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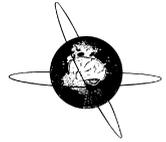
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## Fixation-related potentials in naming speed: A combined EEG and eye-tracking study on children with dyslexia



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### HIGHLIGHTS

- Novel framework for integrative analysis of neurophysiological and eye-gaze data in examining young readers' cognitive processes under serial rapid-automatized naming (RAN) tasks.
- Fixation-Related Potentials during the serial RAN capture neural components that differentiate between children with dyslexia (DYS) and chronological age controls (CAC).
- Differences between DYS and CAC groups were observed in the phonological but not in the RAN tasks' visual conditions.

### ABSTRACT

**Objective:** We combined electroencephalography (EEG) and eye-tracking recordings to examine the underlying factors elicited during the serial Rapid-Automatized Naming (RAN) task that may differentiate between children with dyslexia (DYS) and chronologically age controls (CAC).

**Methods:** Thirty children with DYS and 30 CAC ( $M_{age} = 9.79$  years; age range 7.6 through 12.1 years) performed a set of serial RAN tasks. We extracted fixation-related potentials (FRPs) under phonologically similar (rime-confound) or visually similar (resembling lowercase letters) and dissimilar (non-confounding and discrete uppercase letters, respectively) control tasks.

**Results:** Results revealed significant differences in FRP amplitudes between DYS and CAC groups under the phonologically similar and phonologically non-confounding conditions. No differences were observed in the case of the visual conditions. Moreover, regression analysis showed that the average amplitude of the extracted components significantly predicted RAN performance.

**Conclusion:** FRPs capture neural components during the serial RAN task informative of differences between DYS and CAC and establish a relationship between neurocognitive processes during serial RAN and dyslexia.

**Significance:** We suggest our approach as a methodological model for the concurrent analysis of neurophysiological and eye-gaze data to decipher the role of RAN in reading.

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**Abbreviations:** EEG, Electroencephalography; RAN, Rapid Automatized Naming; DYS, Children with Dyslexia group; CAC, Chronologically Aged Controlled group; FRP, Fixation-Related Potentials; fMRI, Functional Magnetic Resonance Imaging; ERP, Event-Related Potentials; ERS-AB, Early Reading Skills Assessment Battery; CPT, Cluster-based Permutation Test.

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### 1. Introduction

One of the most examined underlying cognitive factors of reading development and dyslexia is naming speed, known as rapid automatized naming (RAN). RAN is defined as the ability to name as fast as possible visually presented stimuli such as colors, objects, digits, and letters (Kirby et al., 2010). Studies investigating the

RAN-reading relationship have focused on the construct's conceptualization (e.g., Papadopoulos et al., 2016) and its assessment (e.g., Georgiou et al., 2013). This focus is based on the strong relationship reported between RAN and reading at various stages of children's development (e.g., Caravolas et al., 2013; Georgiou et al., 2014; Kirby et al., 2003; Puolakanaho et al., 2007) and adults (e.g., Araújo et al., 2019). Recently, the focus switched to deciphering the role of RAN to predicting reading through the use of eye-tracking (e.g., Easson et al., 2020), electroencephalography (EEG) methods (e.g., Bakos et al., 2020) or functional magnetic resonance imaging (fMRI) measures (e.g., Al Dahhan et al., 2020; Cummine et al., 2015). As expected, because the interest in understanding the RAN-reading relationship through imaging and electrophysiological measures is recent, the field is open to new approaches. The purpose of the present study was to go one step further and combine electroencephalography (EEG) and eye-tracking recordings and examine the underlying components of RAN through fixation-related potentials.

Naming speed performance on the RAN task is a powerful predictor of concurrent and future reading ability in alphabetic writing systems (in both consistent: Aarnoutse et al., 2005; Georgiou et al., 2008a; Landerl et al., 2019; Papadopoulos et al., 2016; Verhagen et al., 2008 and inconsistent orthographies: Cardoso-Martins and Pennington, 2004; Furnes and Samuelsson, 2011; Kirby et al., 2003; Landerl et al., 2019) and in non-alphabetic languages, such as Chinese (Liao et al., 2008; Wang et al., 2015). Conversely, naming speed deficits are a characteristic of reading difficulty from childhood to adulthood (Georgiou et al., 2012; Georgiou et al., 2018). As reported in a recent meta-analytic study, the size of the RAN-reading relationship is 0.48 (Araújo et al., 2015). These findings underscore RAN's significant role in reading and justify additional investigation with neurophysiological methods to explain the nature of RAN as a construct, expected to decipher further how RAN relates to reading.

In that direction, earlier studies have attempted to distinguish processes associated with phonological retrieval of the letter name from other processes requiring visual processing (e.g., Jones et al., 2010; Jones et al., 2013). The manipulation of the RAN tasks' visual versus phonological requirements has provided a means of investigating whether different processes are related to the naming process (Jones et al., 2008). To test the contribution of different processes, for example, Compton (2003) constructed three variations of the RAN task by manipulating the original letter matrix to increase (a) phonological confusion, (b) visual confusion, and (c) both phonological and visual confusion. Compton (2003) found that RAN naming speed and accuracy can be significantly affected by visually confusing letters. Specifically, the increase of visual confusion of the RAN stimuli affected both speed and accuracy adversely. However, the underlying neural processes that drive these behavioral effects were not sufficiently understood.

Studies like the above rely on cognitive measurements tapping RAN with primary emphasis on reaction (in discrete RAN tasks) or response (in serial RAN tasks) time (Georgiou et al., 2013). Thus, cognitive measurements are generally considered to capture efficiency (work per unit time) and, to a much lesser, almost negligible extent, effectiveness (how well the user can perform a given RAN task). However, this general approach in performing a naming speed task can only provide a single time point in different experimental conditions at the output stage (i.e., the outcome at the end of the process). This means that the internal cognitive stages at which the actual information processing occurs (e.g., Breznitz, 2003) are ignored or not adequately studied. Relevant research has even attempted to partition RAN total time into its constituent components, namely articulation and pause time (e.g., Neuhaus et al., 2001; Georgiou et al., 2014). Although this approach has generated significant knowledge about the proportion of RAN's predic-

tive variance in reading fluency accounted for by what articulate and pause time shared, we still need to know what kind of processing RAN reflects. Thus, more advanced methods are needed, which recent research has begun to employ, to explain the underlying cognitive processes involved during naming speed.

Recent research investigating the RAN neuro-cognitive processes has used neurophysiological and imaging methods, such as eye-tracking (e.g., Easson et al., 2020), electroencephalography (EEG) (e.g., Bakos et al., 2020) or fMRI (e.g., Al Dahhan et al., 2020; Cummine et al., 2015). For example, research employing eye-tracking has shown that older readers (such as college and Grade 7/8 students) are generally more efficient, have shorter fixation durations, and make fewer saccades and regressions than younger groups (Grades 2 and 4; Easson et al., 2020) when they perform typical RAN-letter tasks. Similar findings are yielded for children (e.g., Al Dahhan et al., 2017) and adults (e.g., Al Dahhan et al., 2020) with dyslexia compared to chronological-age controls. Furthermore, when naming tasks involve visually, or phonologically similar letters or objects, tasks similar to those employed in the present study, the naming speed performance has been found to be significantly affected for both participants with dyslexia and their chronological-age controls (e.g., see Al Dahhan et al., 2017; Araújo et al., 2020, for relevant findings with children and adults, respectively). Even more, Araújo et al. (2020) have reported that although significant interactions of the frequency of the object name and phonological neighborhood were observed in first fixation and gaze duration measures, none of the group interactions was significant. Such findings are confirmed through fMRI methods, where poorer behavioural performance and greater activation are reported in similar conditions involving adult populations (Al Dahhan et al., 2020).

Research employing EEG methods has been limited and focuses only on adults with developmental dyslexia and their chronological-age controls (e.g., Araújo et al., 2016). For example, Araújo and colleagues using a discrete naming task, reported attenuated N/P190 component indexing early visual processing and N300 component indexing late visual processing in naming pictures preceded by perceptually related (vs. unrelated) primes in the age controls but not in the group with dyslexia. The authors interpreted these findings as an indication of suboptimal processing in the early stages of object processing in individuals with dyslexia. This processing makes it difficult to map and integrate perceptual information to a more specific form of perception in memory.

Although these studies have reported reliable findings of the RAN neurocognitive processes, understanding naming speed performance mechanisms remains an open question. Naming speed is essentially an active sensor-motor process, where the consecutive saccadic eye movements subserve visual stimulus sampling, the focus of attention, and the efficient use of processing speed and working memory (Papadopoulos et al., 2016). Therefore, investigating neural processes of naming speed using concurrent methods that provide complementary data, such as EEG and eye movement registration, is necessary to eliminate eye movement artifacts and uncover the naming speed's neural substrates. We developed an experimental framework to address these challenges, aiming to the fixation onset-related EEG activity, based on the simultaneous recording of eye-tracking and EEG data. We return to this framework next.

### 1.1. Current approaches and limitations to EEG and Event-Related Potentials (ERPs) analysis

Event-Related Potentials (ERPs) - an average stereotypical neural waveform evoked in response to physical stimuli - are interpreted as indices of cognitive processes involved in specific tasks.

ERPs have been used to study psychological processes such as attention, memory and cognition, perception, and intelligence (for example, see Sokhadze et al., 2017 and references therein). Several machine-learning-driven approaches have also been proposed to analyze EEGs in the study of the neuro-cognitive processes (Christoforou et al., 2017, 2018, 2010; Christoforou and Theodorou, 2021). Such methods aim to identify neural correlates of different cognitive functions and often find application in scenarios where traditional average ERPs fail to capture the true nature of the underlying neural components or overcome the intrinsic limitation of the ERP analysis (Sokhadze et al., 2017). For example, multivariate, single-trial discriminant analysis has been proposed to capture the neural representation of task difficulty and decision making during perceptual categorization tasks (Philiastides and Sajda, 2006). Likewise, multivariate single-trial correlation analysis (Christoforou et al., 2013) has been proposed to capture neural components that maximally correlate with continuous behavior observations.

Thus, we argue that a similar type of analysis is expected to help identify which neurophysiological processes and at which stage of the process could differentiate typically developing children from children with dyslexia during the serial naming process of a set of stimuli with increased phonological and visual confusion. To our knowledge, there are no studies that have explored the concurrent use of neurophysiological techniques, such as ERP and eye-tracking recordings to investigate neural circuitry during serial RAN tasks. This is primarily due to the methodological challenges in isolating informative neural components during naming tasks because of the lack of experimenter-controlled time-locked events necessary to extract ERPs. Instead of dealing with the methodological challenges that arise from the paradigm, researchers have focused on employing variations of RAN tasks, such as the discrete RAN task, on bypassing paradigm constraints. In this variation, RAN symbols are presented in sequence one after another at predefined time intervals to introduce the time-locked events needed for the ERP generation artificially (Bakos et al., 2020).

Even though the discrete RAN format is related to reading fluency (e.g., Altani et al., 2017) and individuals with reading difficulties also exhibit deficits in this task (e.g., Gasperini et al., 2014), these effects and associations are more strongly present in the serial RAN task (Bakos et al., 2020). In particular, serial RAN format engages more - and likely different - cognitive processing related to reading. For example, looking ahead and pre-processing subsequent items, backtracking, and resolving confounding effects - as in phonological or visual confusable symbols - reflect the cognitive processing involved. Hence identifying neurophysiological components engaged during the serial RAN task is likely to provide more relevant information about the underlying cognitive processes involved during the naming process. Accordingly, overcoming the methodological limitation associated with analyzing neurophysiological measures during non-time-locked paradigms is a critical prerequisite.

## 1.2. The present study

Thus, this study aims to identify neurophysiological components elicited during the serial Rapid-Automatized Naming task that may differentiate between children with dyslexia and typically developing children (Question 1). We examine these neurophysiological components combining electroencephalography (EEG) and eye-tracking recordings under a set of phonological and visual confounding serial RAN tasks to address the limitations of prior research. Moreover, we examine which extracted neural components better predict overall RAN performance (Question 2).

To the best of our knowledge, this is the first study that integrates two modalities (i.e., EEG measures and eye-tracking) to explore the neurophysiological effects in children with varying reading ability during a serial RAN task. Importantly, our proposed analysis approach acts as a methodological model for the integrative analysis of neurophysiological and eye-gaze data to study cognitive processing in children under serial RAN, on which traditional ERP analysis would not be applicable.

## 2. Methods

### 2.1. Participants

The study's sample was recruited from Grades 3 and 6 from inner-city public elementary schools in Cyprus. Two groups were formed, a group of children with dyslexia (DYS) and a chronological-age control group (CAC) based on a stepwise group selection process, as described below.

*Step 1:* Because a formal diagnosis of dyslexia is rare in Cyprus, to identify the children with dyslexia, we first asked teachers to nominate children experiencing reading difficulties with no sensory, intellectual or attentional problems. After obtaining parental consent, nominated children were tested on reading fluency and general cognitive ability measures to ensure that they met the inclusionary criteria for reading difficulties, as described in the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 2013). Thirty children (19 males, 11 females; mean age = 9.6, SD = 1.5), who scored at least one standard deviation below their respective age group mean on the reading fluency tasks (word reading fluency and phonemic decoding fluency; ERS-AB; Papadopoulos et al., 2009b) and within the average range on verbal (Vocabulary Wechsler Intelligence Scale for Children—Third Edition, Wechsler, 1992; Greek standardization: Georgas et al., 1997) and non-verbal ability (Nonverbal Matrices from the DN-CAS, (Naglieri, and Das, 1997); Greek standardization: Papadopoulos et al., 2009b) met the inclusionary criteria and included in the group with dyslexia.

*Step 2:* A group of 30 chronological-age controls (CAC) were randomly chosen from the same classes (17 males, 13 females; mean age = 9.92 years, SD = 1.62). These participants performed within the average range on reading fluency and verbal and non-verbal ability tasks. The two groups differed in reading fluency measures, Wilks'  $\Lambda = .491$ ,  $F(2, 57) = 29.51$ ,  $p < .001$ ,  $\eta^2 = .51$ , but not in verbal and non-verbal ability measures, Wilks'  $\Lambda = 0.976$ ,  $F(2, 57) = 0.699$ , ns,  $\eta^2 = 0.02$ . They also differed in phonological awareness (Phoneme Elision; Papadopoulos et al., 2009c) and orthographic processing (Spelling Choice; Papadopoulos et al., 2009c) abilities, Wilks'  $\Lambda = 0.772$ ,  $F(2, 57) = 8.43$ ,  $p = .001$ ,  $\eta^2 = 0.23$ . We tested groups' performance on these skills since phonological and orthographical processing skills have been found to mediate RAN's effects on reading fluency (Papadopoulos et al., 2016) and are intrinsically linked to dyslexia (Papadopoulos et al., 2021, 2009a). Participants' characteristics are summarized in Table 1. All schools followed the same reading curriculum developed by the Ministry of Education Culture, Sport and Youth.

### 2.2. Statement of ethical considerations

The study was carried out per the Cyprus National Bioethics Committee recommendations (EEBK/EP/2011/10). It also received approval from the Ministry of Education and Culture, Cyprus (#7.15.01.27/17). Written Parental consent and school consent were obtained prior to each assessment.

**Table 1**  
Data on participants' ability and reading-related measures.

|                           | Groups |         |            |       |        |             | F     |     |
|---------------------------|--------|---------|------------|-------|--------|-------------|-------|-----|
|                           | DYS    |         |            | CAC   |        |             |       |     |
|                           | M      | (SD)    | R          | M     | (SD)   | R           |       |     |
| Verbal Ability            | 23.10  | (5.15)  | 14–33      | 24.33 | (5.24) | 17–35       | 0.85  |     |
| Nonverbal Ability         | 14.50  | (4.05)  | 10–23      | 14.20 | (3.89) | 7–21        | 0.09  |     |
| Word Reading Fluency      | 39.10  | (12.37) | 13–56      | 60.37 | (8.88) | 32–81       | 58.56 | *** |
| Phonemic Decoding Fluency | 24.00  | (7.25)  | 10–37      | 35.87 | (5.82) | 26–45       | 48.86 | *** |
| Phoneme Elision           | 12.18  | (2.23)  | 6.97–14.85 | 13.63 | (1.26) | 10.61–15.00 | 9.57  | *** |
| Spelling Choice           | 12.56  | (3.13)  | 7.20–18.40 | 15.44 | (2.58) | 10.20–19.20 | 15.13 | *** |

Notes: DYS: Group with dyslexia; CAC: Chronological-age controls; R: Range; M: Mean; SD: Standard Deviation; \*\*\*  $p < .001$ .

### 2.3. Measures and Selection Criteria

**Reading measures.** Participants' word reading skills were assessed with two measures from the standardized Early Reading Skills Assessment Battery (ERS-AB; Papadopoulos et al., 2009c), a word reading and phonemic decoding (nonword reading) tasks. ERS-AB includes several tasks to assess word reading, spelling, reading comprehension and related skills (e.g., phonological, naming) from age 5 through 18. The reported Cronbach's alpha for the word reading task in the standardization sample are 0.92 and 0.93 for grades 3 and 6, respectively. Participants were asked to read a list of words as accurately and quickly as possible in both tasks. Fluency scores (the number of words read correctly within 60 s) were recorded for each participant.

**Verbal ability measure.** The vocabulary subtest from the WISC-III (Wechsler, 1992) was used to assess participants' verbal ability. Georgas et al. (1997) reported Cronbach's alpha reliability coefficients were 0.81 in Grades 3 and 6.

**Non-verbal ability measure.** The Matrices task from the DN-Cognitive Assessment System was used to assess participants' non-verbal ability. Papadopoulos et al., 2009b reported Cronbach's alpha reliability coefficients were 0.73 and 0.78 for Grades 3 and 6, respectively.

**Phoneme Elision.** This task was used to assess participants' phonological skills at the phonemic sensitivity level. It comes from a standardized battery of phonological tasks (Papadopoulos et al., 2012, 2009c, 2009d). It includes 15 testing items and is discontinued after four consecutive mistakes. Participants were asked to repeat a word after deleting an identified phoneme. The targeted phonemes were either vowels or consonants, and their positions varied across items. After deleting the target phoneme, the remaining phonemes formed a word (e.g., Say the word  $\tau\acute{o}\rho\alpha$ ; [/ $to\alpha$ /; now], after deleting the sound  $/t/ \rightarrow \acute{o}\rho\alpha$ ; [/ $o\alpha$ /; time]). Participants' score was the total number of correct responses. Papadopoulos et al., 2009c reported Cronbach's alpha reliability coefficient to be 0.92 for both grades.

**Spelling Choice.** This task consisted of 20 items. Each target word was presented together with two homophonic distractors (e.g.,  $\kappa\alpha\lambda\eta\nu\acute{o}\chi\tau\alpha/\kappa\alpha\lambda\eta\nu\acute{\eta}\chi\tau\alpha/\kappa\alpha\lambda\eta\nu\acute{\iota}\chi\tau\alpha$ ; / $kalinihta$ /; goodnight). Participants had to use their orthographic knowledge to identify the word with the correct spelling among the three available options. Cronbach's alpha reliability coefficient in the standardization sample is 0.77 in Grade 3 and 0.82 in Grade 6 (Papadopoulos et al., 2009c).

### 2.4. Serial rapid naming speed (RAN)

We developed a computerized version of a rapid naming task to allow for simultaneous eye-tracking and EEG measurements' recording. This task was an adaptation of the work by Jones et al.

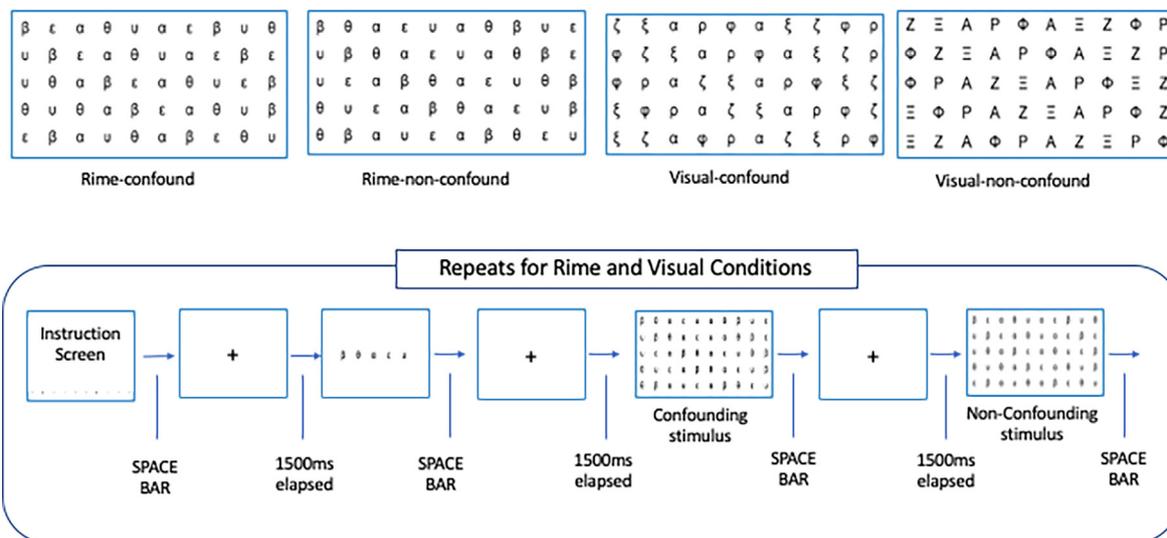
(2008). Our experiment manipulated whether the RAN array was either phonologically or visually challenging to process. Phonological manipulation involved naming eighteen pairs of letters, either *rime-confusable* (Condition 1) or *rime non-confusable* (Condition 2). *Rime-confusable* items were presented adjacently to promote confusability ( $\beta$ - $\theta$ ,  $\epsilon$ - $\upsilon$ ; beta-theta, epsilon-upsilon) or non-adjacently to minimize confusability ( $\beta$ - $\epsilon$ ,  $\theta$ - $\upsilon$ ; beta-epsilon, theta-upsilon). In turn, visual manipulation involved the naming of eighteen pairs of letters that were either visually confusable or visually non-confusable. Confusability, in this task, was manipulated by letters that are often confused by poor readers in Greek. Thus, *visual-confusable* letters (Condition 1) were presented in lower case ( $z$ - $\xi$ ,  $\rho$ - $\phi$ ; zeta-xi, rho-phi), while *visual non-confusable* items (Condition 2) included the same letters but in upper case ( $Z$ - $\Xi$ ,  $P$ - $\Phi$ ) to avoid visual similarity. In each letter set, a filler item  $/a/$  appeared ten times. Likewise, each of the four targets was used as a filler item (see Fig. 1). Thus, 45% of the consecutive letter-pairs introduced either a visual or phonological confusability in the stimuli in confusable tasks.

Participants were presented with the letter matrix organized in five rows and ten columns (total of 50 letters) in each condition. Participants' task was to name out loud each letter from left to right and from top to bottom as fast and as accurately as possible and press the SPACE bar once they read the last letter in each stimulus<sup>1</sup>. At the beginning of the experiment, an instruction screen was first shown to the participants stating the task's objective (i.e., reading all letters presented as fast and accurate as possible, press the SPACE bar to begin and once they read the last character). The experimenter triggered the onset of the block by pressing the SPACE bar after at the instruction screen. At the start of each trial, a centered fixation cross was presented on a gray background for 1500 ms before the letter-matrix stimulus replaced it. When participants read the last character on the stimuli and the experimenter pressed the SPACE bar that marked the trial's end, the next stimulus in the sequence appeared, and a TTL signal was sent (via a parallel port) to both recording devices to allow for EEG and eye-gaze signal synchronization. The paradigm was created and presented using Experiment Builder (SR Research, Kanata, ON, Canada). A schematic representation of the experimental paradigm and example stimuli is shown in Fig. 1.

### 2.5. Procedure

Participants were individually tested in a session lasting approximately 60 min. The tests' administration order was the same for all the participants. The reading, cognitive ability, phono-

<sup>1</sup> To ensure the timely transition between stimuli, the experimenter was monitoring the participants during the experiment and administered the pressing of the SPACE bar.



**Fig. 1.** Sample stimuli and schematic representation of the behavioral paradigm. In each task, participants are instructed to fixate on the center of the screen. They were subsequently presented the letter-matrix. First, a sample trial was presented to familiarize the participant with the specific task's stimulus. Then a full letter matrix was presented. Participants repeated these sequences for each of the four tasks (i.e., Rime-confound, Rime-non-confound, Visual-confound, Visual-non-confound).

logical awareness, and spelling choice tasks were administered first, followed by the RAN tasks. In the naming tasks, the administration of the non-confusable condition preceded the confusable condition. After the completion of each RAN task, the participant took a 1-minute break to control likely fatigue. At the beginning of each task, participants performed a practice trial to read a single line of characters that included the letters from the corresponding upcoming task. This was done to ensure that participants were familiar with the upcoming stimuli and could recognize the characters. After each practice trial, participants were exposed to the letter-matrix stimuli associated with the corresponding RAN tasks.

**2.5.1. Eye-tracking data acquisition and pre-processing**

Eye movement data were recorded using the EyeLink 1000 Plus eye-tracker (SR Research, Kanata, ON, Canada) at a 1000 Hz sampling rate. The stimuli were presented on a Dell Precision T5500 workstation with an ASUS VG-236 monitor (1920 × 1080, 120 Hz, 52 × 29 ch) at a viewing distance of 60 cm. To improve eye-gaze measurement stability, participants held their heads in a chin rest for the duration of the data collection session. A 9-point calibration routine was run at the beginning of the experiment. Before each task, a fixation cross was shown on the screen to ensure a common gaze onset. On-line detection and analysis of eye-motion events such as saccades and fixations were performed by the EyeLink Parser and were recorded along with raw gaze points. Markers indicating each trial's beginning and ending were recorded in the eye-gaze data file using Ethernet log messages to achieve event synchronization between the eye-gaze stream and the stimulus. Subsequent processing and analysis of the eye-tracking data were implemented using custom python and the pyGaze Analyzer library.

**2.5.2. EEG acquisition and pre-processing**

Continuous EEG data were collected using a BioSemi Active-two system (BioSemi, Amsterdam, Netherlands) at a sampling rate of 256 Hz. Participants were fitted with a standard 64-electrode cap following the international 10–20 system<sup>2</sup>. The preparation procedure took about 10 min for electrodes to be placed, and the DC offset

of all sensors was kept below 20 μV. EEG data were collected for the entire duration of the experiment.

All EEG data preprocessing was performed offline using custom python code and the MNE library<sup>3</sup>. As part of the preprocessing, a software-based 0.5 Hz high-pass filter was employed on the continuous EEG to remove DC drifts, and notch filters at 50 Hz and 100 Hz were used to minimize the power-line noise interference. Subsequently, four EEG sub-segments were extracted from the continuous EEG, one for each RAN task, spanning 2 seconds before the task's onset (i.e., the onset being the moment the letter-matrix appeared on the screen) until completing the corresponding RAN task (i.e., the SPACE BAR was pressed after participants read the last letter in the matrix). The baseline amplitude of each segment (i.e., from –2000 ms to 0 ms of task onset time) was removed from each segment in the EEG and channels were re-referenced to the average reference. The resulting EEG segments were further processed to generate the fixation-related potentials.

**2.5.3. Fixation related potential modeling**

As pointed out in the introduction, the serial RAN experiment design does not provide experimenter-controlled time-locked trials necessary to extract Event-Related Potentials (i.e., the stereotypical neural components from the EEG signals following a repeatable event). To overcome this inherent constrain of the paradigm (and allow the study of reading under realistic scenarios, like in natural reading), we explored the integration of eye-gaze measurements and EEG measurements to identify and isolate neural components that differentiate between the group with dyslexia and typically developing children. This section presents the methodology for calculating these components, referred to as Fixation Related Potentials (FRPs).

The eye-gaze measurements and pre-processed EEG data (see relevant sections above) data were used to estimate the FRPs. First, the fixation data were loaded from the eye-tracking recording files using custom python code and the pygaze analyzer library<sup>4</sup>. Eye-tracking data included accurate timestamps, raw gaze points, fixations, saccades and timestamped log messages for signal synchronization. Then, for each participant and each task, the set of all

<sup>2</sup> Head cap layout specification <https://www.biosemi.com/headcap.htm>

<sup>3</sup> MNE Python Library available at <https://mne.tools/stable/index.html>

<sup>4</sup> The library is available at <http://www.pygaze.org>

fixation onsets, fixation offsets and fixation duration were extracted, along with their respective timestamps relative to the task's onset. To ensure data quality, gaze points were visually inspected by overlaying them over the stimuli image. The set of all valid fixations (i.e., fixations that fall within the viewing area) from each participant and task served as time markers in the estimation of the fixation-related potential. We will refer to this set of fixations as *Fixation\_set(p,t)*, denoting the set of fixations from participant *p* and task *t*.

For each EEG segment *EEG(p,t)* (i.e., the EEG recording of a participant *p* during a specific task *t*), the trail-fixation set *Fixation\_set(p,t)* was used to extract epochs starting at each fixation's onset. In particular, epochs starting –200 ms before a fixation onset and 500 ms following the fixation onset were extracted (total epoch duration 700 ms). A low-pass filter at 30 Hz cut-off frequency was employed on each epoch. Also, the baseline average amplitude from –200 ms to 0 ms was subtracted from each epoch. To minimize the effect of muscle artifacts from participants' movement and rapid impedance changes on the calculation of the FRPs, channel-time pairs whose absolute amplitude exceeded the mean channel amplitude (i.e., mean across time) by two standard deviations, or whose absolute amplitude exceeded the mean amplitude across trials by more than 3 standard deviations were excluded from the subsequent calculation<sup>5</sup>. Subsequent mean calculations used the 'nanmean' function to ensure that the 'nan' values had no effect on the mean estimation. Finally, the average fixation relation potential *frp(p,t)* was calculated as the mean across all epochs in the fixation set. Thus, for every participant and every task, the preprocessing generates a fixation related potential *frp(p,t)* which represents multivariate time signals for each channel (i.e.,  $frp(p,t) \in \mathbb{R}^{D \times T}$ , where  $D = 64$  channels,  $T = 128$  time samples). A visual inspection of the resulting FRPs showcase similar stereotypical responses one typically sees in an Event-Related Potentials Experiment analysis. A visual illustration of the steps involved in calculating each *frp(p,t)* is shown in Fig. 2.

## 2.6. Statistical analysis

### 2.6.1. Cluster-based permutation test for comparing neural components between groups

To examine if neural activation in the Fixation Related Potentials differentiates between groups, we employed a cluster-based permutation statistical test (Maris and Oostenveld, 2007) on the resulting FRPs. In brief, the cluster-based permutation test (CPT) is a nonparametric statistical test that aims to find clusters of samples (i.e., connected subsets of EEG channels and time points) that are significantly different between groups or conditions. The test also accounts for the family-wise error due to multiple comparisons. In particular, CPT first identifies a set of channel-time pairs of interest by applying multiple univariate base tests (i.e., ANOVA or T-test) to quantify the effect at each sample. It then groups significantly different samples (i.e., channel-time pairs whose effect is above a threshold) in connected sets based on temporal and spatial adjacency. Maximally connected sets form the spatio-temporal clusters of interests, each comprising a subset of channels and time points. The CPT calculates the cluster-level statistic by aggregating the individual univariate-test statistic values of all (channel-time)-pairs that belong to that cluster. Finally, the CPT uses the Monte-Carlo approximation to calculate the significant probability of the reference distribution on the cluster-level statistic<sup>6</sup>.

<sup>5</sup> Channel-time pairs whose value exceeded the threshold were set to the value 'nan' in python (denoting non-a-number value)

<sup>6</sup> For more details on the cluster-based permutation test, we refer the interested reader to the work of Maris and Oostenveld (2007) and the implementation documentation in FieldTrip Toolbox [https://www.fieldtriptoolbox.org/tutorial/cluster\\_permutation\\_timelock/#structure-in-experiment-and-data](https://www.fieldtriptoolbox.org/tutorial/cluster_permutation_timelock/#structure-in-experiment-and-data).

In particular, in our study, we tested between-group differences with a cluster-based permutation test with a one-way ANOVA as the base test. The cluster statistic was the weighted sum of all nodes' statistical scores in a cluster. The electrode spatial neighborhood templates were defined using the automatic symmetric triangulation method on the 64 channel Biosemi electrode layout<sup>7</sup>. The temporal cluster connectivity parameter was set to 5. The time window for running the cluster permutation test was defined between 50 and 300 ms following the FRP's onset; this was done to allow sufficient time for the visual information to propagate to the visual cortex and for reading processes to be activated (Loberg et al., 2019). Statistical analysis was performed using custom scripts and the MNE library. The cluster-based permutation test was performed using the *spatio\_temporal\_cluster\_test* implemented in the MNE library, and the number of permutations was set to 30,000.

### 2.6.2. Regression model for exploratory FRP waveform analysis

We employed a univariate linear regression model to explore the relationship between neural activity within each significant spatial-temporal cluster and behavioral performance scores during serial RAN (i.e., Naming speed). We considered the mean amplitude of each FRP across the subset of channels and time samples associated with the identified spatio-temporal cluster (i.e., the significant clusters identified by the cluster-based permutation test) as the independent variable. We also considered the RAN performance scores (i.e., Naming speed, the time taken to complete the RAN task) as the dependent variable. Coefficients were estimated through a least-squares approach.

## 3. Results

### 3.1. Naming speed behavioral data analysis

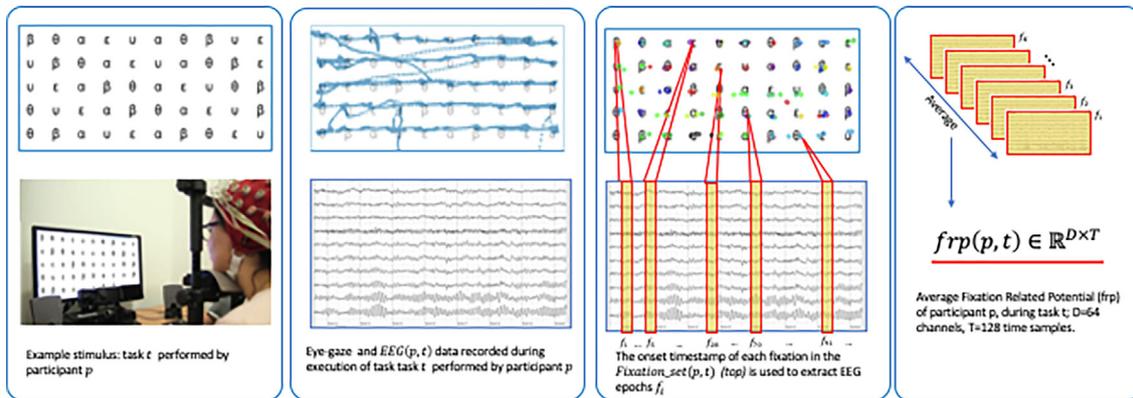
A MANOVA analysis, with the naming speed performance time for each of the 4 RAN tasks as dependent measures and Group (2) as a fixed factor, was performed. The main group effects was significant, Wilks'  $\Lambda = 0.754$ ,  $F(4,55) = 4.48$ ,  $p < .01$ ,  $\eta^2 = 0.20$ . Subsequent univariate analyses demonstrated that the group's main effect was significant for all individual measures after Bonferroni adjustments (Table 2). The DYS group performed significantly poorer than the chronological-age controls in all naming speed measures.

### 3.2. Comparing neural components between DYS and CAC

To examine differences between DYS and CAC groups' neural activation, we compared the amplitudes of FRPs of each group for each of the four experimental tasks (*Rime-confusable*, *Rime-non-confusable*, *Visual-confusable* and *Visual-non-confusable*) separately. A cluster-based permutation test revealed a significant difference between DYS and CAC groups during the *Rime-non-confusable* task. These differences were visible in a cluster that emerged around 128–270 ms in frontal channels ( $p < .01$ ). Cluster-based permutation test also revealed significant differences between the groups during the *Rime-confound* task; this was supported by a cluster that emerged in the occipital channels between 80–160 ms post-fixation onset ( $p < .05$ ). There were no significant differences between the groups under the *visual-confound* and *visual non-confound* tasks (ns). The average FRP across selected channels and the significant clusters' topology are illustrated in Fig. 3.

### 3.3. Exploratory FRP waveform analysis

<sup>7</sup> Biosemi layout used is available here <http://www.fieldtriptoolbox.org/template/neighbors/>.

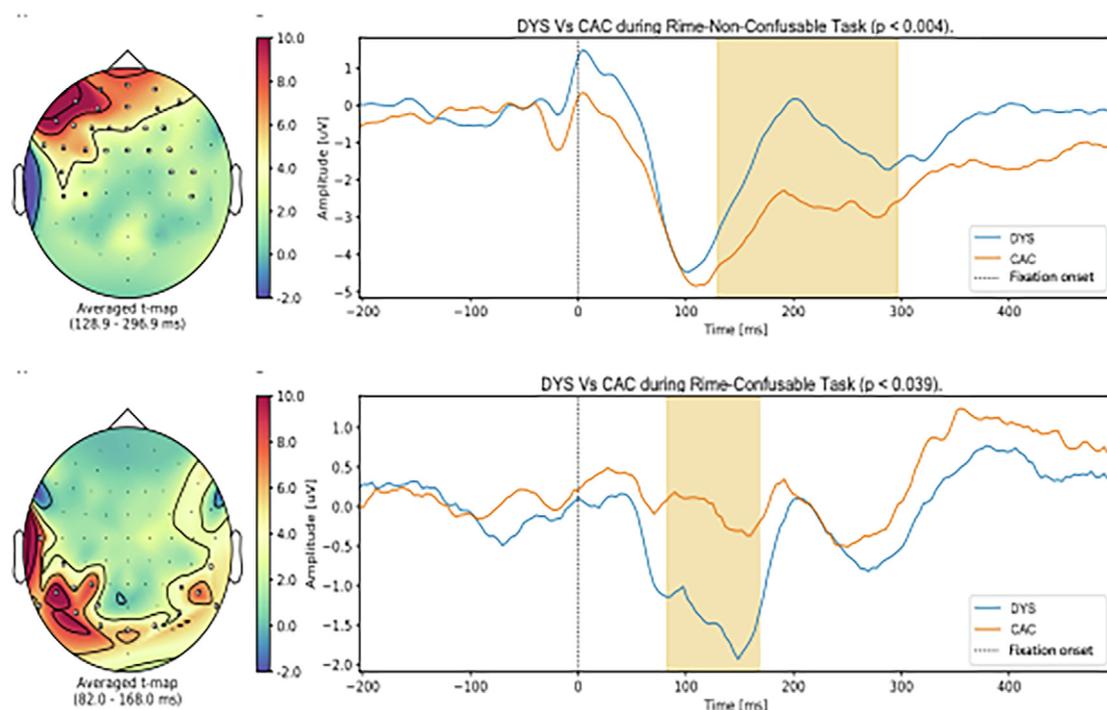


**Fig. 2.** Illustration of the steps involved in the calculation of fixation-related potentials. For each participant and task, EEG and eye-tracking data are collected. The timestamps of the onset of each fixation during the task are used to extract event-locked EEG epochs. FRPs (Fixation-Related Potentials) are calculated as the average across all event-locked EEG epochs of each task.

**Table 2**  
Naming Speed Analysis of Behavioral data.

|                       | Groups |         |       |        | F     |     |
|-----------------------|--------|---------|-------|--------|-------|-----|
|                       | DYS    |         | CAC   |        |       |     |
|                       | M      | (SD)    | M     | (SD)   |       |     |
| Rime confusable       | 40.08  | (10.89) | 34.14 | (6.79) | 6.44  | **  |
| Rime non-confusable   | 43.45  | (12.40) | 35.60 | (6.49) | 9.36  | **  |
| Visual confusable     | 56.85  | (13.53) | 44.41 | (9.97) | 16.43 | *** |
| Visual non-confusable | 49.35  | (11.60) | 39.13 | (7.70) | 16.17 | *** |

Note. **DYS:** Group with dyslexia; **CAC:** Chronological-age controls; **M:** Mean Naming speed (reported in seconds); **SD:** standard deviation; **\*\***  $p < .01$ ; **\*\*\***  $p < .001$ .



**Fig. 3.** Average FRP amplitude (group average; across channels in the selected significant cluster) over time for DYS and CAC, under rime-non-confusable (top row) and rime-confusable (bottom row) conditions. Circled electrodes in the topographic map identify the position of the channels in the selected cluster. The plot shows the average FRP amplitudes time response for each of the two groups. The dotted line indicates the fixation onset of the FRP. The shaded area identifies the time window the corresponding significant cluster appears ( $p < 0.05$ , permutation test). **Abbreviations:** **DYS,** Children with Dyslexia group; **CAC,** Chronological Age Control group; **FRP,** Fixation-Related Potentials.

We further explored the relationship between the mean amplitude of FRPs within the significant spatiotemporal clusters and the RAN behavioral performance (i.e., Naming speed, the time taken to

complete the RAN task) on the corresponding RAN condition. In the rime non-confound task, the regression analysis results showed that the average FRP amplitude significantly predicted RAN Nam-

ing speed in the corresponding task,  $b = 1.2724$ ,  $t(51) = 3.0$ ,  $p < .01$ . The average amplitude also explained 15% of the variance,  $R^2 = 0.152$ ,  $F(1,51) = 8.97$ ,  $p < .01$ . In the rime confound task, regression analysis showed that the average FRP amplitude within the corresponding spatiotemporal cluster significantly predicted RAN performance scores in the relevant task,  $b = -0.62$ ,  $t(50) = -2.68$ ,  $p < .01$ . The average amplitude also explained 13% of the variance  $R^2 = 0.13$ ,  $F(1,50) = 7.19$ ,  $p < .01$ .

#### 4. Discussion

This study examined the differences between children with dyslexia and their chronological-age controls on a serial RAN task, using a novel methodological approach that integrates neurophysiological and eye-gaze data (Fixation Related Potentials amplitudes-FRP). The study findings contribute to the relevant research because previous research has overlooked the contribution of neurophysiological measurements during serial RAN tasks and their relation to behavioural measures (i.e., Naming speed) that together might explain reading performance and related difficulties. We argued that the lack of studies in this direction resulted from the relative methodological difficulty in using neurophysiological techniques to investigate the neural components elicited during the serial RAN task. While behavioural measurements capture information at the output stage, they tend to ignore the internal cognitive stages at which the actual information processing occurs (e.g., Breznitz, 2003). Thus, the present results provide insights into the underlying cognitive processes involved in naming speed and identify at which time point and which neurocognitive processes differentiate between children with and without reading difficulties. In this study, we introduced an analytical framework that alleviates the methodological difficulties and enables the concurrent analysis of neurophysiological and eye-gaze data to decipher the role of RAN in serial paradigms. The results revealed significant differences between groups in FRP amplitudes. Importantly, these differences were observed during phonologically confusable and phonologically non-confusable RAN tasks. Also, a relation between the extracted neural components and behaviour measures of RAN naming speed was observed. We discuss these findings in detail next.

Regarding the first question of the study, namely, the contribution of neural components in differentiating between children with and without dyslexia, the results confirmed our hypothesis. We observed significant differences between groups in FRP amplitudes. Specifically, the group differences were visible in a cluster that emerged between 80 ms and 160 ms in temporal-occipital channels in the phonologically confusable condition. Given that the initial stages of reading correspond to specialized visual brain processes that occur within 200 ms of stimulus presentation in occipitotemporal regions (McCandliss et al., 2003), our findings suggest that the suggested methodological approach is appropriate in distinguishing poor readers from their typically developing counterparts from the early stages of the reading process. Readers in the control group seem to benefit from the optimal information transfer between the visual and language systems during access and retrieval of letter names in a serial RAN task (e.g., Georgiou et al., 2013) as it happens in visual word processing (Fáisca et al., 2019). As a result, they quickly named the array of letters.

In contrast, in the readers with dyslexia, the visual code's rapid mapping to its phonological equivalent is impaired. Such a result means that although children with reading difficulties form correct representations of the letters, they cannot access these patterns at an appropriate rate (see Papadopoulos et al., 2020, for a similar discussion). Recently, eye-movement studies have shown that, compared to normal readers, children and adults with dyslexia

process RAN stimuli one at a time and do not take as much advantage of parafoveal processing as good readers (e.g., Pan et al., 2013; Yan et al., 2013).

Our results also show that group differences were evident in the phonological but not in the RAN tasks' visual conditions. These findings support the assumption that phonological ability plays a significant role in the RAN-reading relationship. It may also be considered a universal cause of dyslexia, particularly in consistent orthographies (Parrila et al., 2020). Since the early '90s, many studies have revealed the detrimental effects of phonological ability deficits on reading development (e.g., Kairaluoma et al., 2013; Kirby et al., 2003; Melby-Lervåg et al., 2012). Based on these findings, the DYS group's difficulties in the RAN tasks' phonological conditions are likely to result from poor phonological ability.

Furthermore, our results showed that the children with dyslexia performed roughly the same as the control group in the RAN task's visual conditions. In Greek, the orthographic inconsistencies are found primarily in one direction, from phonemes to graphemes [i.e., the phoneme /i/ can be written in five different ways ( $\eta$ ,  $\iota$ ,  $\upsilon$ ,  $\epsilon\iota$  and  $\omicron\iota$ ), the phoneme /o/ in two different ways ( $\omega$  and  $\omicron$ ) and the phoneme /e/ in two different ways ( $\epsilon$  and  $\alpha\iota$ )] (e.g., Protopapas and Vlahou, 2009). As a result, both children with dyslexia and controls need prolonged times to access the letters' orthographic representations.

Regarding the second question of the study, namely, the relation between the extracted neural components and the RAN performance measures, the present findings showed that the average FRP amplitude in phonologically non-confusable task significantly predicted RAN naming speed. In terms of the eye movement parameters, longer fixation durations are associated with more effortful language processing (Engbert et al., 2005; Nuthmann and Henderson, 2012). Thus, FRP amplitudes in phonological conditions may be related to the effort to retrieve phonological representations or achieve a comparable degree of automaticity in this process. Furthermore, these findings fit nicely with empirical evidence from RAN component studies (e.g., Araújo et al., 2011; Georgiou et al., 2006; Georgiou et al., 2008b) in which variability in RAN total time was found to be associated more strongly with variability in pause time (the mean inter-stimulus intervals) than with variability in articulation time (the mean time to articulate the stimuli in a RAN array). The retrieval of the name of any given stimulus (and thus the speed of access to phonological information) is part of the pause time.

From a methodological perspective, this study's analytical approach constitutes a novel framework for the integrative analysis of neurophysiological and eye-gaze data in examining young readers' cognitive processes under serial RAN paradigms. Indeed, the analysis of continuous EEG measures obtained during serial tasks constitutes a challenge for traditional Event-Related Potential analysis methods. This led experimenters to modify or attenuate their experimental paradigms to fit the constraints of ERP analysis methods, resulting in paradigms that do not necessarily capture the same factors as the original experimental paradigm intended. For example, in their study, Bakos et al. (2020) chose to test a similar hypothesis using a discrete RAN version because "the implementation of the serial RAN task in combination with ERP measures poses severe difficulties" (p. 352). That is, although the authors recognized that the serial RAN is "more strongly associated with reading because it captures additional cognitive factors which are important to fluent reading" (p. 352), such as pre-processing of the following item during sequential processing, they did not use such a task.

The proposed framework overcomes those "severe difficulties" recognized in Bakos et al. (2020) and provides reading researchers with the tools to analyze and study neural correlates directly under the serial RAN. Thus, our approach is customized to fit the experimental paradigm's analysis requirements and not the other way

around (i.e., customizing the paradigm to comply with the restrictions of analysis methods). It helps, in turn, uncover the underlying processing explaining the RAN-reading relationship. Importantly, the approach proposed here could find applications in the study of other neurocognitive processes using neurophysiological data on serial experimental paradigms and in the absence of experimenter-controlled time-locked events necessary to extract ERPs. To the degree these findings are replicable, a future direction of the relevant research could address similar issues in different age groups and languages.

To conclude, the study examined the differences between children with dyslexia and their chronological age controls on a serial RAN task, using an innovative methodological approach that integrates neurophysiological and eye-gaze data. Our analysis identified neural components elicited during the unprompted serial RAN during phonological (confusable and non-confusable) conditions that differentiate the two groups of readers. Moreover, the resulting neural components are predictive of RAN naming speed measures and its components, associated with reading at various stages of children's development (e.g., Caravolas et al., 2013; Georgiou et al., 2014). Thus, the resulting neural components show promise to explain better the underlying neural factors that drive the RAN-reading relationship beyond the evidence available from separate imaging and electrophysiological measures to date.

### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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