 2010, Peterson et al., 2013). Being able to recognize words rapidly requires having a stable and readily accessible representation of the word forms stored in memory.

Various traits have been associated with dyslexia. An extensive body of research shows that many individuals with dyslexia have deficits in phonological processing skills: Compared to typical peers, their accuracy and speed is lower when dissecting words into individual phonemes and making changes to their sequence (Bradley and Bryant, 1983, Fletcher et al., 1994), uploading and storing phonemes in short-term memory during nonword imitation tasks, retrieving phoneme sequences from long-term memory in naming tasks (Catts, 1986, Denckla and Rudel, 1976), and producing complex strings of phonemes (Catts, 1986, 1989). Other neurocognitive deficits underlying dyslexia include slowed processing speed across task types and sensory modalities (Cardillo et al., 2017, Peter et al., 2011, Shanahan et al., 2006, Stoodley and Stein, 2006) and difficulty with perceiving and processing sequential information across task types and sensory modalities (Cowan et al., 2017, Hachmann et al., 2014, Peter et al., 2018). It is debatable whether these phonological and domain-general deficits are simultaneously present in the majority of individuals with dyslexia, where they present competing explanations for the dyslexia phenotype, or whether one or more of these traits contribute to the dyslexia phenotype in distinct subsets of individuals with dyslexia, where they constitute dyslexia subtypes.

Recent work suggests that many individuals with dyslexia have difficulty with implicit learning tasks in verbal as well as nonverbal tasks that require extracting regularities and probabilities from repeated exposure to stimuli, a problem that interferes with forming stable mental representations of the essential features of the stimuli. An illustration of how implicit learning capacity is associated with reading ability is given by a study of implicit learning in typically developing children and healthy adults who were shown multiple sets of three pictured objects repeatedly, then were asked which of two test triplets was included in the exposure series (Arciuli and Simpson, 2012). One test triplet was identical to one of the triplets shown repeatedly during the exposure series, thus had a transition probability of 1 (i.e., the three objects had always occurred in the same sequence), whereas the other was a combination never shown during the exposure series, with a transition probability of 0 (i.e., the three objects had never occurred together). The accuracy of the responses was associated with word reading ability. The authors interpret their findings as evidence that repeated exposure to structured information triggers implicit learning that is automatic, leads to stable representations in memory, and subserves acquisition of written words. A domain-general nature of implicit learning with respect to sensory modalities, cognitive processes, and brain regions including thalamus, inferior frontal gyrus, caudate, and hippocampus that support it is described in a recent review (Frost et al., 2015).

Regarding dyslexia, the deficit in implicit learning has been observed during perceptual and perceptual-motor tasks (Gabay and Holt, 2015, Lum et al., 2013, Menghini et al., 2006, Menghini et al., 2011, Stoodley et al., 2008) and in difficulties with recognizing visual or auditory stimuli presented in background noise (Sperling et al., 2005, Ziegler et al., 2009).

A special case of poor implicit learning is difficulty with filtering out redundant from essential information during repeated exposure to stimuli. This has been observed in adults with dyslexia as failure to adapt to repetitive stimuli across a variety of modalities, where novelty responses occur despite repeated presentations of a given stimulus. In a recent study (Perrachione et al., 2016), neural adaptations were measured with functional magnetic resonance imaging (fMRI) blood-oxygen level dependent (BOLD) signals to repetitive presentations of the same speaker voice. Response adaptations were diminished in 19 adults with dyslexia, whose response levels remained high despite the repetitive nature of the stimuli, but not in typical controls, whose response levels to repetitive stimuli decreased. In this study, the same failure to adapt to repetition was also observed when the stimuli were spoken words, written words, visual objects, and pictures of faces. Group differences in brain activation were localized to various brain regions depending on stimulus type, e.g., left and right superior temporal gyri when listening to speaker voices and left fusiform gyrus when viewing words. Higher levels of repetition-induced neural adaptation were associated with better performance on tests of word reading. The authors interpret their findings as reduced rapid neural adaptation in dyslexia that is domain-general across modalities and stimulus types and that interferes with extracting core features in a complex signal. This results in failure to create a mental representation of these features, which has relevance for the dyslexia phenotype because it also prevents stable letter-sound and letter-word associations from forming. Here, we argue that this failure may underlie difficulty with rapid word recognition via the lexical route in individuals with dyslexia. An additional aspect is that failure to filter out redundant information may be associated with attention deficit hyperactivity disorder (ADHD), as recently reviewed (Hendren et al., 2018). This aspect is relevant because ADHD is frequently comorbid with dyslexia (Germano et al., 2010, Wadsworth et al., 2015).

Regarding the methodology in the Perrachione et al. (2016) study, stimuli were presented in blocks of repeated items ("Adaptation" condition) or various different items ("No Adaptation" condition). BOLD signals were computed over a 20 second interval that included 6 seconds preceding the canonical onset of the BOLD response, which is 2 seconds after stimulus onset. This experimental fMRI design is ideally suited to obtain high spatial but not temporal resolution.

To date, rapid adaptation failure in individuals with dyslexia has not been measured with higher temporal resolution. Knowledge of precise temporal events while processing recurring stimuli would elucidate the neural infrastructure of adaptation processes and deficits. One approach toward this goal is using cortical event-related potentials (ERPs), which are changes in voltage in the cortical electrophysicologic signal in response to a stimulus, measured at the scalp. In humans, ERPs can be observed as discrete components occurring at characteristic post-stimulus latencies, depending on the nature of the stimulus. For instance, auditory stimuli elicit positive deflections at approximately 50 ms post stimulus onset (P1 or P50), 200 ms (P2 or P200), and 300 ms (P3 or P300), and negative deflections at 100 ms (N1 or N100) and 200 ms (N2 or N200).

Sensory gating paradigms using ERPs are ideally suited to study the time course of neural adaptation responses to stimuli that are redundant and, hence, should trigger lower response levels than novel stimuli. Sensory gating refers to the brain's ability to automatically filter out redundant information, retaining only relevant information, thus preventing a sensory overload. It is thought that the thalamus and the prefrontal cortex play a crucial role in sensory gating by performing an automatized filtering process before passing sensory information along to other brain regions (Green et al., 2017, Mayer et al., 2009). Sensory gating is thought to occur when a set of sensory neurons is activated by the first of the two stimuli while a different set of interneurons is activated to produce an inhibitory response (Adler et al., 1985). Typically, in an ERP gating paradigm, pairs of stimuli separated by an intervening interval of up to 1 second duration are presented. The response amplitude of the P1, N1, and P2 components to the second stimulus is reduced, compared to the first stimulus (Boutros and Belger, 1999, Boutros et al., 2005, Freedman et al., 1987). This adaptation has been observed robustly in the visual as well as auditory modality (Luck et al., 1990). Auditory sensory gating has been studied extensively in typical and clinical populations (Boutros and Belger, 1999). Failure to attenuate to repeated stimuli is considered an indication of hyperexcitability and a problem with inhibitory processes when a neural response to a repeating stimulus should be suppressed. ERP studies of failure to attenuate responses have been conducted in individuals with autism spectrum disorder (ASD) where adaptation failures were seen in the P1 component (Madsen et al., 2015), Fragile X Syndrome where the N1 component was implicated (Ethridge et al., 2016), and schizophrenia, where gating was observed in the P1, N1, and P2 components (Freedman et al., 1996, Nagamoto et al., 1991, Schubring et al., 2018), but not yet in dyslexia. Whereas other studies of temporal processing such as tone frequency, rise time, duration discrimination, amplitude modulation, and frequency modulation using ERP designs, have indicated various neurophysiological deficits in individuals with dyslexia (Hamalainen et al., 2013), to our knowledge, the present study is the first to investigate neural adaptation using an ERP sensory gating design in this population. Using ERP approaches to study adaptation failures in dyslexia may provide the opportunity to study this deficit at a high temporal resolution, thus critically complementing recent fMRI findings of localized effects.

To position our ERP study of gating within the context of the fMRI study of diminished neural adaptation (Perrachione et al., 2016), we hypothesize that an intact gating mechanism will allow only sensory information that is novel and relevant to proceed from a modality-general filter in thalamic and prefrontal regions to modality-specific cortical regions where they trigger brain activity that is measurable with fMRI. Neither the ERP nor the fMRI design captures the gating process directly. The ERP design measures gating at the level of the cortex in terms of diminished response to the second of two tones presented in sequence, where the response to the second tone is presumed to be inhibited via the gating mechanism deeper in the brain of typical individuals, whereas the fMRI design captures the brain activity in the regions that received input passed to them by the implicit learning filters, where in typical individuals, repetitive information is recognized as such and filtered out. In this way, implicit learning and gating refer to the same construct of building a representation of a stimulus by recognizing it in repeated exposures and suppressing a novelty response. We further hypothesize that an intact gating mechanism is needed to form stable representations of written words. An individual who has stable word form representations in memory must have been able to form these representations by gradually decreasing novelty responses when exposed to the word forms over time. If this is the case, strong associations would be observed between word identification skills and measures of neural adaptation captured not only with fMRI but also with ERP.

Here, we report on adults with dyslexia and controls who participated in an auditory gating experiment using an ERP approach and a visual word discrimination task that requires rapid word recognition and, hence, a stable representation of the words. Selecting adults for this study allows a direct comparison to the Perrachione et al. (2016) that also reported on adults. The following research questions and hypotheses were addressed:

1. Compared to control adults, do adults with dyslexia show diminished adaptation to the second of two auditory stimuli? We hypothesize that the domain-general failure to adapt to repetitive stimuli in a previous study (Perrachione et al., 2016) can be observed in an ERP paradigm at high temporal resolution (Hypothesis 1). We predict rapid neural adaptation in the control participants but not in the participants with dyslexia.
2. Which ERP component is most strongly associated with the failure to suppress the novelty response to the second stimulus in paired sounds? We hypothesize that, although both N1 and P2 are robust auditory components with neural sources in auditory regions (Crowley and Colrain, 2004) (Godey et al., 2001, Naatanen and Picton, 1987), the gating effect is most strongly expressed in the earlier of these two components based on previous gating studies in other neurodevelopmental disorders (Madsen et al., 2015) that point to a preattentive mechanism underlying the gating process (Hypothesis 2a). Alternatively, the lack of adaptation may be evident mainly in the P2 component, given the role of attention deficit during gating and the relevance of ADHD for dyslexia (Hypothesis 2b).
3. Are measures of neural adaptation associated with behavioral measures of rapid word recognition, which relies on a solid representation of words in memory? In a task requiring the participants to evaluate two words presented side by side for being identical or different, we predict that the participants with dyslexia but not the controls will have difficulty and/or take longer to correctly identify two words as different because they may not have captured the essential features of the two words well enough detect the differences, which are subtle by design (Hypothesis 3a). Conversely, they may have difficulty and/or take longer to correctly identify two words as identical if the second word triggers an exaggerated novelty response (Hypothesis 3b). Overall, we predict that the measure that most clearly differentiates the participants with dyslexia and controls, either difficulty with detecting subtle differences or difficulty detecting the identical status of two words, is associated with the measure of gating identified with Research Question 2 because both are associated with stable word representations in memory (Hypothesis 3c).

## 2. Methods

### 2.1. Participants

In accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki), this study was conducted with the approval of the Internal Review Board at the University of Washington, acting on its own behalf as well as on behalf of Arizona State University. All participants gave written consent prior to the experiment.

Participants were 14 adults with dyslexia (6 males and 8 females; $M_{age}$ = 36.2 years, $SD_{age}$ = 17.2, age range 17–70 years) and 14 typical controls (5 males and 9 females; $M_{age}$ = 28.2 years, $SD_{age}$ = 15.5, age range 19–71 years). Group differences for age ($t(26) = 1.07$, $p = 0.293$, $d = 0.41$) and male/female distributions ($chi^2 = 0.15$, $p = 0.699$) were not statistically significant.

All participants passed a hearing screen at 20 dB SPL for 0.5, 1, 2, and 4 kHz and were free of current or past sensory, cognitive, psychological, or neurological disorders that could confound the results of this study. To be included in the control group, participants had to have no previous diagnosis of dyslexia and to have scores higher than one standard deviation below the mean on four tests of reading and one spelling test, described below. To be included in the dyslexia group, participants had to have a professional diagnosis of dyslexia and scores lower than one standard deviation below the mean on at least one of these tests (Berninger et al., 2001, Hsu et al., 2002, Raskind et al., 2000). The average number of low reading and/or spelling scores in the dyslexia group was 1.9 (range: 1–5). To rule out intellectual disability as a potential confounder, all participants had to have scores within or above normal limits on a standardized test of nonverbal cognition, described below. Because verbal processing ability can predict reading ability to a certain extent (Swanson et al., 1996), a similar requirement regarding a test of verbal cognition was only applied to the control group.

### 2.2. Diagnostic and experimental measures

Participants completed four standardized reading tasks and one standardized spelling task. Two subtests from the Woodcock Reading Mastery Tests–Revised (Woodcock et al., 2001) were administered. Word Identification (WID) and Word Attack (WATT) measure sight word reading and nonword decoding ability, respectively, under untimed conditions. Two subtests from the Test of Word Reading Efficiency (Torgesen et al., 2012) were administered. The Sight Word Efficiency (SWE) and Phonemic Decoding Efficiency (PDE) subtests measure sight word reading and nonword decoding ability, respectively, under timed conditions. The Spelling (SP) subtest from the Wechsler Individual Achievement Test – II (WIAT-II) (Wechsler, 2005) measures spelling ability. Because deficits in phonemic awareness are widely accepted as a component phenotype of dyslexia, a measure of phonemic awareness, the Nonword Repetition (NWR) subtest of the Comprehensive Test of Phonological Processing (CTOPP) (Wagner et al., 1999) was administered to validate this attribute.

To include measures of verbal and nonverbal processing ability, participants completed two verbal and two nonverbal subtests from the Reynolds Intellectual Assessment Scales (RIAS) (Reynolds and Kamphaus, 2003) that provide the basis for the Verbal Intelligence Index (VIX) and the Nonverbal Intelligence Index (NIX).

Table 1 summarizes diagnostic and inclusionary measures in terms of descriptive statistics and group differences. As expected, the two groups did not differ on verbal and nonverbal ability, but the dyslexia group obtained significantly lower measures of reading and spelling, compared to the control group. Despite a large effect size, the group difference with respect to NWR was not statistically significant, likely because the average NWR standard scores in both groups were below the population mean.

### 2.3. Electroencephalographic recordings

During the ERP experiment, participants were seated in a quiet room in front of a computer monitor with eyes approximately 60 cm away from the monitor. Participants were instructed to keep their eyes open and look at a fixation cross on the monitor while listening to sounds. Auditory stimuli were presented via insert earphones using E-Prime 2 (Psychology Software Tools, Sharpsburg, PA). Each trial consisted of a pair of pure tones (65 dB SPL; 1.5 kHz; 25 ms duration, 10 ms rise/fall time) with an interstimulus duration of 500 ms. The experiment consisted of 50 trials with approximately 5 s inter-trial-intervals (range 2–9 s).

Continuous electroencephalographic (EEG) data were collected using a high-density EEG recording system (Electrical Geodesics Incorporated, Eugene, OR) running Net Station 2.0. The EEG net held 128 electrodes (HydroCel Geodesic Sensor Net) including electrodes for recording eye-movements (horizontal and vertical) and two electrodes on the left and right mastoids. During the recording, data were collected with reference to the vertex electrode (at 250 Hz sampling rate). Impedance of all electrodes was ensured to stay below 40 kΩ during the data recording.

Offline data analyses were conducted using the EEGLAB toolbox (Delorme and Makeig, 2004) and custom-written Matlab (Mathworks, Matick, MA) scripts. Prior to data analysis, data from the two mastoid electrodes were averaged and used as a reference signal for all EEG electrodes. The EEG signals were low-pass filtered with a cut-off frequency of 55 Hz, using a finite impulse response (FIR) filter implemented in EEGLAB (Kaiser windowed sinc FIR filter; deviation: 0.005; transition bandwidth: 1 Hz). Automatic artifact correction and removal were done on the continuous data,

**Table 1**
Diagnostic and inclusionary variables for the two groups and measures of group differences.

| Variable | Controls | | Dyslexia | | t | 2-Tailed p | Cohen's d |
|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | | | |
| Word Identification* | 104.9 | 5.6 | 92.2 | 7.8 | 4.96 | <0.001 | 1.87 |
| Word Attack* | 105.4 | 6.9 | 95.6 | 9.2 | 3.18 | 0.004 | 1.20 |
| Sight Word Efficiency* | 108.1 | 9.1 | 88.5 | 14.1 | 4.37 | <0.001 | 1.65 |
| Phonemic Decoding Efficiency* | 97.8 | 9.9 | 78.5 | 8.3 | 5.59 | <0.001 | 2.11 |
| WIAT Spelling* | 113.4 | 7.6 | 91.6 | 17.8 | 4.24 | <0.001 | 1.60 |
| Nonword Repetition** | 8.7 | 1.6 | 7.4 | 1.7 | 2.05 | 0.052 | 0.77 |
| RIAS Verbal Intelligence Index* | 114.4 | 9.5 | 111.6 | 8.9 | 0.99 | 0.334 | 0.44 |
| RIAS Nonverbal Intelligence Index* | 114.5 | 6.7 | 114.1 | 11.8 | 0.10 | 0.918 | 0.04 |

* Population mean = 100, standard deviation = 15.
** Population mean = 10, standard deviation = 3.

using the clean_rawdata plugin of EEGLAB. The clean_rawdata plug-in has several procedures for noise removal from continuous data. We used its "BurstCriterion" procedure with 4 standard deviations as a threshold to find and to remove data portions that fall beyond the threshold. For consistency purposes, we did not exclude channels. The clean continuous data were segmented into epochs of 500 ms length (from 100 ms prior to auditory stimuli to 400 ms after the stimuli) and were baseline corrected (based on the first 100 ms of each epoch). We used automatic bad trial rejection to reject trials that contained large deviations in the baseline period (exceeding ± 50 μV) or large deviations in the entire epoch (exceeding ± 120 μV). Additionally, trials were visually inspected to exclude trials that were contaminated with excessive muscle artifact, eye movements, or blinking. The total number of artifact-free epochs were highly similar for the two groups ($t(26) = -0.17$, $p = 0.867$). Finally, for each participant, artifact free epochs were averaged to compute the evoked potentials in response to each of the auditory stimuli. For this study, we focused on N1 and P2 components because they are well-defined auditory components (Naatanen and Picton, 1987, Tremblay et al., 2001) with relevance to gating (Ethridge et al., 2016, Freedman et al., 1996, Matsuzaki et al., 2014, Nagamoto et al., 1991, Schubring et al., 2018). Whereas the N1 component is thought to be preattentive, the P2 component is influenced by attentional factors, at least in the visual domain (Luck, 1994). Given that both N1 and P2 components are maximal over frontocentral electrodes (Doallo et al., 2007, Lightfoot, 2016), evoked responses from 19 electrodes in the central region were averaged as a measure of the final evoked potential for each participant. Note that the electrode locations were based on the EGI electrode system (E55 (Cpz), E31, E80, E30 (C1), E7, E106, E105 (C2), E13 (FC1), E6 (Fcz), E112 (FC2), E12, E5, E11 (Fz), E20, E118, E19 (F1), E4 (F2), E29 (FC3), E111 (FC4)). As electrophysiological dependent measures, the amplitude and latency of both the N1 and P2 components of the final evoked potential were extracted for responses to each of the auditory stimuli and for each participant. The N1 component was defined as the largest negative peak occurring 70–130 ms post stimulus. The P2 component was defined as the largest positive peak occurring 150–250 ms post stimulus. These measures were used to calculate auditory gating for N1 and P2 components (i.e., comparison between N1 or P2 in response to the first tone and those in response to the second tone). Additionally, topographical scalp maps were created using the data from all electrodes. These maps were used to visually inspect distribution of N1 and P2 as well as N1 and P2 gating over the scalp. It should be noted that we focused on N1 and P2 because these are relatively robust components in comparison with earlier components such as P1 (Fuerst et al., 2007, Rentzsch et al., 2008). We argue that the absence of gating at P1 implies that it is also absent at P50.

### 2.4. Word comparison

The experimental behavioral task was a word comparison task. Participants were seated in front of a computer screen on which word pairs were displayed side by side, using E-Prime 2. Participants were given a response box and instructed to press the key labeled "1" if the words were the same, e.g., "cod cod," and the key labeled "4" if they were different, e.g., "cod cob." Following a brief practice set and a start prompt, the first word pair appeared on the screen. The response key press triggered the next word pair. Using the response information captured with E-Prime 2, average reaction time in ms was calculated as a measure of speed of performance. Accuracy of performance was calculated as a proportion of accurate out of the sum of responses. Because this variable is bounded by [0, 1], it was logit transformed.

The word pairs were constructed from 5th and 6th grade vocabulary words that consisted of one or two syllables and three to seven letters. Of the 576 word pairs, shown in Supplementary File 1, 291 were two identical words, whereas 285 represented two different words, so that the two conditions Same (S) and Different (D) occurred with nearly equal probability. Of the word pairs in the D condition, the following categories of subtle differences were represented: word length differed by one letter (58 word pairs, e.g., "world word"), visual letter similarities that were not symmetrical (51, e.g., "neat heat"), visual similarities that were symmetrical (47, e.g., "cob cod," cub cup"), and sequential letter arrangement (12, e.g., "form from"). The remaining differences were slightly less subtle and consisted of substitutions of one letter that was visually dissimilar (39, e.g., "think thank"), changes representing two letters (3, e.g., "seen seam"), and homophones (76, e.g., "write right"). All word pairs thus shared substantial numbers of letters and/or phonemes in their spoken forms, a feature that provided the advantage of probing access to the lexical route of word recognition with more stringency than standard tests of word identification such as the WID or SWE.

Given that the words were obtained from 5th and 6th grade vocabulary terms, it can be assumed that they were familiar to adults. Rapidly recognizing familiar words as lexical units, as proficient readers routinely do, requires having a well-established representation of the words in memory. The lack of such a solid representation leads to failure to detect subtle differences or, alternatively, to reliance on the comparison of the words in terms of letter arrangement using the sublexical route, which is a slower and more error-prone process. Under the assumption of underspecified word representations, one would expect a greater error rate during the D condition where the subtle word differences were not recognized and the word pair was incorrectly labeled as "same." The side-by-side presentation of the two words provides opportunities for an alternate error type where the second word may trigger a novelty response that remains unrepressed by some individuals with dyslexia, causing them to incorrectly identify two identical words as different.

### 2.5. Statistical analyses

All statistical analyses were conducted using the IBM SPSS Statistics 24 software package. To test Hypotheses 1, 2a, and 2b, four separate repeated measures ANOVA for each of the dependent measures (N1 amplitude and latency, P2 amplitude and latency) were conducted. For these analyses, Group (control, dyslexia) was used as a between-subjects variable and Tone (first tone, second tone) as a within-subjects variable. Statistically significant interactions were followed up with posthoc analyses of the gating magnitude using t-tests. The magnitude of the gating effect was calculated as the difference in response to the first and second tones, divided into the response to the first tone.

Prior to testing hypotheses 3a, 3b, and 3c regarding the word pair comparison task, the two groups were compared on their overall reaction times and accuracy. Large differences were evident in both domains (Table 2), which questions the use of raw reaction time and accuracy for tests of group differences regarding the S and D conditions, as large group differences would be expected a priori.

To make comparisons in the S and D conditions more meaningful, relativized scores were computed. For reaction time in ms, the difference between the S and D condition was divided into the S value to arrive at the Proportional Reaction Time (PRT). For accuracy, the logit-transformed D value was subtracted from the value in the S condition to arrive at a Differential Accuracy Score (DAS). PRT and DAS thus each capture the aspects of interest, S and D, in a single variable. For both types of relative scores, a positive value indicates lower performance when the word pairs consisted

**Table 2**
Measures of central tendency and group differences for overall reaction time in ms and logit-transformed accuracy.

| Variable | Control Mean | Control SD | Dyslexia Mean | Dyslexia SD | t | p | Cohen's d |
|---|---|---|---|---|---|---|---|
| Overall reaction time (ms) | 968.9 | 171.8 | 1241.0 | 282.2 | 3.501 | <0.001 | 1.152 |
| Overall Acc. (logit) | 2.852 | 0.430 | 2.362 | 0.534 | 3.256 | 0.001 | 0.356 |

of two different words, compared to two same words, which would be consistent with Hypothesis 3a that the dyslexia group would take longer and/or produce more errors in the D condition by selecting the S response for D word pairs because of a lack of a representation of the stimulus words in long-term memory. A negative PRT and/or DAS value indicates lower performance when the word pairs consisted of two same words, compared to two different words, which would be consistent with Hypothesis 3b that the dyslexia group would take longer and/or incorrectly identify S word pairs as D because of an unsuppressed novelty response to the second word. To test Hypotheses 3a and 3b, t tests of PRT and DAS were computed.

To test Hypothesis 3c that the behavioral responses to the word pairs are associated with the electrophysiological measure of gating, the most significant outcome from the word pair t tests, PRT or DAS, was selected for association testing with the most significant outcome measure of gating, amplitude or latency of N1 or P2, identified with the statistical testing of the electrophysiological responses. In addition to correlation testing, these two variables were entered into an iterative hierarchical cluster analysis using average linkage, followed by k-means clustering where k was based on the number of clusters in the hierarchical clustering. Finally, cluster membership was compared to dyslexia/control group membership with chi square testing.

## 3. Results

### 3.1. Electroencephalographic results

The N1 and P2 components of the ERPs were investigated. The N1 component was defined as the largest negative peak occurring 70–130 ms post stimulus. The P2 component was defined as the largest positive peak occurring 150–250 ms post stimulus. Regarding N1 amplitude, a statistically significant main effect of Tone, $F(1,26) = 47.76$, $p < 0.001$, was found, with a more negative response amplitude for the first tone, compared to the second. A nominally statistically significant Tone by Group interaction, $F(1,26) = 6.10$, $p = 0.020$, was evident. No significant main effect of Group was found ($F(1,26) = 0.35$, $p = 0.560$), suggesting that the overall N1 amplitude was similar between the two groups (Fig. 1). As shown in Figs. 1 and 2A, the Tone by Group interaction indicated that the change in N1 amplitude of responses to the second tone relative to responses to the first tone (N1 gating magnitude) in the control group was significantly larger than the N1 gating magnitude in the dyslexia group ($t(26) = 2.75$, $p = 0.005$), with means (and standard deviations) for the control and dyslexia groups, respectively, 0.45 (0.22) and 0.20 (0.07), an effect size (Cohen's d) of 1.04.

Regarding N1 latency, the ANOVA test did not reveal a statistically significant main effect of Tone, $F(1,26) = 2.81$, $p = 0.105$, main effect of Group, $F(1,26) = 0.87$, $p = 0.359$, or Tone by Group interaction, $F(1,26) = 0.16$, $p = 0.689$ (Fig. 2B).

Regarding P2 amplitude, a statistically significant main effect of Tone, $F(1,26) = 22.39$, $p < 0.001$, was found, with larger P2 amplitude in response to the first tone compared to the P2 amplitude of response to the second tone. No statistically significant main effect of Group, $F(1,26) = 0.08$, $p = 0.777$, or Tone by Group interaction, $F(1,26) = 2.38$, $p = 0.135$, was evident. Together, these results suggest that P2 gating was statistically significant and that the magnitude of P2 gating was similar for the two groups (Fig. 2C).

Regarding P2 latency, similar to results for N1 latency, no statistically significant results were found for main effect of Tone, $F(1,26) = 0.19$, $p = 0.665$, main effect of Group, $F(1,26) = 1.15$, $p = 0.294$, or Tone by Group interaction, $F(1,26) = 0.33$, $p = 0.572$ (Fig. 2D).

Fig. 1 shows grand average evoked responses to the first and the second tones for the two groups. Fig. 2 summarizes N1 and P2 amplitudes and latencies for the two tones and both groups

In both participant groups, the N1 responses were largest in the frontocentral region (Fig. 3). This confirms previous findings in gating experiments (Doallo et al., 2007, Lightfoot, 2016) and validates the choice of the 19 frontocentral electrodes for statistical analysis. Fig. 3 shows the topographical N1 distributions for both groups in response to the first and second tones.

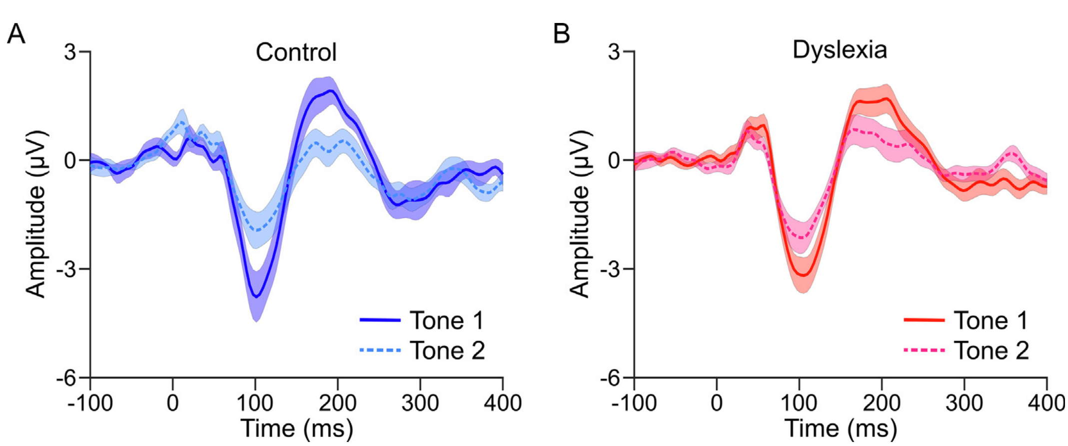


**Fig. 1.** Waveforms. Grand average ERP waveforms in response to the first and the second tones for the frontocentral electrodes in control participants (A) and participants with dyslexia (B). The shaded area corresponds to standard error of the mean in each time point.

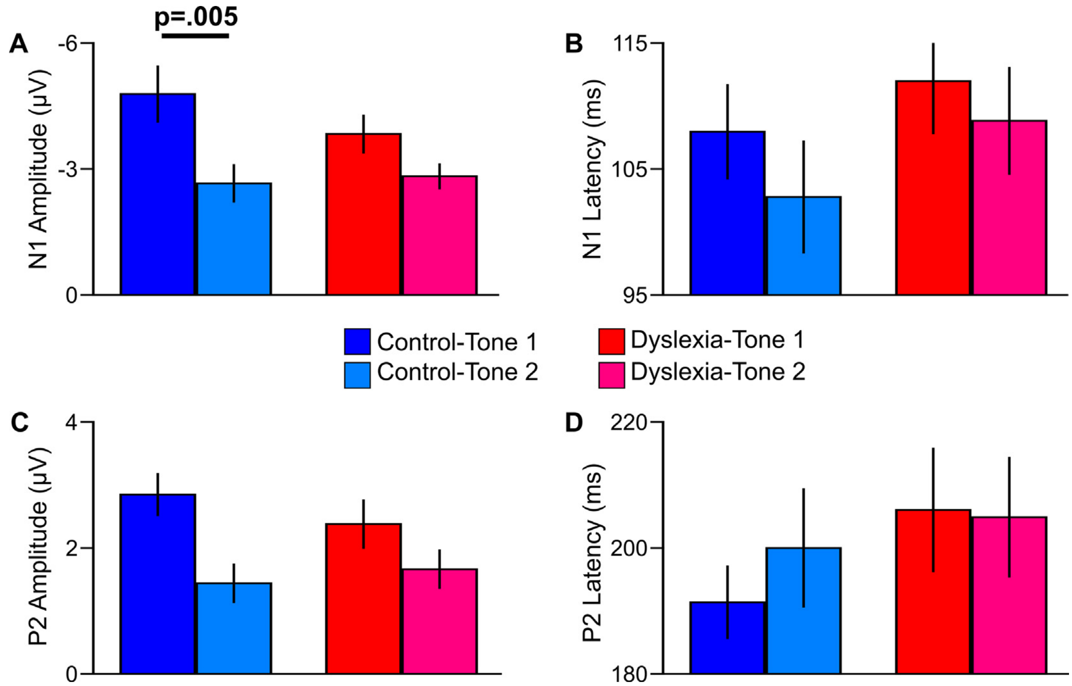


**Fig. 2.** N1 and P2 results. Group means and standard errors (error bars) of the mean for N1 amplitude and latency (A and B) and P2 amplitude and latency (C and D) for the first and the second tones.

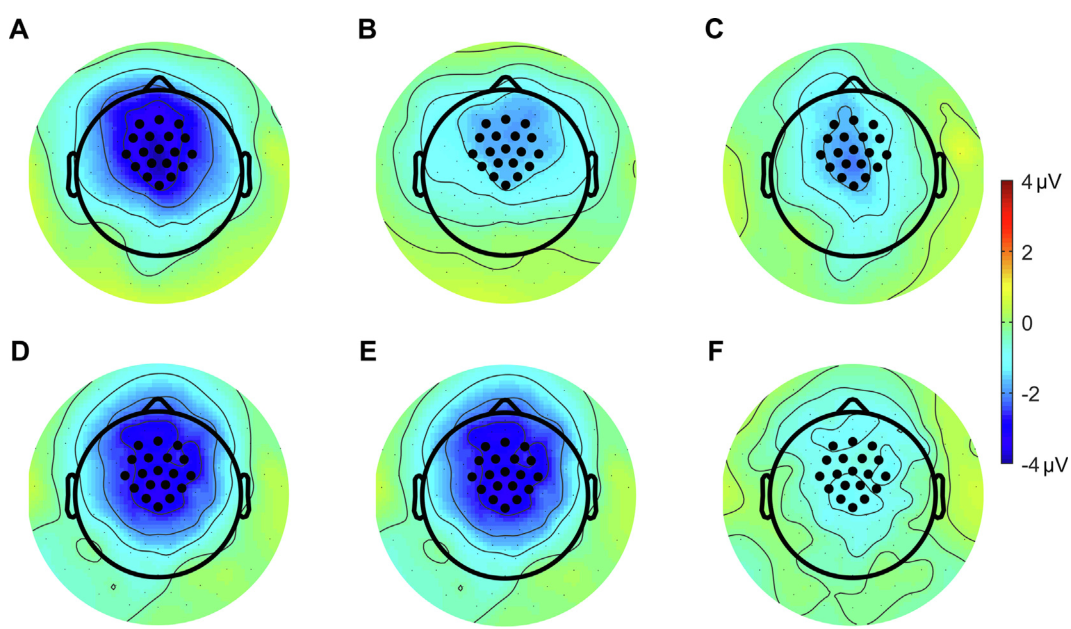


**Fig. 3.** Topographic amplitude distributions. Topographic maps for N1 amplitude of the response to the first (left column, A and D) and the second tones (center column, B and E) show typical N1 topographical maps for the control group (top row) and dyslexia group (bottom row). Individual electrode channels contributing to the frontocentral region of interest are colored as black circles in the topographical scalp map. Topographic maps in the right column (C and F) show the topographical map of N1 gating magnitude (N1 amplitude of the first tone minus N1 amplitude of the second tone).

### *3.2. Word pair speed and accuracy*

As expected due to the overall findings, group differences in reaction times and accuracy were highly statistically significant. Regarding the variables of interest, relative measures of reaction time (PRT) and accuracy (DAS), t tests showed a significant group difference for DAS but not for PRT (Table 3). This indicates generally longer reaction times in the dyslexia group, compared to the control group, that are not specific to the S and D conditions. Accuracy was lower in the dyslexia group, compared to the control group, not only in general but specifically in the D condition. Table 3 summarizes measures of central tendency and group differences for the direct and relative measures of reaction time and accuracy. Figs. 4 and 5 illustrate the reaction times and logit-transformed accuracy individually for the two conditions of interest, S and D, and the two participant groups.

Accuracy during the word pair task differentiated more significantly between the groups than reaction time, and regarding ERP,

**Table 3**
Measures of central tendency and group differences for direct and relative reaction time and accuracy.

| | Control | | Dyslexia | | t | p | Cohen's d |
|---|---|---|---|---|---|---|---|
| Variable | Mean | SD | Mean | SD | | | |
| *RT Same (ms)* | *936.5* | *173.2* | *1208.9* | *306.0* | *3.73* | *<0.001* | *1.082* |
| *RT Diff. (ms)* | *1001.7* | *183.0* | *1273.4* | *277.3* | *3.708* | *<0.001* | *1.146* |
| PRT | 0.074 | 0.102 | 0.068 | 0.133 | 0.158 | 0.438 | 0.049 |
| *Acc. (logit) Same* | *2.978* | *0.367* | *2.676* | *0.409* | *2.504* | *0.008* | *0.774* |
| *Acc. (logit) Diff.* | *2.775* | *0.554* | *2.159* | *0.740* | *3.029* | *0.002* | *0.936* |
| DAS | 0.203 | 0.448 | 0.515 | 0.686 | 1.732 | 0.046 | 0.535 |

Note: Italic font = variables with group differences that were expected a priori.

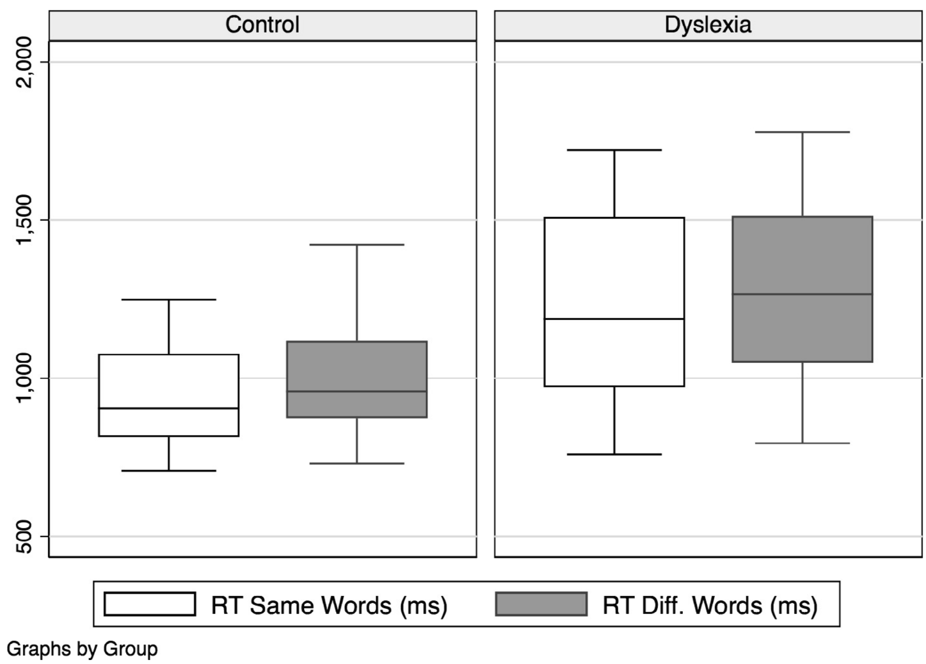


**Fig. 4.** Reaction time during word pair comparisons. Reaction time in ms for the same and different word pair condition, separately for the control and dyslexia group.

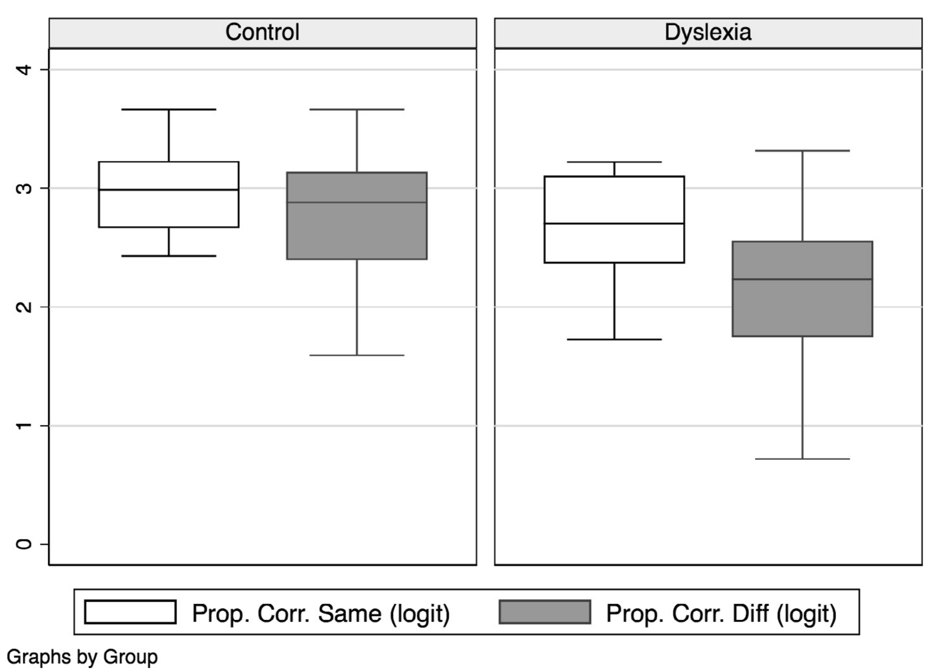


**Fig. 5.** Accuracy during word pair comparisons. Proportion correct (logit) for the same and different word pair condition, separately for the control and dyslexia group.

N1 resulted in more significant group differences than P2. Hence, DAS was the aspect of the word pair task and N1 gating magnitude was the ERP aspect selected for association testing. Across all subjects, a statistically significant negative correlation between the normalized N1 gating index and DAS was evident ($r = -0.503$, $p = 0.006$). This correlation was present in the dyslexia group ($r = -0.560$, $p = 0.037$) but not in the control participants ($r = -0.029$, $p = 0.922$). Fig. 6 confirms that the overall association between the two variables of interest is mainly driven by the dyslexia group.

Results from hierarchical iterative clustering revealed three distinct clusters. K-means clustering (Fig. 6) showed that Cluster 1 with the highest gating magnitude and intermediate DAS scores consisted of three controls, Cluster 2 with intermediate gating magnitude and DAS scores consisted of 7 participants with dyslexia and 10 controls, and Cluster 3 with the lowest gating and highest DAS scores consisted of 7 participants with dyslexia and 1 control. Thus, the dyslexia and control groups differed significantly with respect to cluster membership (chi2(2) = 8.03, $p = 0.013$).

## 4. Discussion

Previous research using an fMRI design with high spatial but low temporal resolution showed that adults with dyslexia had diminished neural adaptation when responding to repetitive stimuli; this was observed across several stimulus types, both in the visual and auditory domain (Perrachione et al., 2016). Here, we show complementary evidence of diminished neural adaptation associated with dyslexia using an ERP design, providing insights into the temporal time course of the responses. Specifically, the N1 response amplitude to the second of two tones was significantly lower, compared to the response to the first tone, and this adaptation was significantly greater in the control participants, compared to the participants with dyslexia. An adaptation of responses to the second tone was also seen in the P2 component, but the dyslexia group did not differ significantly from the typical controls.

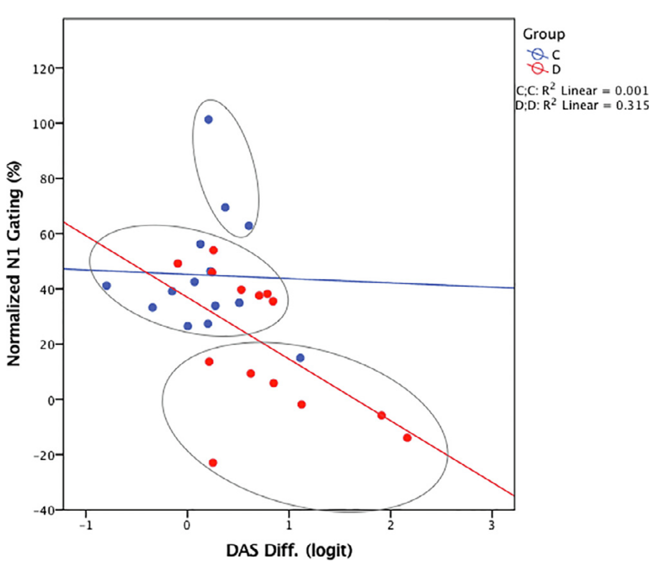


**Fig. 6.** Gating magnitude and differential accuracy score (DAS) during word pair comparisons. Normalized N1 gating index as a function of the accuracy (logit) difference between the same and different condition of the word pair comparisons. Gray ovals designate three clusters identified with hierarchical and k-means clustering.

The N1 component is known to decrease in amplitude as a function of repetitiveness, both in the visual and the auditory domain. Whereas failure to adapt to repetitive stimuli have been documented with early-occurring ERP amplitudes in other neurodevelopmental disorders, e.g., autism spectrum disorder and schizophrenia, and interpreted as failure to filter out irrelevant information, the present ERP results show for the first time that a similar mechanism is at work in dyslexia.

Whereas the fMRI study of dyslexia (Perrachione et al., 2016) implicated various predictable brain regions depending on stimulus modality (e.g., temporal regions for auditory stimuli) where response attenuation occurred in the control participants but not in the participants with dyslexia, the present study implicates the N1 component and, by implication, prior time points, as the corresponding time window when the response attenuation occurs in the control participants but less so in the participants with dyslexia. In the present ERP study, the measured N1 responses were most salient in frontocentral regions, as expected given well-established previous findings of gating in other populations (Doallo et al., 2007, Lightfoot, 2016). By itself, this cortical ERP localization cannot be interpreted with respect to its neural generators. Based on the findings regarding auditory stimuli in the fMRI study (Perrachione et al., 2016), one would assume that the neural generators of the auditory response are in temporal regions, whereas the neural generators of the gating processes preceding the auditory response are thought to occur in the thalamus and prefrontal cortex (Green et al., 2017, Mayer et al., 2009). The main contribution of the N1 results is not the spatial, but rather, the temporal information contained in it.

The N1 component is an early-occurring component representing preattentive sensory processing of information. Given that many individuals with dyslexia also have ADHD, this finding may imply that the attention deficit has early-occurring sensory precursors. However, clinical measures of ADHD were not available for the participants in the present study. Future studies should investigate N1 responses in individuals with dyslexia with and without concomitant ADHD. The fact that both participant groups showed gating effects at the P2 time window shows that the salient time window associated with the ability to filter out extraneous information occurs earlier.

During the word pair discrimination task, the participants with dyslexia showed generally longer reaction times, compared to the typical controls, regardless of word pair condition (S or D), but a group difference in proportional reaction times was not found. This indicates that the dyslexia group showed longer reaction times in general, regardless of word pair condition. Similar general differences in reaction times and processing speeds have been observed previously across many different domains (Cardillo et al., 2017, Peter et al., 2011, Shanahan et al., 2006).

More relevant for Hypotheses 3a and 3b is the significant difference in not only direct but also relative accuracy between the two groups. The participants in the control group processed the word pairs rapidly and with high accuracy, which is consistent with using the lexical route, especially given that the words were common and familiar. The accuracy in the dyslexia group regarding the D condition was highly variable. Those participants with low accuracy in this condition clicked the button for the S condition when the words actually differed in subtle ways. Consistent with Hypothesis 3a, this implies that they failed to detect these differences, likely because they did not have a stable representation for the stimuli stored or accessible in memory. These findings cannot disambiguate whether the participants in the dylsexia group simply overlooked the suble word differences in the D condition or whether they relied on visual inspection of the letter sequences, letter shapes, and word lengths via the sublexical route, a challenging, time-consuming, and error-prone task given the subtleness of the differences in many of the word pairs.

Some support was found for Hypothesis 3b that participants with dyslexia would incorrectly identify S word pairs as D. Their accuracy in the S condition was slightly lower than that in the control group, although this difference was not as great as in the D condition. However, the relative accuracy scores in the dyslexia group was positive, which indicates that in this group, accuracy in the S condition was higher than in the D condition. Whether or not seeing two identical words side by side triggers sufficient novelty responses to label the second word as different from the first should be evaluated in further studies.

Hypothesis 3c was supported by the significant correlation between the amplitude of the N1 gating effect and the accuracy of responses to word pairs in the D condition, relative to the S condition. Both of these measures reflect aspects of forming stable representations of exemplars. In the case of gating, this aspect is the ability to extract regularities from exemplars by filtering out irrelevant information. In the case of detecting subtle differences between two written words, this aspect is the presence of stable word representations. The measure of gating thus reflects the process of forming a stable representation, whereas the accuracy when detecting subtle differences between words reflects the end result of having formed such a representation. The fact that the correlation between the electrophysiologic measure of gating and the accuracy during the D condition, relative to the S condition, of the word comparison task, was driven largely by the dyslexia group, especially by some participants with very low gating and poor relative accuracy in the D condition, is consistent with the idea that there are several subtypes of dyslexia and diminished gating may only characterize a subset of the participants in this study, here represented as Cluster 3 that emerged from the clustering procedure.

### *4.1. Limitations and future studies*

This study has several limitations that should be addressed in future studies. First, the sample size was relatively small. Future studies should replicate our findings in a larger sample of individuals with, and without, dyslexia to show the association between gating and word representation with more statistical power. Second, we focused on the N1 and P2 components because they are more robust than earlier components such as the P1 or midlatency components. Although a lack of N1 gating in the dyslexia group implies a lack of gating in any earlier components as well, future studies should evaluate this assumption explicitly in larger samples of individuals with, and without, dyslexia, using a larger number of trials. Additionally, the neural generators of gating in individuals with, and without, dyslexia should be investigated more directly, as here, we report evidence of gating at the level of the cortex using EEG technology, where deep structures are not readily accessible.

Taken together, the findings from this study are consistent with an early-occurring auditory adaptation that is reduced in some individuals with dyslexia and that is associated with poor word form representation in memory. Future studies should investigate this lack of adaptation in other modalities including visual to complement previous fMRI studies of implicated brain regions with information regarding the time course. The findings from this study have implications for clinical management that targets the formation of stable representations in memory, not only regarding letters and words but also more generally regarding implicit learning across many modalities.

## Declaration of Competing Interest

None.

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## Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clinph.2019.07.028.

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