Chapter

The Neurobiological Development of Reading Fluency

Bobbie Jean Koen

Abstract

This chapter offers an extensive review of current and foundational research literature on the neurodevelopment of dyslexia and reading fluency worldwide. The impact of different languages and their orthographies on the acquisition of phonological analysis and orthographical features by beginning readers is explored. Contributions from the Psycholinguistic Grain Size Theory and new assessments, i.e. rapid automatized naming, have focused and advanced the understanding of slow phonological and visual processing skills. Recently, the development of new definitions of fluency has led to a proposed continuum of automatized decoding and processing skills required for students of English. Computer technology has enhanced the use of visual hemisphere-specific stimulation to affect the neurodevelopment of efficient word retrieval pathways and to increase reading speed. Processes for subtyping students based on reading behaviors and then stimulating a particular hemisphere of the brain with the fast presentation of words and phrases have been found to change levels of activation in key brain locations and increase the fluent processing of connected text. Newer technologies such as diffusion tensor imaging, while somewhat suspect, may provide the evidence that ultimately will document the changes in communication between regions of interest regulating the automaticity of brain functions in reading.

Keywords: dyslexia, rapid automatized naming (RAN), phonological processing, visual processing, visual hemisphere-specific stimulation (VHSS), fluency

1. Introduction

The worldwide narrative around fluency has grown dramatically in the last 10 years. This surge in interest has been driven, perhaps, by new working definitions of fluency, and the growing realization that different languages pose variable challenges to students with dyslexia who exhibit problems with reading fluency. While analyzing their own language's nuances, researchers have inundated these students with behavioral measures of nonverbal and verbal intelligence, reading accuracy, phonological skill, spelling, orthographic patterns, short-term memory, vocabulary – receptive and expressive, visual information processing and memory, and speed of processing. Through these various behavioral assessments, the strengths and weaknesses of struggling readers of every language are quantified, modeled and correlated to describe the multitude of possible different literacy actions displayed.

It seems inevitable that some kind of labels would need to be created to identify these special readers. The dual route model of reading constitutes the background of dyslexia subtyping [1]. Its central axiom is that no single processing procedure produces the correct pronunciations of both nonwords or pseudo-words (e.g. slint) and exception or irregular words (e.g. pint) [2]. It is theorized that nonwords can only be correctly pronounced using the grapheme-phoneme correspondence rules, the "non-lexical" route; exception words require an additional procedure, the "lexical" route, because they cannot be pronounced by the rules and readers must use context to figure them out. In many studies, subjects are classified in terms of accuracy either as "phonological dyslexics" when pseudo-word reading ability is impaired but irregular word reading is spared, or as "surface dyslexics" when the reverse occurs- irregular word reading is compromised while pseudo-word reading is intact [3]. For example, in accuracy-based studies in Spanish, surface dyslexics were more frequent than phonological dyslexics [4]. However unlike English, most orthographies have highly regular grapheme-phoneme correspondences with relatively few "exception" words [5], so the applicability of the dual-route framework beyond English has been questioned [6]. More recently, researchers have focused on those children who display Single Deficits (phonological processing weakness) and those who have the dreaded Double Deficit or Double Dissociation (phonological processing and processing speed deficits) [7]. They have worked hard comparing disabled reading and cognitive skill performances with normal readers who are carefully matched by chronological age or reading level (reading age), who are younger, or who represent a different ethnicity. The subtyping, use of labels, and multi-control-group comparisons all serve to refine and focus the discussion of how these students learn to read fluently or not.

To a lesser extent, investigators have used neurobiological technology to explore various brain activations: post-mortem studies of brains of individuals with dyslexia [8], Magnetoencephalography (MEG) and Magnetic Source Imaging (MSI) to provide information both on the spatial localization and on the timing of neurophysiological processes [9], positron emission topography (PET) to examine differences in resting state blood flow in regions of interest in the brain [10], and computerized tomography (CT) and structural magnetic resonance imaging (MRI) to examine noninvasively structural brain differences [11]. Decreased activation in the left temporal–parietal cortex of adults with dyslexia was first found using functional magnetic resonance imaging (fMRI) by Constable et al. [12]. These technologies were developed and implemented in an effort to understand better the growth of the phonological and visual processing systems and verbal retrieval systems in beginning learners that for many readers seem automatic. The crucial issue is the reliability of the different sub-types, which differ according to the type of response taken into account (accuracy, speed, or both) and the type of orthography (opaque/transparent) being evaluated [13].

2. Considerations for expressions of dyslexia

It is clear that depending on what is emphasized in any given language (e.g. fluency in German; visual–spatial memory in Chinese; phonological skills in English), there will be somewhat different manifestations of dyslexia, as well as different predictors of reading failure. Cross-language studies highlight the importance, not only of regular language features, but also the influence of the writing system (orthography) on reading performance [14]. The type of orthography that the child is acquiring is a primary cultural factor that influences reading acquisition in both typical and atypical development [15]. It has been considered that the cognitive processes underpinning reading ability may be differently involved in producing the symptoms of Developmental Dyslexia, depending on orthographic transparency [16]. Generally, languages that are considered more transparent with regular orthographies are Spanish, German, Finnish, Dutch, Greek, Italian and Hebrew, while English and French are considered less regular and therefore, more opaque.

A particularly challenging example is found in the standard Arabic language. Most Arabic words are morphologically derived from roots and written Arabic uses three basic diacritical marks corresponding to short vowels. Arabic script is also made with different degrees of internal connectivity or ligation between the letters within a word. In Algeria, standard Arabic is the first written language taught in the first 3 years of schooling, and there is a transition from vowelized to un-vowelized forms of reading starting from the third grade. Although the vowelized form of Arabic is highly transparent, the non-vowelized form is rather opaque [13]. Clearly, even though the language itself is fairly regular, the features of orthography present unique difficulties to students.

A central hypothesis in the area of reading accuracy and speed across orthographies is the Psycholinguistic Grain Size Theory of reading. This idea suggests that differences in reading accuracy and speed across orthographies reflect basic differences in the nature of the phonological recoding and reading strategies [17]. Learning to read in orthographically inconsistent languages cannot rely on letter to sound correspondences (small grain size), forcing the reader to develop flexible unit size recoding strategies, such as morphological units, analogy and whole-word recognition. It would follow that these processing differences would also reflect variable activations in key processing areas in the brain. This theory would seem to impact the less regular features of a language and, particularly, languages such as English and French that are highly irregular and opaque.

Another important idea in this field is the growing body of work demonstrating the predictive ability of "rapid automatized naming" or RAN tasks [18] in reading performance. Several researchers have used these tasks where children are presented with separate arrays of different primary colors, common objects, numerals from 0 to 9, and/or single letters, and are timed while they name the stimuli as quickly as they can. It has been claimed that RAN, and in particular, the RAN alphanumeric component (digit naming and letter naming), is associated with reading success [19]. A predominate and somewhat controversial view is that reading and RAN could be linked together through the general phonological processing system because they both tap the speed of accessing phonological representations in long-term memory [20]. However, some studies suggest that RAN is independent of phonological processing and can, itself, account for variance in reading. This implies that a naming deficit is directly related to orthographic processing- if letters are recognized at a slower rate, letter representations of words are not activated with sufficient speed to create a strong trace of common orthographic features [21]. Further support for this view is found in research that confirms that later in reading skill development, the role of non-alphanumeric RAN diminishes, while that of alphanumeric RAN (letters and digits) increases and becomes the sole predictor of reading at this stage [22]. From a global perspective, this naming speed deficit seems to be more prominent than the phonological deficit, and this appears to be true in both transparent orthographies like Spanish, Finnish, and German, as well as in entirely different and diverse orthographies, such as Hebrew, Chinese, and Japanese [23].

3. A review of international studies and phonological processing/speed

International researchers have investigated many of the most important factors identified in fluent reading. In Dutch, Vaessen and Blomert found that RAN contributed uniquely and substantially to the development of word reading fluency from grade 1 to grade 6 in primary school students [24], and when both accuracy and speed measures were considered in French, readers with dyslexia displayed deficiency in word-level reading skills [25]. A similar speed deficit of lexical and sub-lexical reading was also suggested by findings in French dyslexic children. The suggestion here being that the sub-lexical route shares with the lexical one the initial processing of the letter string, but then the lexical processing applies grapheme-phoneme rules in a serial mode [26]. This deficiency in sub-lexical processing is also a crucial feature in American dyslexic definitions and treatment, a language system known for its irregular words and "exceptions to the rule".

Researchers have proposed that between English and German dyslexic children with the same underlying phonological processing deficit, the English children show more severe reading impairment because of differences in orthographic consistency [27]. Mann and Wimmer [28] assessed readers in English and German at the end of kindergarten, and regression analyses showed that the only significant predictor of reading accuracy and speed in English was phonological awareness. Initial studies in German children found few problems with accuracy after the first year of instruction in contrast to English-based research and led to a German-English dyslexia comparison [27]. However, the reading fluency deficit of German dyslexic readers (found for all types of reading tasks) was found to be highly persistent [29] and hard to remediate [30].

Extensive research with German and Italian dyslexic children found reduced reading fluency as the main dyslexic impairment [6, 31]. Impairment on tasks that require implicit phonological processing, such as those evaluating verbal short-term memory, has been identified most clearly in transparent orthographies such as Italian and German [32]. Italian is a relatively shallow orthography, characterized by a high consistency of grapheme-phoneme correspondences and a simple syllabic structure. Also there are few irregular words and non-homographic homophones [15]. In spite of this regular orthography, Italian children with Developmental Dyslexia still present with a relevant difficulty which is primarily a deficit in reading speed [33] markedly affected by stimulus length [34]. Tobia and Marzocchi worked to define the cognitive profile of Italian children with Developmental Dyslexia. They found that 43.7% of children with DD had a profile that included deficits in both verbal and nonverbal domains. Some measures (visual search, syllable blending, and syllable deletion) were not significantly different among the three groups: dyslexic children, typically developing children of the same age (CA) and a control group of younger children equated for reading ability. Phoneme blending was the only variable that showed a large effect size [35].

The viability of accuracy/fluency-based typology of reading impairments has been investigated in Hebrew by Shany and Share [2]. Using a full battery of behavioral assessments including "pointed texts" (with all diacritical vowel markings included) and "unpointed texts" (with partial vowel markings included), these researchers found clear processing differences between the performances of students identified as rate-disabled and those identified as accuracy-disabled. Especially for word reading, the doubly-disabled subgroup of students was the most severely incapacitated with the lowest accuracy and reading rates.

The Korean handwriting system is an "alpha-syllabic" orthography, called Hangul. There are 24 graphemes, 14 are consonants and 10 are basic vowels. Hangul graphemes consistently represent sounds with a one-to-one correspondence and are combined in a limited number of patterns [36]. In a study using Hangul, researchers investigated the association of RAN and regular/irregular words in 4- and 5-year-old Korean children and found that RAN was uniquely associated with reading ability of both regular and irregular words [37]. Other research examined the cognitive abilities that predict reading and spelling performance in Korean children in Grades 1–4. Park and Uno [36] found that the contribution of phonological awareness to Hangul reading accuracy appears to occur only during the first 2 years of schooling, and RAN speed significantly predicted word-reading accuracy only in Grade 1. Further, the results of path analysis revealed that receptive vocabulary contributed exclusively and substantially to Hangul word-reading accuracy in Grades 1–4. This is unusual in light of the accepted idea that vocabulary plays a more important role in reading in less consistent orthographies [17]. Park and Uno argue that these results may be due to characteristics of the Hangul writing system that support the decoding of two-syllable words based on partial decoding and knowledge of the phonological and lexical aspects of a known, corresponding spoken word. In this case, the strategies needed to read accurately and with speed in Hangul differ with expertise and reading experience. A recent cross-language investigation measured reading performance (both reading accuracy and fluency), phonological short-term memory, RAN, receptive vocabulary and non-verbal intelligence in grade 2 children in five European countries (Finland, France, Hungary, Netherlands, and Portugal). While it is often proposed that extensive familiarity with the words of a language affects reading performance, the results here suggest that vocabulary was not a unique predictor of reading accuracy and fluency in these languages, except for Finnish [38].

In conclusion, phonological awareness represents the main predictive factor in normal and disabled readers of different languages. However, it may be less relevant in consistent orthographies, especially for reading accuracy where language –specific patterns appear to exist [39]. Research in German [40], Dutch [41], Norwegian [42], Italian [33], Greek [43], Finnish [44], Hungarian [45], and Hebrew [46], shows that most dyslexics in these languages attain high levels of reading accuracy but remain slow. It is possible that orthographies that are relatively regular in their letter-sound correspondences such as the Arabic require rapid development of the "direct access route". Perhaps it is only with increasing practice that improvements in efficiency lead to the reliable use of "direct access processes". Consequently, it is unclear whether the sub-lexical route accesses semantics after the phonology is assembled, and it is still debated whether direct visual access can occur without phonological mediation [47]. See **Table 1** for a time-ordered summary of the international studies cited regarding phonological processing.

Researchers	National origin of subjects	Year	Subjects- age or grade	Major findings
Wimmer	Germany	1993	Grades 2, 3, 4	German dyslexics attain high levels of reading accuracy but remain slow in processing speed.
Yap, Van der Leij	Netherlands	1993	Mean age: 10.2 years	Dutch dyslexics attain high levels of reading accuracy but remain slow in processing speed.
Bjaalid, Hoien, Lundberg	Norway	1996	Grade 3	Norwegian dyslexics attain high levels of reading accuracy but remain slow in processing speed.
Breznitz	Israel	1997	Normal mean age: 6.9 years; Dyslexic: 9.1 years	Hebrew dyslexics attain high levels of reading accuracy but remain slow in processing speed.
Landerl, Wimmer, Frith	Germany, England	1997	8 year olds	English children seem more impaired because of orthographic differences; German children had few problems with accuracy after the first year of instruction.

Researchers	National origin of subjects	Year	Subjects- age or grade	Major findings
Wimmer, Mayringer, Landerl	Germany, Italy	1998	Beginning Gr. 1 and End Gr. 2	Impairment on verbal short-term memory has been identified most clearly in transparent orthographies.
Porpodas	Greece	1999	Grade 1	Greek dyslexics attain high levels of reading accuracy but remain slow in processing speed.
Zoccolotti, De Luca, Di Pace, Judica, Orlandi, et al.	Italy	1999	11–15 years old	Italian children with DD demonstrate primarily a deficit in reading speed.
De Luca, Borrelli, Judica, Spinelli, Zoccolotti	Germany, Italy	2002	11–16 years old	Reduced reading fluency is the main impairment in German and Italian dyslexic children.
Mann, Wimmer	Germany, England	2002	End of Kindergarten	Phonological awareness was the only significant predictor of reading accuracy and speed in English students.
Hutzler, Wimmer	Germany, Italy	2004	13 yr. olds	Reduced reading fluency is the main impairment in German and Italian dyslexic children.
Thaler, Ebner, Wimmer, Landerl	Germany	2004	8–11 years old	Reading fluency deficit in German Dyslexic readers is hard to remediate.
Zoccolotti, De Luca, Di Pace, Gasperini, Judica, et al.	Italy	2005	Grades 1, 2, 3	Reading speed deficits in Italian children with DD are markedly affected by stimulus length.
Puolakanaho, Ahonen, Aro, Eklund, Leppanen, et al.	Finland	2007	3.5, 4.5, and 5.5 years old	Finnish dyslexics attain high levels of reading accuracy but remain slow in processing speed.
Cho, Mcbride-Chang, Park	Korea	2008	4 and 5 yr. olds	RAN was uniquely associated with reading ability of both regular and irregular words.
Georgiou, Parrila, Papadopoulos		2008	Grades 1 and 2	Phonological awareness may be less relevant in consistent orthographies.
Landerl, Wimmer	Germany	2008	Gr. 1, 4, 8	Reading fluency deficit in German dyslexic readers is highly persistent.
Vaessen, Blomert	Netherlands	2010	Grade 1–6	RAN contributed uniquely and substantially to word reading fluency.
Ziegler, Bertrand, Tóth, Csépe, Reis, et al.	Finland, France, Hungary, Portugal, Netherlands	2010	Grade 2	Vocabulary was not a significant predictor of reading accuracy and fluency in these languages, except for Finnish.

Researchers	National origin of subjects	Year	Subjects- age or grade	Major findings
Shany, Share	Israel	2011	Grades 2, 4, 6	There are processing differences between rate-disabled and accuracy-disabled readers; the doubly-disabled readers had the lowest accuracy and reading rates.
Sprenger-Charolles	France, Spain, England	2011	7 yr. olds	French dyslexics were weak in word reading when both accuracy and speed were measured.
Csépe, Honbolygó, Paavo, Leppänen	Hungary	2012	Grades 2–4	Hungarian dyslexics attain high levels of reading accuracy but remain slow in processing speed.
Tobia, Marzocchi	Italy	2014	DD grp. Mean age: 9.76 years; Control grp. 9.82 years; RA grp. 7.38 years	Results show that 43.7% of Italian children with DD showed deficits in both verbal and nonverbal domains; phoneme blending was the only variable that predicted reading disability.
Park, Uno	Korea	2015	Grades 1–4	RAN speed significantly predicted word-reading accuracy only in Grade 1; receptive vocabulary contributed exclusively and significantly to word reading accuracy.

Table 1.
International studies of phonological processing in time order.

4. A review of international studies and visual processing

An interesting element of learning to read in a regular orthography is the relative ease of attaining high levels of accuracy. Correct reading in transparent orthographies is already at ceiling level after the first year of formal instruction [5, 17]. The advantage of regular orthography was further documented in studies comparing a substantial number of regular European writing systems with English [5, 48]. Due to the transparency of the language system, visual processing deficits are often found to contribute to dyslexia. In a Norwegian study, Talcott et al. demonstrated the presence of visual processing deficits characteristic of poor readers in a sample of poor readers [49]. Finnish is one of the most regular alphabetic orthographies and dyslexia primarily means slow dysfluent reading, however a major dysfunction of the occipito-temporal reading circuit is suggested by a series of MEG studies with Finnish dyslexic adults [50]. A dysfunction of left occipito-temporal reading areas was also found in the cross-linguistic PET study by Paulesu et al. [51] which included dyslexic adult readers from the regular Italian orthography and from less regular orthographies of French and English. There is also a good deal of evidence that children with Developmental Dyslexia also experience difficulties in visuo-attentional tasks [52], such as visual search [53], visual recognition [54], and low-level (occurring within the first 300 milliseconds of visual analysis) visual information processing [55]. Thai researchers examined the performance of good and poor 10 year-old Thai readers on visual processing and reading accuracy tests and found a difference between the good and poor Thai readers in their performance on visual processing tests [56].

Schiff et al., [57] examined the effects of orthographic transparency on the reading ability of fourth-grade children with dyslexia on two Hebrew scripts. In addition to documenting reading accuracy and speed, this study also investigated the role of vowelization in the reading ability of un-vowelized script among readers with dyslexia. These results showed that fourth-grade children with dyslexia read the vowelized script with less accuracy than that found in typically developing second-graders. Also, the children with dyslexia demonstrated no significant differences in the reading accuracy or speed between the vowelized and unvowelized scripts. However, for these readers with dyslexia, accuracy in reading both vowelized and un-vowelized words mediated the reading speed of un-vowelized scripts. These findings underscore the idea that if grapheme-phoneme conversion skills are flawed in Hebrew children with dyslexia, they are unable to use the vowelized script as a self-teaching mechanism for acquiring an autonomous orthographic lexicon that would enable future word recognition.

The hypothesis of poor phonological-orthographic integration suggests impaired neural connectivity between regions engaged by orthographic processes and regions engaged in phonological processes [58]. There are first reports suggesting abnormalities of the left-hemisphere tracts that connect occipito-temporal brain regions engaged by visual-orthographic processes with temporo-parietal and the left inferior frontal areas engaged by phonological processes [59]. Functional imaging findings- some with German dyslexic readers -show reduced reading related activation in a left ventral occipito-temporal brain region, which is assumed to function as an interface between high-level visual orthographic codes and phonology and meaning. As expected, dysfluent readers exhibited underactivation of the left occipito-temporal region of interest-ROI (engaged by fast word processing) and increased activation of the left inferior frontal ROI (engaged by phonological decoding) [60]. Voxel-based analysis showed that for fluent readers, extended activations were found in the left temporal cortex mainly along the superior temporal sulcus and in left inferior frontal and precentral regions. The left temporal activation extended into the supramarginal gyrus and inferior occipito-temporal cortex. More issues regarding neural connectivity will be investigated in depth later.

A fascinating example of an opaque and complex orthographic system used in India is found in the Urdu language system. There are 38 letters with no vowel letters, and diacritics, which serve as vowel markings in its script, are omitted. The graphemic system called Nastaliq is cursive, and is characterized by many to one mappings between graphic symbols and sounds. Further, the same letter is written differently in different positions in a word, [61] greatly increasing the possible variations of each letter. Most Indian children speak Punjabi as their first language, but Urdu is the national language and the language of the media. It is the medium of instruction at schools, and another first language for some children, depending on the social class. In all Pakistani schools, English is taught and evaluated as a compulsory subject from grade 1, but in Urdu medium schools, all subjects are taught in Urdu, and English is taught as a subject, and in English medium schools, all subjects are taught in English, and Urdu is taught as a subject. There are clearly differences in the instruction and informal practice of reading and writing the Urdu language in different settings. For both the control group and the reading disability group, both RAN letters and RAN digits significantly predicted fluency with RAN letters being the stronger predictor. For the control group, non-word reading was the most significant predictor of accuracy and RAN letters was the other significant predictor. For the reading disability group, only RAN letters predicted accuracy [61]. So even in a visually complicated, reading-in-a-second (or third) language, rapid naming is shown to be an important predictor of reading accuracy. However, the most compelling issue regarding fluency around the world may be that in spite of different orthographies and language regularities, commonly-used instructional interventions still do not result in lasting remediation for the majority of this population. See **Table 2** for a time-ordered summary of the international studies cited regarding orthographic processing.

Researchers	National origin of subjects	Year	Subjects	Major Findings
Slaghuis, Lovegrove	Australia	1987	13 year olds	Children with DD show difficulties with low-level visual information processing.
Eden, Vanmeter, Rumsey, Maisog, Woods, et al.	United States	1996	Adult men	Men with DD show difficulties with visuo-attentional tasks.
Paulesu, Demonet, Fazio, Mccrory, Chanoine, et al.	England, France, Italy	2001	Dyslexic adults	In a cross-linguistic PET study, a dysfunction of left occipito-temporal reading areas was found.
Seymour, Aro, Erskine	Denmark, England, Finland, France, Germany, Greece, Iceland, Italy, Netherlands, Norway, Portugal, Spain, Sweden	2003	6, 7, 8, yr. olds	Reading accuracy in transparent orthographies is at ceiling level after the first year of instruction.
Talcott, Gram, van Ingelghem, Witton, Stein, et al.	Norway	2003	12, 13, 14 yr. olds	Visual processing deficits were characteristic of poor readers.
Kim, Davis, Burnham, Luksaneeyanawin	Thailand	2004	10-year old children	There is a difference in good and poor Thai readers in their performance on visual processing tests.
Salmelin, Helenius	Finland	2004	Dyslexic adults	MEG studies reveal a major dysfunction of the occipito-temporal reading circuit
Deutsch, Dougherty, Bammer, Siok, Gabrieli, et al.	United States	2005	7–13 year olds	First reports suggesting abnormalities of the left-hemisphere tracts that connect occipito-temporal brain regions with temporo-parietal and left inferior frontal areas.
Kronbichler, Hutzler, Staffen, Mair, Ladurner, et al.	Germany	2006	14–16 year olds	Dysfluent readers showed underactivation of the left occipito-temporal region and increased activation in a left inferior frontal region.
Geiger, Cattaneo, Galli, Pozzoli, Lorusso, et al.	Italy	2008	9–13 year olds	Children with DD show difficulties with visual recognition.
Vidyasagar, Pammer	Australia	2010	7–12 year olds	Children with DD show difficulties with visual search.
Schiff, Katzir, Shoshan	Israel	2013	Grade 4	There were no significant differences in reading accuracy or speed in dyslexic readers regardless of the text (vowelized or un-vowelized).

Table 2.
International studies of orthographic processing in time order.

5. The development of fluency in English

The American focus on the development of reading proficiency has been far-ranging and often perplexing, perhaps due to the intricacies of the English language. It has been considered that the cognitive processes underpinning reading ability may be differently involved in producing the symptoms of Developmental Dyslexia, depending on orthographic transparency [29]. Converging data from a variety of neurobiological investigations, but especially from functional magnetic resonance imaging, support the current belief that there are differences in the temporo-parieto-occipital brain regions between dyslexic and nonimpaired readers. Goswami [62] found that analysis of results from different technologies, including PET, fMRI, MEG, and EEG using different research questions, consistently show that children with Developmental Dyslexia display hypoactivation of crucial parts of the network of areas involved in word recognition and an atypical pattern of continuing right hemisphere involvement.

The neurobiological origins of fluency can actually be seen in the early work of physiologist, Donald Hebb. In 1950, he proposed the concept of unitization when he observed patterns of cells in the visual cortex activating together after multiple exposures to novel visual stimuli [63]. LaBerge and Samuels went on to apply this idea to more complex visual levels such as familiar letter patterns, and in other modalities such as phonological representations. They focused on the automaticity of processing that decreases response time in learning and reading and is believed to increase the neurological resources allocated to comprehension [64]. American educators have historically used fluency as a measure of reading performance and a precursor of superior comprehension, but continue to fail in developing instructional exercises that improve reading speed, especially for those with specific reading disabilities. The expectation is that students will read fluently as a function of age and experience. Oral reading inventories and running records of reading performance commonly measure fluency as the rate and accuracy of oral reading and ignore the other aspects of fluency, particularly the contributions of lower level subskills: graphological features of letters, orthographic regularities of letter combinations, the semantic features of words, and the semantic-syntactic constraints of word sequences.

Ultimately, Kame'enui, Simmons, Good, and Harn suggested a developmental conceptualization of fluency that included the building of proficiency in foundational component skills of reading, effectively merging the influences of skill development with processing speed and accuracy into a continuum of reading proficiency [65]. It is this continuum that Wolf and Katzir-Cohen refer to in their comprehensive definition of fluency:

"In its beginnings, reading fluency is the product of the initial development of accuracy and the subsequent development of automaticity in underlying sublexical process, lexical processes, and their integration in single-word reading and connected text. These include perceptual, phonological, orthographic, and morphological processes at the letter, letter-pattern, and word levels, as well as semantic and syntactic processes at the word level and the connected text level. After it is fully developed, reading fluency refers to a level of accuracy and rate where decoding is relatively effortless; where oral reading is smooth and accurate with correct prosody; and where attention can be allocated to comprehension." [66]

Since the development of fluency is founded in every process and skill used in reading, Kame'enui [67] advises that it also requires an increase in proficiency and speed in every underlying component. It seems obvious that failure to acquire these processes and skills would result in critical and persistent reading disabilities.

Researchers have been diligent to identify the progressive neurodevelopment of those underlying processes. It is clear that Frith's 1997 phonological deficit hypothesis which suggests that Developmental Dyslexia results from an underlying phonological impairment, and accounts for a wide range of behavioral symptoms associated with dyslexia, especially lexical retrieval and verbal short-term memory, has been thoroughly validated [68].

Further, the issue of general intellectual ability has been explored with regard to phonological processing. Although the 2004 reauthorization of the U.S.'s Individuals with Disabilities Act mandates that states can no longer require school districts to use IQ tests to identify individuals with learning disabilities [69], the majority of schools and school psychologists still rely on the discrepancy between reading achievement and IQ to define dyslexia [70]: requiring that reading skill should be significantly below the level expected given an individual's IQ. Tanaka et al. used fMRI, univariate, and multivariate pattern analysis to observe whether differences in brain activation during phonological processing that are characteristic of readers with dyslexia were the same or different in dyslexic children with poor reading ability who had high IQ scores (discrepant readers) and in dyslexic children with poor reading ability who had low IQ scores (non-discrepant readers) as compared to the phonological processing of typically developing readers [71]. The results show that discrepant and non-discrepant poor readers exhibited similar patterns of reduced activation in brain areas such as left parieto-temporal and occipito-temporal regions; there were no reliable functional brain differences between the two types of poor readers. The validity of the discrepancy definition of dyslexia is called into question. Even though the discrepancy criterion may be intuitively appealing, its strict application would deprive non-discrepant children of the educational interventions that could promote their advancement in reading.

American researchers have also found distinctions in the use of RAN for identifying impaired processing. Using multi-variant analysis of the results of a battery of reading skills measures of 123 dyslexic 2nd and 3rd graders, Katzir et al. found that rapid naming, orthographic pattern recognition, and word reading fluency moderately predicted rate, accuracy, and comprehension of connected-text reading, while phonological awareness contributed only to the comprehension dimension of connected-text reading [72]. The unanticipated result that rapid naming was more related to reading speed than phonological awareness may help explain the limited success of phonology-based reading intervention programs for achieving improvements in fluency and comprehension.

6. Intervention studies impacting English

Researchers in the U.S. have also investigated the effects of focused instruction and other interventions. Several post-intervention studies show different patterns of activation in the reading networks, evidence of the strength of experimental results in suggesting effective neurobiologically-based remedial instructional practices. Shaywitz et al. found increased LH activation of the inferior frontal gyrus (IFG) and the middle temporal gyrus only in children with the characteristics of dyslexia who participated in daily tutoring of the alphabetic principle and phonological processing and not in those children who participated in a variety of common reading interventions exclusive of explicit phonology [73]. Their longitudinal data also indicated a continuation of correct activation patterns 1 year past, suggesting the durable nature of the processing change. Similarly, Simos, Breier, Fletcher, Bergman, and Papanicolaou using MSI found that after 80 hours of intensive phonological intervention, dyslexic children showed a dramatic increase in the activation of left temporo-parietal regions, predominately in the left posterior superior temporal gyrus (STG), the network that supports grapheme-phoneme recoding in typical developing readers. However, even after intervention, neural activity was delayed in the dyslexic children relative to the controls (837 ms on average for dyslexics and 600 ms for controls), indicating that even with intensive phonological remediation, dyslexic children are slower to achieve the same reading fluency shown by non-dyslexic children. Further, high-risk children, who were nonresponsive to the phonological remediation package that was being offered, were distinct in showing earlier onset of activity in IFG compared to the temporo-parietal regions [74]. This would indicate a persistent processing anomaly that influences ineffective decoding as well as decreased processing speed.

However, it is the work of Dutch and Italian researchers that provided the foundation for a fluency intervention that appears to address the processing anomalies that are prevalent in American dyslexics. Employing the commonly accepted differences in the hemispheric contributions in learning to read, Bakker and Vinke identified Dutch children with dyslexia as L-dyslexics or P-dyslexics based on oral reading error analysis, the distribution of brain responses, and other behavioral measures [75]. They proposed that L-dyslexics are insensitive to the perceptual features of text because they predominately developed left hemisphere strategies from the very onset of learning to read. Behaviorally, L-dyslexics exhibit a hurried and inaccurate style of reading with many word substitution errors. Conversely, P-dyslexics are overly sensitive to perceptual features of the text because they began the learning-to-read process in the right hemisphere, but never advanced from there. These P-dyslexics read slowly with a fragmented style. Bakker and Vinke hypothesized that since L-type dyslexics had trouble using right hemispheric strategies during reading, they might profit from specific stimulation of the right hemisphere and the opposite for P-dyslexics: they had not naturally shifted to left hemisphere processing and so would benefit from specific stimulation of the left hemisphere [75].

As a general rule, specific stimulation of a hemisphere (HSS) can be achieved by the lateral presentation of a stimulus (reading material) in the left visual field or to the fingers of the left hand in L-dyslexics, and in the right visual field or to the fingers of the right hand in P-dyslexics. Bakker and Vinke actually treated the children with a wooden tactile training box, in which the child would place their target arm through a hole in the side and manipulate plastic letters in grooves out of sight. L-type children were given regularly-formed concrete words to configure and trace with their left hand, to stimulate the right hemisphere. P-type children were given difficult-to-visualize abstract words to configure and trace with their right hand, to stimulate the left hemisphere. The results indicated that P-dyslexics showed a decrease in sound/symbol errors on both word and text reading, while L-dyslexics decreased substantive errors only on text reading [75]. In spite of several limitations in their methodology and intervention, the positive effects of even motor stimulation to the less activated hemisphere on reading performance are encouraging. Further, these findings imply that the dyslexia sub-typing procedures appear to be valid techniques for matching reading interventions to brain processing systems.

Based on the potency of these theoretical and neurobiological foundations, Lorusso, Facoetti, Paganoni, Pezzani, and Molteni achieved much stronger results in a study of Italian impaired readers employing computer technology. These researchers implemented the sub-typing of dyslexic students used by Bakker and Vinke, and added M- type dyslexia: a mixed type demonstrating both slow and inaccurate reading, indicating impaired processing in both hemispheres [76]. Their new technology included a modified version of a computerized system for visual hemisphere-specific stimulation (VHSS), "FlashWord" [77]. After 1440 minutes (24 h) of intervention, Lorusso et al. applied only behavioral measures and found that all students with the characteristics of dyslexia, regardless of their sub-type, improved not only in accuracy and fluency as compared to non-impaired controls, but also showed gains in spelling, memory, and general processing speed. Further, the dyslexic students gained 0.33 syllables / second more in reading speed over the same period of time than their non-impaired controls [76]. These extraordinary results suggest that requiring very fast processing of the presented visual stimuli in a targeted brain hemisphere may produce a greater degree of automatisation of the component processes. It is this automatisation of the underlying lexical and sublexical processes that Wolfe and Katzir-Cohen validate as critical influences on fluent reading of connected text in their comprehensive definition of fluency [66].

7. VHSS intervention in English

Subsequent research using FlashWord in English with American students has built on the successes in Dutch and Italian. Koen et al. used fMRI technology to localize brain activity before and after VHSS training in students who qualified with the characteristics of developmental dyslexia. This research was designed to test the hypothesis that subtyping students with the characteristics of dyslexia based on their reading behaviors as Bakker proposed, and administering VHSS intervention based on those subtypes (FlashWord-modified and in English), would improve fluency performance across dyslexia sub-types more effectively than other currently used reading fluency programs. Secondarily, the location and level of activation differences from pre-intervention and post-intervention scans were analyzed for evidence of developing automaticity in regions of interest [78].

FlashWord, Ver. 2.2, written by Franco Fabbro and Cristina Masutto (copyright, 1995–2004 by Editrice TecnoScuola) is a computer program that uses a game-format to present words or phrases in the right or left visual hemi-field at increasingly rapid rates. According to their dyslexia sub-type, each student sees the words (or phrases) projected on either the right or left side of the computer screen, stimulating either the right or left visual field and the opposite brain hemisphere. Ocular fixation is confirmed by directing the child to watch a luminous dot oscillating up and down on the screen at an adjustable speed. A word is revealed only when the child clicks the mouse exactly when the dot is crossing the central target. This ensures visual attention to the stimulus. The child's task is to read the words as they are flashed on the screen in ever shortening durations. Reading rates of 250–100 ms for single words are generally considered to reflect "emerging fluency" [75]. For this study, students repeated all of the lessons in their assigned program (34 for the LH program and 27 for the RH program) at their own speed, matching the Italian students in total time spent: 1440 minutes (or 24 hours) total.

This fMRI experiment used a mixed design, in that the events of interest (Word Pair analysis) are randomized with perceptual controls (Letter Match analysis) to provide robust event-related activation maps and estimates of hemodynamic response. The Letter Match task demands that the child decide whether two letter strings (e.g., szpy and sxpy), printed in all black letters and shown simultaneously one above the other, match exactly. The length of the letter strings is comparable to the length of the pseudo-words used in the phonological analysis task. As this is the control task, attention to all letter positions is necessary but the assignment of speech sounds to letters is not. For the phonological analysis task, the Word Pairs were two decodable non-words printed in black, also presented visually, one above the other. Each word contained a letter, or group of letters, printed in pink. The child was instructed to press the button "Yes", if the pink letter(s) in the top word could stand for the same sound as the pink letter(s) in the bottom word, and to press a different button "No", if the pink letters represent different sounds.

Among other statistical procedures, the results of 1440 minutes of intervention measured in milliseconds and representing a change in speed of processing was used as a measure of achieved fluency in the Intervention group only. This sub-grouping was necessary because three individuals in the Intervention group did not achieve fluent processing with the FastWord program. This evidence of processing change was analyzed by means of a two-way mixed design ANOVA having two levels of reading fluency scores (pre- and post-intervention) as a within-subjects factor and two levels of fluency: those students (N = 6) who reached levels of emerging fluency, 100 ms or less, and those (N = 3) who did not, as a between-subjects factor. The between-subjects main effect of the fluency rate achieved during intervention was significant, $F(1,8) = 5.38$, $p = .05$, indicating significant differences between the students who achieved fluent processing and those who did not [78].

The fMRI results were remarkable for their corroboration of brain activations found during tasks requiring phoneme analysis. This analysis focused on three Regions of Interest (ROIs) within the core sub-systems supporting the processing of written language in normal readers: the left hemisphere (LH) superior temporal gyrus (STG) in the inferior parietal lobule within the temporoparietal system associated with word meaning; the posterior aspect of the inferior frontal gyrus (IFG) within the anterior system associated with sound/symbol associations; and the LH inferior occipito-temporal/fusiform area (VWFA) within the ventral system associated with quick recall of high frequency words first documented by Shaywitz et al. [73]. It was hypothesized that achieving fluency in reading will involve automaticity within each of these ROIs and that the brain activation maps of phonological processing of Word Pairs greater than perceptual control of Letter Match condition would show changes in activation patterns. Through comparisons of pre-intervention processing and post-intervention processing, there are clearly subjects who demonstrate much more focused activation bilaterally in the temporal regions around the STG and Postcentral Gyrus with very little activation in the visual word form area (VWFA) in the LH occipital lobe, and others who show an increase in left hemisphere activation around the IFG and VWFA [78].

Using a clustering threshold of five voxels, a sample of the activation locations were found post-intervention in the condition of Word Pairs over Letter Match in a fluent subject. **Table 3** contains a partial list of left hemisphere only activation sites, noting the location, relative size, and maximum recorded t-score.

These data confirm some anticipated activation areas with sizeable groups of voxels contributing and some remarkable lack of activation within the ROIs studied. The largest activated cluster in the IFG ROI is the Inferior Frontal Gyrus (1.52), but activation in the STG (3.10), and Brodmann areas 41 (3.17) and 42 (3.94) is much stronger. This could indicate that most of the processing in this region involved sound/symbol associations with support in the primary and auditory association cortex. The weak activation in the IFG, which supports the encoding of phonological features, could mean that less effort was required to accomplish the phonological analysis task by this subject.

The largest activated cluster in the STG ROI is the STG (2.56), but again, other areas show stronger levels of stimulation. The Postcentral Gyrus activation (3.87) is odd in that this area is the primary somatosensory cortex receiving all sensory input, especially touch. However, except for the pressing of the response button, there was no variation in the motor demands of the scanner task that would explain activation in this area. The activation found in Brodmann areas 13 (3.08) and 40

Structure	*x*	y	z	Cluster size	Max t score
ROI-IFG					
LH inferior frontal gyrus	−48	24	12	523	1.52
LH superior temporal gyrus	−60	−28	12	352	3.10
LH Brodmann area 41	−56	−20	12	147	3.71
LH insula	−36	−16	12	119	1.97
LH Brodmann area 42	−60	−20	−12	114	3.94
LH Brodmann area 13	−40	−16	12	73	1.93
LH precentral gyrus	−56	−8	12	67	1.66
ROI-STG					
LH superior temporal gyrus	−40	−40	16	233	2.56
LH angular gyrus	−52	−64	36	86	2.46
LH insula	−42	−16	16	68	2.21
LH postcentral gyrus	−52	−31	52	33	3.87
LH Brodmann area 13	−44	−16	16	29	3.08
LH inferior parietal lobule	−52	−36	28	26	2.74
ROI-VWFA					
LH sub-gyral	−36	−4	−32	30	1.54
LH middle temporal gyrus	−40	0	−32	19	1.42
LH Brodmann area 20	−44	−8	−32	7	1.80
LH Brodmann area 21	−40	−4	−32	5	2.05
LH Brodmann area 35	−24	−16	−32	5	2.01
LH fusiform (aal)	−28	−24	−32	5	3.06

Table 3.
Post-intervention activation locations in a fluent subject.

(3.16) makes sense in that area 40 is part of Wernicke's Gyrus where sound/symbol associations are refined and area 13 is a bridge between lateral and medial layers. The Postcentral activation could be evidence of compensatory systems being used for phonological analysis in immature processing systems.

The largest activation in the VWFA ROI is found in the smallest clusters detected. The Brodmann areas 21 (2.05) and 35 (2.01) appear to support automatic processing through their connection to Middle Temporal Gyrus, believed to access word meaning, and the perirhinal cortex, critical to memory. The left aspect of the Fusiform Gyrus shows the strongest activation (3.06) as would be expected if automatic retrieval of letter patterns was triggered [78]. So taken together, the activation locations identified in the subjects of this study, generally follow activation patterns found in the literature. Shaywitz et al. found that activation in the left occipito-temporal cortex increases with reading skill [79].

Even more unexpected, was the finding that only 1440 minutes of intervention resulted in increases in the reading speed of connected text for many subjects. Since the training mostly involved single word reading and some phrases, it was not anticipated that the intervention would make any difference in the reading of longer passages of connected text. However, this was found to be false. Six of the nine students in the Intervention Group who achieved levels of automatic

Intervention Group (N = 9)			Delayed Intervention Group (N = 6)		
Pre-intervention reading fluency range (average)	Post-intervention reading fluency range (average)	Net gain	Pre-intervention reading fluency range (average)	Post-intervention reading fluency range (average)	Net gain
40–115 wpm (78 wpm)	51–131 wpm (90 wpm)	11.9 wpm	24–128 wpm (77 wpm)	50–120 wpm (85 wpm)	7.3

Table 4.
Summary of behavioral results.

processing (<100 ms) in either the left- or right visual hemi-field, also increased their reading rate by an average of 20 wpm [78]. See **Table 4**.

There is considerable evidence that different students responded to the intervention differently. Those students who only displayed phonics-based errors in reading connected text and worked for the entire intervention time in the LH Program seemed to make the most substantial increases in both processing and reading speed. Only one student who demonstrated meaning-based errors and used the RH Program exclusively showed faster processing during intervention. The students who displayed both types of errors and split their time between programs made the least amount of progress; two reached fluency in the LH Program, but not in the RH Program. It is suggested that continued work with the intervention program could achieve the desired level of automaticity and that strengthening processing in the right hemisphere is inherently more difficult than strengthening the left hemisphere [78].

Wolf cautions that another source of reading disability could be an impediment in the circuit connections among the brain structures, stressing the importance of understanding the connectivity among the various regions instrumental to reading performance. She proposed at least three forms of disconnections which are consistently studied: between the frontal and posterior language regions based on underactivity in the connecting insula; and between the occipital-temporal region or the left angular gyrus region; and frontal areas in the left hemisphere. She suggests that children with dyslexia use an altogether different reading circuitry. Instead of a progressive disentanglement of the right hemisphere's larger visual recognition system in reading words and an increasing engagement of left hemisphere's frontal, temporal, and occipital-temporal regions, they used more frontal regions, showed less activity in the left-hemisphere angular gyrus, and created potentially compensatory "auxillary" right-hemisphere regions which performed functions usually handled by more efficient left-hemisphere areas [14]. The fMRI results from this study underscore Wolf's proposal. It may be that much of the diffuse frontal activation that was observed in many pre-intervention scans and some post-intervention scans of nonfluent subjects is evidence of these compensatory "auxillary" strategies. It may be that in older readers who have over time consolidated less efficient pathways for reading, more exposure is required for specific hemispheric stimulation (intervention) to supplant frontal and right hemisphere functions with effective left hemisphere processing.

8. Case studies OF VHSS intervention

Subject 1, coded MC, was one of the students who reached very fast processing speeds during the intervention using the left hemisphere program. The pre-intervention scan showed mostly diffuse activation in the right hemisphere occipital-parietal areas. Based on all phonetic reading errors in the pre-intervention fluency measure, this student was labeled a "P-type" and assigned the LH intervention program. MC was a very willing subject and engaged with the program easily. After progressing through the LH program (34 lessons) nearly six times during the 1440 minutes of training, the fastest processing was 80 ms with 100% accuracy. This student also achieved fluent processing rather quickly on the thirteenth day of treatment. MC gained 26 wpm on the final fluency measure. Analyzing this subject's scanner data, there was an almost perfect performance when processing the letter matches: 98% accuracy during Scan 1 and 89% accuracy during Scan 2. MC's analysis of phonemic elements improved from Scan 1–2. During Scan 1, 54% of the word pairs were correctly identified and 70% were right in Scan 2. Overall this subject demonstrated a 5% improvement in fast decoding skills. The post-intervention scan shows much more focused activation bilaterally in the temporal regions around the superior temporal gyrus and postcentral gyrus, and there is very little activation in the VWFA in the LH occipital lobe [78].

Subject 2, coded PE, was one of the students who achieved processing speeds that approached fluency using the left hemisphere program. The pre-intervention scan showed a lot of bilateral frontal activation and more RH activation than LH activation in the occipital areas. Five out of six reading errors were phonics-based, so this student was labeled "P-type" and assigned the LH program. PE completed the LH program six times during 1440 minutes of treatment, but there were only 24 lessons included because some of the orthographic patterns were not taught at this reading level. This student was one of the younger participants in the study and only reached levels of fluent processing for words, not for phrases. PE's fastest processing score was 125 ms with 83% accuracy and during post-intervention fluency measures, reading speed was increased by 11 wpm. Analyzing the scanner data, there is evidence of significant learning, perhaps due to the young age and the nature of reading instruction in the lower grades. PE showed a lot of confusion when analyzing the letter strings: only 49% were judged correctly in Scan 1 and 57% in Scan 2. Growth in decoding skills is evident in the correct identification of the word pairs: 45% during Scan 1 and 62% during Scan 2. Overall, this subject demonstrated a 13% improvement in fast visual processing. The post-intervention scan indicates an increase in left hemisphere activation around the inferior frontal gyrus and VWFA [78].

So if the focus is on automatic word retrieval, the Visual Word Form Area, has to be a region of exceptional interest. There remains much to understand regarding the activation of the Visual Word Form Area in the left fusiform gyrus and its relationship to the development of fluent reading. According to Cohen et al., a standard model of word reading proposes that visual information is initially processed by occipito-temporal areas contra-lateral to the stimulated hemi-field. Then it is transferred to the visual word form system (VWFA), a left temporal region devoted to the processing of letter strings. Using fMRI, they identified a highly significant activation in the left fusiform gyrus (Talairach coordinates: $x = -42$, $y = -57$, $z = -6$) that was strictly unilateral and remarkably stable across subjects [80]. Since their research also included comparisons of activation from the right and left visual hemi-fields, they concluded that the VWFA lies at the convergence of retinotopically organized visual pathways and contain visual neurons with receptive fields in both hemi-fields. They hypothesize that the VWFA may be homologous to inferotemporal areas in the monkey where cells with wide receptive fields, selectivity to high-level visual features, and size and position invariance have been found. If this is the case, it is possible that the human VWFA holds a distributed representation of the visual shapes of letters such that specific alphabetic strings are distinguished and is thought to supply instantaneous recognition of learned letters, letter patterns, and unique words.

Van der Mark et al. researched areas of the fusiform gyrus for activations related to visual processing. Initially, they found a posterior–anterior measure of change to print specificity with higher anterior response to letter strings but higher posterior response to false-fonts. Additionally, there was a constant sensitivity to orthographic familiarity demonstrated by higher response for unfamiliar than familiar word-forms. These variations along the VWF-System could only be detected in controls. They used functional connectivity MRI (fcMRI) to correlate signal changes in a seed region with signal changes in other parts of the brain and reveal functional interactions between brain areas. Five non-overlapping seed regions of interest (ROIs; spheres with a 6 mm radius) centered on the VWFA of the fusiform gyrus and covering neighboring areas along a posterior–anterior axis in the left hemisphere were defined, with ROI3 being the VWFA itself. Results showed that functional connectivity in children with dyslexia was significantly reduced only between the VWFA proper (ROI3) and classical left hemispheric language related regions, including the inferior parietal lobule and the inferior frontal gyrus. Significantly greater connectivity for the dyslexia than the control group was observed between ROI3 and the left middle temporal and middle occipital gyrus, and between ROI4 and the left superior temporal gyrus and the left insula. The strength of the functional connections between VWFA (ROI3) and the left middle temporal gyrus and between ROI4 and the left superior temporal gyrus did not correlate significantly with the behavioral measures in either the control group or the children with dyslexia. Correlating these increases in connectivity does not reflect better performance, but instead compensation efforts. They conclude, as did Wolf, that dyslexics may not use the network in the same way as controls [81].

9. Evidence from diffusion tensor imaging

A "disconnection syndrome" in which functional connectivity of the relevant cortical networks in the left hemisphere is disrupted has been proposed as a potential basis for reading difficulties [82]. Diffusion Tensor Imaging (DTI), a technology similar to fMRI, allows probing the distance and direction of water molecule movement in the brain, producing form and orientation information about the underlying white matter structures [83]. White matter exhibits anisotropic water movement, with water molecules showing various degrees of diffusion in each direction. In typical DTI studies, diffusion images from at least six directions are analyzed using an ellipsoid tensor model—a symmetrical 3×3 matrix. Parallel and perpendicular diffusivities are then calculated and used to estimate properties of underlying tissues [84]. DTI has demonstrated a correlation between the microstructural integrity of the left temporo-parietal white matter and reading ability in dyslexic and control adults [85]. It seems that this technology could be instrumental in measuring not only the degree of connectedness between crucial brain features, but also in determining the amount of pressure needed by these systems to change functioning.

Fractional anisotropy (FA) is a related technology that is used to index structural information regarding a brain area. It measures the anisotropy of the diffusion of water molecules [86] and is sensitive to axonal density, size, myelination, and the coherence of organization of fibers within a voxel, thus providing an index of the structural integrity of white matter. FA is measured from 0 (isotropic diffusion) to 1 (anisotropic diffusion) [83]. Beaulieu et al. propose that FA may be reduced in poor readers due to a number of possible differences in the microstructural properties of white matter. These possible differences include reduced myelination, reduced axonal packing density, decreased axonal diameter, or reduced coherence of the orientation of axons within the region, all of which might impact the efficiency of communication (bandwidth) among cortical areas [87]. Further, their findings suggest that there are regional brain structural correlations over a wide range of reading ability even within a so-called normal population. Keller and Just examined the diffusivity in directions that are perpendicular to the principal axis of diffusion in anisotropic regions of white matter (radial diffusivity) or parallel to it (axial diffusivity). They suggest that the pattern of diffusivity effects signifies that the difference in FA between poor and good readers before remediation is due to initially higher radial diffusivity in the poor readers. Further indicating that the change in FA results from an alteration in some microstructural feature-myelination, packing density, or axon diameter- that affects radial diffusivity. By default, myelination is deemed the plausible mechanism of the microstructural change [88]. It is possible that extended, pressured practice affects the myelinated cortical thickness in key regions of the neuroanatomical correlates of the dual route reading model.

In a meta-analysis focusing on the foci of brain activity in a set of studies, Richlan, Kronbichler, and Wimmer used Activation Likelihood Estimation (ALE) to analyze for agreement by modeling each reported focus as the center of a Gaussian probability distribution. These distributions are then joined to create a whole-brain statistical map that estimates the likelihood of activation for each voxel. The data from 17 studies (12 fMRI and 5 PET) with a total number of 595 participants (294 dyslexics and 301 controls) were included. This approach resulted in three ALE maps: one, presenting brain regions with under-activation in dyslexic readers, another, presenting regions with over-activation and, finally, a subtraction map which allows a formal assessment of differences between the two maps. The results extracted 128 foci of reliable group differences (69 for dyslexic under-activation and 59 for dyslexic over-activation), and localized 80 input foci in the left hemisphere and only 48 in the right hemisphere. They found that 58% of the left and 48% of the right hemisphere foci were under-activation foci. The majority of activation abnormalities identified by separate maps were still present in the conservative thresholded difference map: under-activation in a large cluster in the left hemisphere reaching from dorsal inferior parietal to ventral occipito-temporal regions and to the middle temporal and the inferior frontal under-activation, with over-activation in left hemisphere anterior insula, primary motor cortex, lingual gyrus, caudate nuclei, thalamus and right hemisphere medial frontal cortex. These results provide support for a dysfunction of the VWFA engaged in visual-orthographic word recognition and a dysfunction of the left fusiform region affecting the build-up or the use of an orthographic word lexicon in recognition. Further, over-activation of the left lingual gyrus may reflect prolonged visual processing when dyslexic readers are confronted with a reading task [89].

Voxel Based Analysis (VBA) uses brain images normalized to a standard brain atlas and smoothed, before computing and comparing DTI properties for each individual voxel. This approach greatly reduces the typical biases of ROI analyses, though since it is typically less theoretically driven more drastic corrections for multiple comparisons are often required [90]. Moreau, Stonyer, McKay, and Waldie observed that many DTI studies have investigated significant differences in FA between dyslexic and typical readers, as well as identifying regions where FA values significantly correlate with performance on reading tasks, with problems in replication and little convergence of data. Using a very stringent process of examination, they identified research that used VBA to identify cortical coordinates where significant differences in FA existed between dyslexic and typical readers, and research that used VBA to locate cortical coordinates where FA significantly correlated with reading ability or performance on a reading-based task. Their results were extraordinary. The analysis of 47 foci from 5 experiments (99 subjects), where FA was significantly greater in typical compared to dyslexic readers, and the analysis of 17 foci from 2 experiments (52 subjects), where FA was significantly greater in dyslexic compared to typical readers, yielded no significant clusters when using FDR correction of 0.05. Further, the analysis of 42 foci from 9 experiments (500 subjects), where reading ability was significantly positively correlated with FA, and the analysis of 2 foci from 2 experiments (40 subjects), where reading ability was significantly negatively correlated with FA, also yielded no significant clusters when using FDR correction of 0.05. Studies of children and adults were analyzed separately. No significant clusters were produced when typical readers had significantly higher FA than dyslexic readers or when dyslexic readers had significantly greater FA than typical readers, regardless of age [90]. The fact that these results showed no systematic differences in fractional anisotropy between dyslexic and typical readers, or as a function of reading ability, after correcting for multiple comparisons, underscores the ambiguity inherent in brain research in spite of, or perhaps because of, cutting edge technologies. Hoppenbrouwers, Vandermosten, and Boets noted that despite appearing consistent, each one of the studies they included in their meta-analysis produced coordinates at different locations within the temporo-parietal region and corpus callosum [91]. In fact many studies have also reported differences and correlations in a range of other regions distributed widely throughout the cortex [59, 92]. Turkeltaub et al. pointed out that the software commonly used for these kinds of analysis, GingerALE 2.0.4, has since been updated too correct initial errors which made ALE analysis to lenient, therefore inadequately controlling for spurious findings [93].

10. Conclusion

There is little doubt that neurobiological investigation into the brain activations of struggling readers is messy and incomplete and fraught with misinformation. Reviews of international studies reveal many areas of agreement regarding the factors that result in dyslexia, but the characteristics of different languages and their orthographies introduce differences in the required processing skills. This is also seen in the unequal application of the Psycholinguistic Grain Size Theory, where transparent languages with a regular orthography are less affected than those opaque languages with many irregular words and derivatives. The contribution of RAN to understanding the neurobiological features of dyslexia appears to have global implications as this naming speed deficit has been found to be more common than even the phonological deficit in both regular and irregular orthographies. These methods and techniques used to investigate the manifestations of dyslexia worldwide have advanced the discussion in many useful ways.

Phonological processing and speed have long been in the forefront of international dyslexia research. Particularly in transparent orthographies, phonological impairments have supported the idea of lexical and sub-lexical routes of decoding that utilize different areas in the brain. Difficulties with phoneme blending often precede and contribute to a slower rate of reading. These processing weaknesses eventually produce students who display the dreaded Double Deficit- a condition that in many languages has been identified as the most severely incapacitating. However, in some languages, RAN is useful as a predictor of reading accuracy only in the early grades. Receptive vocabulary, often an important factor in less

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consistent orthographies, has been found to play a role in reading accuracy in more regular orthographies as readers become more experienced, but this seems to rely on specific language features that promote decoding based on lexical aspects of known, related words. So in languages where these language-specific patterns are prevalent, most dyslexics achieve high levels of reading accuracy but remain deficit in reading speed.

Research into the visual processing of struggling readers has focused mainly on the functions of the occipito-temporal reading circuit. Dysfunction in a variety of visuo-attentional skills such as visual search, visual recognition, and visual information processing has been documented in several languages, with both transparent and opaque orthographies. Interesting work in languages that use diacritical vowel markings which are absent after instruction emphasizes the theory that when grapheme-phoneme processing skills are weak, students are unable to develop strong connections in the orthographic lexicon to support further autonomous word recognition. In this case, the results also highlight the importance of visual accuracy and memory for the missing vowel markings. Generally, however, functional imaging studies reveal reduced reading related activation in a left ventral occipito-temporal brain area, often associated as an interface between visual orthographic codes and phonology and meaning. There is some assurance of parity for even complex visual languages like Urdu that RAN continues to be a reliable predictor of reading accuracy. Regardless, the question of effective interventions remains largely unanswered.

American researchers have addressed the problems inherent in dyslexia through new conceptualizations of fluency and definitions that acknowledge the crucial role played by the automatization of underlying subskills at the letter, letter-pattern, and word levels. They challenged the validity of the commonly held discrepancy definition of dyslexia which mandates that a student with reading difficulties can be labeled "dyslexic" only if they have an average or higher IQ. Research showed that there were no reliable differences in the brain functioning of poor readers with high IQs and poor readers with low IQs. The effects of instructional intervention have also been explored in studies with American students. Most of this research focuses on explicit instruction in the alphabetic principle and phonological processing. These efforts generally resulted in increases in the activation of left posterior superior temporal gyrus (STG), although processing speed remained unaffected. However, a novel study using visual hemisphere-specific stimulation has shown some advancement in the speed of processing of dyslexic readers. Matching struggling readers to either a left or right hemisphere intervention program by specific oral reading behaviors appears to be helpful in applying an effective remediation program. The differences in the composition of the intervention programs (the left hemisphere lessons are all phonologically decodable words and the right hemisphere lessons are all phonologically decodable non-words) apparently interact with the weak brain processing systems efficiently. The forced pressure of faster and faster recall appears to strengthen the pathways resulting in automatized recall. Brain activations of subjects who achieved levels of automatic processing (recall within 100–250 ms) revealed expected changes: pre-intervention, there was a great deal of diffuse activation in the frontal areas and in the right hemisphere, and post-intervention activation was much more focused bilaterally around the STG and postcentral gyrus with very little activation in the VWFA. Further these documented processing changes were discovered to directly support increases in reading speed in those students reaching automatic levels of visual processing. So, visual hemisphere-specific stimulation has emerged as an intervention tool that influences access to the VWFA in American dyslexic readers.

Other technologies also shed light on the functional connectivity of brain regions important to fluent reading, but, as always, must be scrutinized for reliability. It is well established that diffusion tensor imaging (DTI) and fractional anisotropy are useful tools for understanding the structural integrity of white matter. Many studies have investigated relationships between differences in FA and various reading abilities, and differences in FA in dyslexic and normal readers. Generally these studies identify left hemisphere under-activation from dorsal inferior parietal to ventral occipito-temporal regions and to the middle temporal and the inferior frontal under-activation, with over-activation in left hemisphere anterior insula, primary motor cortex, lingual gyrus, caudate nuclei, thalamus, and right hemisphere medial frontal cortex. However, many researchers have also commented that in spite of apparent consistency, there is substantial disparity in the coordinates locating specific activations in the temporo-parietal region and corpus callosum. These observations led to a careful, but controversial meta-analysis using voxel-based analysis (VBA) to identify cortical coordinates where significant differences in FA existed. These analyses found no systematic differences in FA between dyslexic and typical readers, or as a function of reading ability, and highlighted possible weaknesses in older versions of the software commonly used to make DTI analyses. Clearly, one must engage in this kind of research and rely on these results cautiously.

For many years, the only neurobiological research was done in adults, which did not allow investigation of the developing brain. Granted, it is very challenging to obtain reliable fMRI results with children, but new techniques and a more permissive environment are encouraging, and the promise of bringing new understandings to fruition as effective intervention practices continues to beckon. Instructional intervention that is designed to improve time-sensitive procedural rather than time-free declarative knowledge of grapheme-phoneme correspondences may overcome the temporal deficit in children by decreasing the over-connectivity of brain regions in the executive panel of working memory- that is the left and right inferior frontal gyrus, and increasing the connectivity between the left inferior frontal gyrus and the middle frontal gyrus (working memory) [94]. From a clinical or educational perspective, remediation seems most targeted and effective when it addresses an isolated disability [71]. The challenge in developing strong intervention tools is to make them engaging, accessible, and fun.

Saine et al. conducted a longitudinal intervention study designed to build a model of predictive values of reading fluency using three different instructional techniques to identify the most effective type of intervention for children with different profiles of core pre-reading skills. Their results show that a computerized remedial reading intervention called GraphoGame was the most successful in remediating reading fluency in Finnish children (7 years old) with deficits in letter knowledge, phonological awareness, and rapid automatized naming [95]. Perhaps reflecting its extremely shallow orthography, (there is full symmetric consistency between graphemes and phonemes and the simplest syllabic structure in the Finnish language) and the fairly long duration of intervention (66 hours), increases in fluency were found in both of the other treatments (remedial reading instruction and mainstream instruction) as well, with the least amount of growth shown in the mainstream group. However, evaluation of data by pre-reading profiles shows that all of the tested profile-types responded most strongly in the computerized reading program.

The GraphoGame program is similar to FlashWord in the structure of the phonological analysis, proceeding from early reading competencies to higher-level concepts, and in the forced, fast processing at the word-level. It was developed to affect the cognitive operations that constitute word reading: the visual identification of orthographic units, their transformation into an internal sound and articulation. This program's creators included the appearance of letters and words at an accelerating rate on the screen (although without hemisphere consideration) in an effort to improve automatized naming and visual recognition more effectively than flashcards [95]. The direct comparison of traditional instructional techniques to outcomes produced through a computer-based intervention underscores the power of these types of programs and their impact on the automatization of lexical and sub-lexical reading processes. Perhaps the power of technology in new applications will ultimately provide solutions for the long-suffering dyslexic readers, especially those of opaque orthographies.

Author details

Bobbie Jean Koen
University of Houston, Houston, Texas, United States

*Address all correspondence to: bjkoen@comcast.net

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