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Letters and speech sounds associations in typical and atypical reading
development

PhD thesis

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Abstract

In alphabetic languages, learning letters and speech sounds correspondence is the first and one of the most crucial steps in reading development. Research shows that this process differs depending on how transparent the language is (how constant and repetitive the association of letters and speech sounds is, e.g., Italian is highly transparent, Polish and Dutch are moderately transparent, and English is an opaque language). According to the literature, Dutch kids learn letter-speech sound (LS) associations in their first year of formal schooling. From the neuroscience perspective, we know that the left superior temporal cortex (STC) plays an essential role in LS integration. Developmental dyslexia or family risk of dyslexia are factors that may interfere with this process. The process of LS association seems similar in alphabetic languages but has not been thoroughly examined in the blind who read the Braille alphabet using their sense of touch.

The principal aim of my doctoral dissertation is to investigate how the process of LS association occurs in the typical and atypical reading development in Polish.

In the first behavioral experiment, I checked how much time Polish-speaking children needed to learn the correspondence between LS pairs. As it is the case with the Dutch language, children learn this skill in the first year of schooling, but it takes them longer to automate this process (up to around the third grade of primary school).

In the second experiment, I delineated the brain regions that play a role in LS integration in young readers with and without a family history of dyslexia. Children's STC activity during the LS association task varied considerably between those with and without a family history of dyslexia. The at-risk group showed more robust activation when processing congruent LS pairs than incongruent ones, while the no-risk group showed the opposite pattern – higher activation for incongruent LS pairs.

In the third experiment, I found significant changes in the pattern of brain activation during the first two years of education. While the brain activity decreases in response to unimodally presented speech sounds (auditory) and letters (visually), it increases when children process multimodal LS pairs.

In the last experiment, I checked what the process of LS integration looks in the blind compared to the sighted. The integration process takes place in the STC in both groups. However, the activation pattern is different. The sighted subjects showed higher activity for incongruent LS pairs in the bilateral STC, similarly to children without the family risk of dyslexia in the early stages of learning to read. In the blind, congruent pairs resulted in an increased response in the right STC. These differences may be related to lower exposure to letters in the blind or more sequential processing of Braille as compared to print reading.

The experiments that comprise my doctoral dissertation lead to a conclusion that the process of letter and speech sound association in Polish takes place in the STC. Its exact course is influenced by dyslexia, family risk of dyslexia, and reading modality.

Streszczenie

W językach alfabetycznych, integracja głoski i litery, czyli nauka asocjacji głosek z odpowiadającymi im literami" jest pierwszym i jednym z najważniejszych kroków w rozwoju umiejętności czytania. Badania pokazują, że proces ten różni się w zależności od tego jak przejrzysty jest język (jak stała i powtarzalna jest asocjacja litery i głoski, np. język włoski jest bardzo przejrzysty, polski i holenderski są średnio przejrzyste, a język angielski jest nieprzejrzysty). W literaturze pokazano, że holenderskie dzieci opanowują umiejętność asocjacji litery z głoską podczas pierwszego roku formalnej nauki. Z badań z użyciem neuroobrazowania wiadomo, że lewa górna kora skroniowa (ang. *superior temporal cortex*, STC) odgrywa istotną rolę w procesie integracji głoski i litery. Czynnikiem, który może zaburzać ten proces prowadząc do trudności w czytaniu jest występowanie dysleksji rozwojowej lub rodzinnego ryzyka dysleksji. Pomimo, że proces integracji zdaje się być podobny dla wielu języków alfabetycznych, nie jest dokładnie zbadane, jak wygląda on u osób niewidomych posługujących się alfabetem Braille'a.

Głównym celem mojej pracy doktorskiej było zbadanie jak proces integracji głoski i litery zachodzi w typowym i nietypowym rozwoju czytania, w języku polskim.

W pierwszym badaniu behawioralnym, sprawdziłam ile czasu potrzeba, aby polskojęzyczne dzieci nauczyły się połączenia głoski i litery. Tak jak w języku holenderskim, dzieci opanowują tę umiejętność w ciągu pierwszego roku nauki czytania, jednak automatyzacja tego procesu trwa dłużej (do ok. trzeciej klasy szkoły podstawowej).

W drugim badaniu przedstawiłam wyniki dotyczące mózgowych obszarów integracji głoski i litery u dzieci rozpoczynających naukę czytania z ryzykiem i bez rodzinnego ryzyka dysleksji. Dzieci z rodzinnym ryzykiem dysleksji istotnie różniły się od dzieci bez ryzyka w aktywności STC podczas zadania mierzącego integrację litery i głoski. Aktywność była wyższa w odpowiedzi na niespójne pary liter i głosek w grupie bez ryzyka, a w grupie z ryzykiem była wyższa przy przetwarzaniu spójnych par.

W trzecim badaniu pokazałam, że zachodzą istotne zmiany we wzorcu aktywacji mózgu w czasie pierwszych dwóch lat edukacji. Podczas gdy aktywność mózgu spada w odpowiedzi na głoski prezentowane wyłącznie słuchowo i litery prezentowane jedynie wzrokowo, wzrasta ona, gdy dzieci przetwarzają multimodalne, wzrokowo-słuchowe pary liter i głosek.

W ostatnim badaniu sprawdziłam jak proces integracji głoski i litery przebiega u osób niewidomych w porównaniu do widzących. Proces integracji zachodzi w STC w obu grupach, jednak wzorzec aktywacji jest odmienny. U widzących zaobserwowano większą aktywność dla niespójnych par głosek i liter w obu stronach STC, podobnie jak u dzieci na początkowych etapach nauki czytania, bez rodzinnego ryzyka dysleksji. U niewidomych to spójne pary skutkowały zwiększoną odpowiedzią w prawej STC. Różnice te mogą być związane z mniejszą ekspozycją na litery u osób niewidomych lub bardziej sekwencyjnym przetwarzaniem alfabetu Braille'a.

Z badań składających się na moją pracę doktorską można wnioskować, że proces integracji głoski i litery w języku polskim zachodzi w STC. Na jego dokładny przebieg ma wpływ dysleksja, rodzinne ryzyko dysleksji oraz modalność czytania.

Introduction

Reading is one of the essential skills in everyday life and one of the most prominent cultural inventions. It is even hard to imagine our world without letters that can be combined and read as words and sentences. Since reading is automatic in adult skilled readers, we often forget that learning to read and mastering this ability took a few years of our formal education. Learning to read is also a challenge for our brain, which learns how to process language in the visual modality and we often do not realize the whole neural machinery that sends information from the retina to our brain. Reading is a demanding process on many levels, and one of the first and most crucial steps in literacy acquisition is learning the letter and speech sound association.

The first part of the thesis describes the model of learning to read proposed by Uta Frith (Chapter I.1). Next, a summary of the behavioral and neuronal research on letter and speech sound association is presented (Chapter I.2). Chapter I.3 consists of a quick summary of dyslexia and its mechanisms. The last Chapter I.4 describes Braille reading in the blind.

The second part of the thesis presents four experiments in which we studied the letter and speech sound association. In Experiment 1, we examined the pace of learning letter and speech sound association in Polish. Experiment 2, focused on how the brain activation to letter and speech sound association differs between typically reading children and children at risk of/with dyslexia at the beginning of reading instruction. Experiment 3 is a longitudinal study on how the process of integrating letters and speech sounds in the brain develops in children during the first two years of learning to read and how this developmental trajectory differs in dyslexia. Experiment 4 summarizes the findings from the blind population on letter and speech sound association compared to the sighted subjects.

In this thesis, I present data from a total of 511 participants (participants of Experiment 3 were a subsample of Experiment 2). I did not test all the participants by myself. I took part in all steps of Experiments 1 and 4, including preparation of paradigms, subjects' recruitment and testing, data analysis, and interpretation. In the case of Experiments 2 and 3, I analyzed and interpreted the results of the already collected data.

Therefore, the vast majority of the research presented in this thesis has been conducted in close cooperation with other members and collaborators of the Laboratory of Language Neurobiology.

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Some parts of the experiments and results presented in the second part of the thesis have been published in international journals. The previous publication included the results of Experiment 2 (Plewko et al., 2018). The design and results of Experiment 3 have been submitted for publication (Beck et al., submitted).

Part I: State of the art

Chapter I.1. Learning to read

Spoken language acquisition happens early in child development and does not require much special attention from caregivers. Contrary, reading is a cognitive skill that has to be acquired through instruction and learning to read can be effortful. What is more, reading acquisition impacts the cognitive system both on behavioral and neuronal level (Dehaene, 2009). Skills like visuo-spatial processing, short-term memory and even mathematical thinking are enhanced by reading acquisition. Due to the complexity of the cognitive process of reading both structure and functional organization of brain networks are influenced too (Dehaene et al., 2015).

Learning to read is a multi-stage process, which starts at a very young age. Young children are exposed to letters all the time and absorb knowledge without even realizing it. Children quite easily move from one stage to another, usually over several months or years, depending on orthographic transparency. This parameter indicates how regular letter-phoneme correspondences are in the given script. Studies show that children from most European countries become accurate and fluent in basic-level reading before the end of the first year of formal reading instruction (Seymour et al., 2003, Blomert and Vaessen, 2009). This rule, however, does not apply to less transparent languages like French, Portuguese, Danish, and English. This difference is not linked to differences in the onset of reading education or to letter knowledge.

Most studies state that this delay in learning to read is linked to the fundamental linguistic differences in syllabic complexity and orthographic depth (Richlan, 2014). The letter-speech sound complexity affects decoding, and simultaneously, decoding depth affects reading. The time needed for reading development in English is more than twice longer than in shallow orthographies like Italian (Seymour et al., 2003).

Uta Frith's model

For the purpose of this thesis, I would like to focus on the model of learning to read proposed by Uta Frith in 1985. The schematic summary of this process is presented in Figure I.1.1.

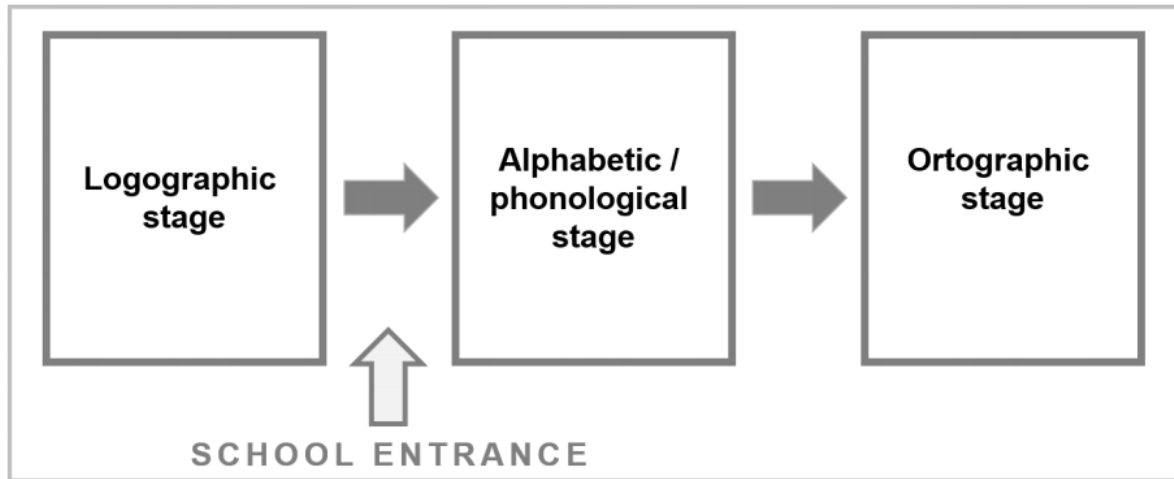


Figure I.1.1. Schematic diagram of the process of learning to read

According to the three-stage model of learning to read (Frith, 1985), the process of reading acquisition starts at the age of five or six with a logographic stage. During this stage, children treat words as whole units and are not fully aware of the nature of letters as building blocks. They can read 'Coca-Cola' on a sign even if they do not know individual letters in this word but would not be able to read another word that consists of the same letters in a different order (Morton, 1989). At this stage, “reading” is more about naming known words than actually combining letters into words. Children know how their own names are spelled and perhaps can recognize a few other common words. Depending on the orthographic transparency, children in different languages have different sizes of sight vocabulary (Ziegler & Goswami, 2006). At this point of word recognition, they make many errors, trying to identify words based on font type instead of decoding words letter by letter. For example, when letters in the word coca-cola are changed to cola-caco, probably children at the logographic stage will name this word as coca-cola if written in a typical brand font. We could say that their visual system attempts to recognize these words as if they were objects. However, recognizing whole words as pictures is only an artificial form of reading.

The next stage in Frith’s model is the phonological stage. Children need to visually represent words in a different format from other visual objects or symbols at this stage, and the concept of letter and speech sound association appears. The children acquire explicit knowledge of phonemes, their correspondences with letters, and how to combine speech sounds into words, as with d - og or d - o – g. The ability to order letters and name them correctly plays a crucial role in developing the ability to read and decode familiar and unfamiliar words. The greatest difficulty is the fact that children often know the names of the letters (ay, bee, see, dee...), which do not provide an auditory indication of what the word sounds like. For instance, it is hard to pronounce even a simple word “dog” if the d is not /d/ but “dee”. Therefore, systematic

and explicit phonics instruction involving the set of letter-sound relationships has been proven the most effective in improving early reading skills, even in less transparent orthographies. The last, the orthographic stage, is reached when readers do not need to pronounce the words repeatedly. They can automatically recognize many words and access their meanings immediately, aligning them with the internal lexicon they have built in the previous stages. Multiple exposures to the exact words allow children to store the entire word's grapheme sequences in the spelling lexicon. This is a much faster process than phonological analysis (i.e., the need to "decode" words letter by letter). Proficient readers are those who have reached this stage and have no trouble choosing the right strategy for decoding a given word. Nevertheless, for new - unfamiliar words or irregular ones, the main strategy will still be the phonological analysis (step 2).

Learning to read in Polish

In Polish studies, researchers also use Uta Frith's model due to its flexibility, as it takes into account the individual nature of this process. However, learning to read differs between countries, and the difference is caused not only by language and its transparency but also by the age of formal reading education. In Poland, pre-schoolers (between ages 3 to 6) develop speaking skills and print awareness (Krasowicz-Kupis et al., 2015b) to prepare for later literacy instruction, which starts in the first grade. Literacy instruction is mainly based on an analytic-synthetic teaching strategy (Awramiuk and Krasowicz-Kupis, 2014), combined with a global strategy (Jaszczyszyn, 2010). Krasowicz-Kupis (1999) conducted a comprehensive study in which she tested children from 6 to 9 y.o (kindergarten to the 2nd grade of primary school). Based on her results, three stages of learning to read in Polish were proposed. Stage I - reading with the help of phonological analytical strategies, using letter-speech sound relation. The next stage (stage II) involves reading using transitional strategies between phonological, analytical, and global expressive. Children adapt the strategy to the type of the reading material. Stage III constitutes the last stage, when holistic expressive and/or phrasal strategies are dominant .

In summary, compared to Frith's model, Polish 6 y.o are already beyond the logographic phase. At the first stage of reading, the mechanism of this activity is definitely linguistic. It has an analytical character and is based on phonemic skills and phonological awareness. As the reading progresses, the strategy becomes global, expressive, or phrasal, depending on metaphonological skill, intellectual level, and some elements of syntactic awareness. Similarly to Frith's model, it is expected that the processes will be automated with time and practice, and that reading efficiency will increase.

Chapter I.2. Letter and speech sound association

Behavioral studies

In order to be able to start decoding written words, a child learning to read in an alphabetic language needs to understand and assimilate how graphemes (letters) and phonemes (speech sounds) are connected (Ehri, 2005, Krasowicz, 1999). Understanding the basic letter-speech sound (LS) associations usually takes place early on, sometimes even before formal reading instruction. Nevertheless, automatization of this knowledge is possible only with repeated exposure to print and requires more time, even several years. This was shown by a study on Dutch speaking children (Froyen et al., 2009). Accuracy and reaction time were measured when children were asked to judge if a letter and a speech sound match. Although most children had accuracy on a ceiling level at the end of the first grade, reaction times of LS matching gradually decreased throughout the entire primary school reading instruction. This was interpreted as slow and steady automatization of LS integration. No precise data on LS association forming timeline is available for other orthographies, including Polish.

Nevertheless, it has been aptly argued that the development of automated LS integration plays a crucial role in the acquisition of fluent reading skills. Efficient ability to form LS associations is a strong predictor of later reading skills across many languages (Caravolas et al., 2012; Schatschneider et al., 2004), and consequently, a failure to develop automated LS integration might result in an impairment of reading fluency (Blomert, 2011).

Behaviorally, there is mixed evidence regarding whether automated LS associations constitute a core deficit in dyslexia and predict reading skills beyond phonological awareness and rapid automatized naming (RAN) or rather reflect the past reading experience and reading-related processes. Supporting data comes from studies that employed a LS learning paradigm of an artificial script (Aravena et al., 2013, 2018). Namely, they revealed a LS binding deficit in dyslexia independent of letter knowledge, which affected reading performance in artificial script. Artificial script-related measures were related to phonological awareness and RAN, but made a unique contribution in predicting individual differences in reading and spelling ability. Even in preliterate children, performance on a similar learning paradigm with morse-code symbols turned out to be a particularly relevant predictor (over other verbal measures) of reading performance one and three years later (Horbach et al., 2015, 2018). However, Law and colleagues (2018) found no differences in LS learning between children with and without dyslexia and no independent contribution of artificial LS learning to reading skills, when they employed the same learning task and assessment procedure as Aravena et al., (2018). Nevertheless, they reported reduced ability of children with dyslexia to use the

newly learned correspondence for reading words presented in artificial script.

Contrasting results were obtained in a priming task based on participants' native language used to assess automatic LS integration (Clayton and Hulme, 2018; Clayton et al., 2020; Nash et al., 2017). Faster responses to speech sounds primed by congruent letters were not related to reading skill and children with dyslexia showed similar priming effects as controls (Clayton & Hulme, 2018). Subsequent longitudinal study in children during the first year of formal reading instruction revealed that automatic integration of LS correspondences could be measured after just 4 months of formal reading instruction, but did not predict variations in word reading skill (Clayton et al., 2020). Finally, Nash et al., (2017) demonstrated that the degree of LS integration in children with dyslexia was appropriate for their reading level, suggesting that compromised LS integration may be a function of reading experience. However, measures of LS integration based on the participant's native language might be under the influence of past orthographic knowledge (Law et al., 2018).

Neural correlates of letter - speech sound mapping

In 2004 Nienke van Atteveldt and colleagues proposed a schematic summary of their findings on letters and speech sounds association in the brain. Basically, letters are processed in the visual cortex and speech sounds in the auditory cortex which includes planum temporale and Heschl's sulcus. Then the information goes to the superior temporal gyrus and sulcus where the integration takes place (see Figure I.2.1.)

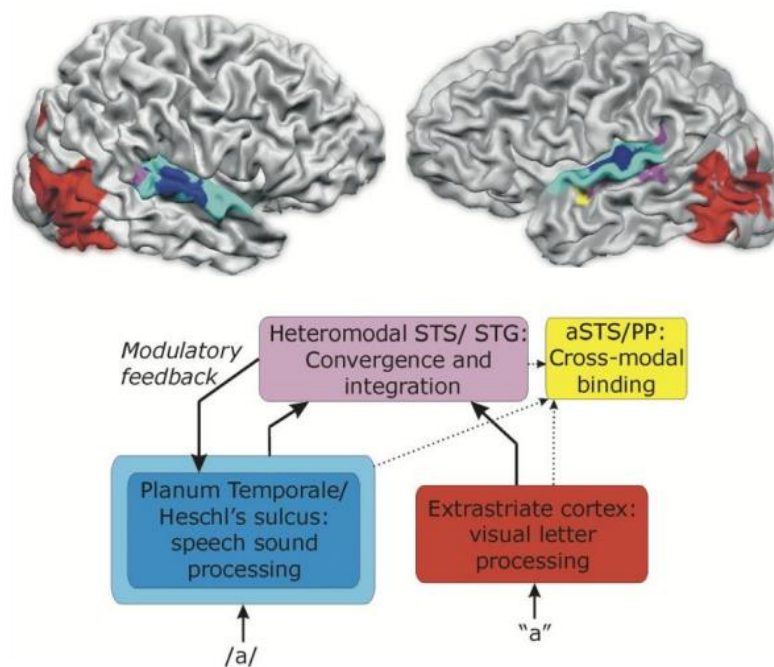


Figure I.2.1 Processing of the visually presented letters (red) and auditory presented speech sounds (blue) as well as integration areas (violet, yellow) in the human brain; figure from van Atteveldt et al., 2004.

The most common way to check which regions are involved in LS association is to simply present two unimodal conditions: letters and speech sounds, and two multimodal conditions: congruent and incongruent LS pairs. Congruent means that the orthographic information represented by the visual letter stimulus matches the phonological information represented by the (simultaneously or sequentially presented) auditory speech sound stimulus. Accordingly, in incongruent LS pairs this information does not match.

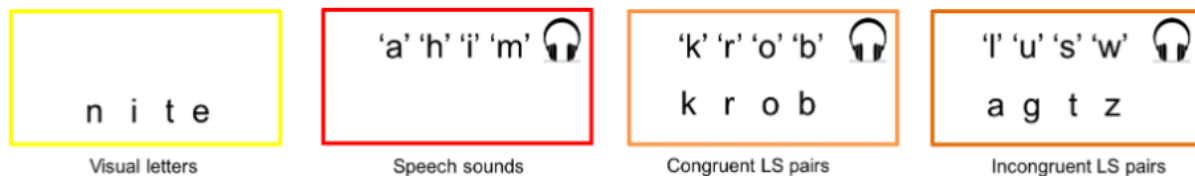


Figure 1.2.2. Exemplary mini-blocks consisting of 4 different stimuli presented consecutively within each condition.

To analyze the data from this type of neuroimaging design we can focus on basic sensory aspects of letter and speech integration and compare multisensory congruent LS activation to unimodal letters and unimodal speech sounds activation (congruent LS > letters + speech sounds). When the activation for a multimodal congruent condition is higher than for summed unimodal conditions we refer to this effect as a super-additive effect. When there is an opposite pattern we obtain a sub-additive effect. This approach is commonly used in letter and speech sound integration studies (Barrós-Loscertales et al., 2013; Kronschnabel et al., 2014; Ross et al., 2022) and was adopted for fMRI from animal electrophysiology studies, where active neurons exhibited a more robust response to multimodal stimuli than to unisensory stimuli (Stein & Stanford, 2008; Xu et al., 2014). The general concept that those criteria are based on is that the brain response to elements processed independently should be additive. Infringement of additivity can indicate the presence of multisensory interactions or (non-additive) attentional or cognitive processes. The ventral part of the human left superior temporal sulcus (STS) was shown to fulfill both super- and sub-additivity criteria (Calvert et al., 2000). However, this conjunction of criteria was relatively often not replicated in fMRI studies (Hocking & Price, 2008) and therefore a relaxed criterion was proposed. The formula for relaxed criterion is: congruent LS > (letters + speech sounds) / 2, which simply compares the mean of unisensory conditions to the multimodal congruent condition (Beauchamp, 2005). Studies show that the left and the right STS and PT have stronger response to multisensory condition than to the mean of unisensory conditions (Calvert et al., 2000; van Atteveldt, Formisano & Blomert et al., 2007; van Atteveldt et al., 2004).

Higher-level associative (orthographic and phonological) aspects of letter and speech sound integration can be studied by comparison of multimodal conditions, and looking for distinguishable brain responses to congruent versus incongruent LS pairs. This effect, called a congruency effect, is a well-established concept proposed by Nienke van Atteveldt in 2004. However, the congruency effect was examined only by a handful of fMRI studies, and the results are inconclusive in terms of its direction, which might depend on age of the participants, language transparency, tasks and stimuli used in fMRI scanner (Richlan, 2019). Some researchers, used active matching paradigm (i.e. indicating via button press whether

the letter and the speech sound match; e.g. van Atteveldt et al., 2007), specific speech sound target detection (i.e. detecting /a/; e.g. Blau et al., 2008), non-letter and non-speech sound target detection (i.e. detecting simple visual – ### –auditory—piano sound—and audiovisual targets among LS pairs; e.g. Kronschnabel et al., 2014) and one-back task (i.e. detecting repeated stimuli; e.g. Francisco et al., 2018). Some of the studies used not only simple letters but also unimodal and multimodal consonant-vowel-consonant (CVC) syllables (Kronschnabel et al., 2014).

As mentioned above, a variety of different fMRI tasks have been employed to examine brain structures involved in LS association testing for the congruency effect. Not surprisingly, the task can have a large effect on the pattern of brain activation (van Atteveldt et al., 2007) and on the presence and/or direction of the congruency effect (Kronschnabel et al., 2014). Among the presented tasks, presentation of letters and speech sounds (unisensory conditions) as well as congruent and incongruent letter-speech sounds (LS) pairs (multisensory conditions) was the most common (van Atteveldt et al., 2004; Blau et al., 2009, Blau et al., 2010).

This paradigm was used in the studies where Dutch-speaking individuals (10-year-old children – Blau et al. 2010 and adults – Blau et al. 2009) with and without dyslexia were compared. Both typically reading adults (van Atteveldt et al., 2004; Blau et al., 2009) and children (Blau et al. 2010) presented congruency effect in the superior temporal cortex. This means that the activation during the presentation of congruent LS pairs was stronger than during the presentation of the incongruent LS pairs. Dyslexia influenced neural correlates of both unimodal and multimodal conditions in both children and adult readers. Independently of age group studied, participants with dyslexia had lower STC activity during speech sounds processing compared to typical readers. Additionally, in children group fusiform gyrus (FG) was also less active in dyslexic group than in typical readers. The STC (and in case of the children group) activity during speech sounds processing was related to phonological skills which in turn predicted reading skills level. When it comes to multimodal condition, both children and adults with dyslexia have shown a decrease in the congruency effect in STC. In children study, the size of the congruency effect was additionally positively correlated with LS matching performance and reading skills level.

As mentioned above not only dyslexia but also orthographic transparency can influence the nature of the differences between the congruent and incongruent conditions-related activations. The relationship between orthographic transparency and the direction of congruent vs incongruent differences is not clear though. To reiterate, Dutch-speaking (semi-transparent orthography) typical readers has shown congruency effect (congruent > incongruent LS pairs activation). Contrary, Swiss-German (also a semi-transparent orthography) typically reading adolescents presented an inverse, incongruency effect

(incongruent > congruent LS pairs activation) in left STG and FG (Kronshabel et al., 2014). In this study the congruency effect was presented by a group of readers with dyslexia. At the same time, the groups did not differ in super-additive effects (examined using a relaxed criterion (Beauchamp, 2005), present in the middle STG clusters nor in sub-additive effects found in superior parietal, middle and superior temporal, and precentral regions. The lack of group differences in super-additivity contrasts argues against a general or basic audiovisual integration deficit in dyslexia (Kronshabel et al., 2014). The incongruency effect was also observed in an opaque orthography – in English-speaking adult typical readers (Holloway et al., 2015). To complicate the matter even more these studies use slightly different paradigm (single letters and speech-sounds pairs of syllable level stimuli). Age of participants may have also play a role here.

In the last two years, the processing of unimodal letters and speech sounds has been examined longitudinally during reading acquisition in typical or atypical reading development. German-speaking children showed early audiovisual integration effects that were characterized by higher activation for incongruent than congruent letter-speech sound pairs in the inferior frontal gyrus and ventral occipitotemporal cortex (Karipidis et al., 2021). Audiovisual processing in the left STG significantly increased from the pre-reading to early reading stages. Additionally, activation in the left STG, inferior frontal gyrus, and ventral occipitotemporal cortex increased in children with typical reading fluency skills. At the same time, poor readers did not show the same development in these regions. Correlations between reading fluency (measured after two years of learning) and (in)congruency effect at the pre-reading stage in bilateral STG were observed suggesting that the latter might be a predictor of reading development (Karipidis et al., 2021).

Additionally, German-speaking children were tested in an implicit audiovisual non-word target detection task aimed at characterizing differential activation to congruent and incongruent audiovisual non-word pairs. The whole design consisted of unimodal auditory or visual non-words and congruent or incongruent multimodal pairs of non-words (like “rof”, “gof”) and children had to press the button whenever the target appeared (turtle (visual) or bell chime (auditory)). While children’s brain activation did not differ between congruent and incongruent non-word pairs in the first grade, an incongruency effect emerged in bilateral inferior temporal and superior frontal gyri in the second grade. The authors discuss this difference by relating the incongruency effect to the detection of audiovisual mismatch during processing LS pairs, which should become progressively automatized with longer reading practice (Wang et al., 2020).

Chapter I.3. Dyslexia

Definition, theory and genes

Dyslexia is defined as specific difficulties in learning to read and write (according to ICD-10 F81.0 and DSM V "315.0"). The diagnostic criteria exclude difficulties resulting from sensory deficit or neurological damage (Silani et al., 2005; World Health Organization, 2008). Dyslexia cannot also be an effect of insufficient educational opportunities or low intelligence. Morbidity of dyslexia is usually estimated to be around 5 to 12% of the population, independently of the language studied (Shaywitz, 1998), however a recent study suggest that it may affect even 20% of children.

The symptoms of dyslexia, apart from deficits in reading accuracy and fluency, are diverse. Phonological awareness, attentional and automatization processes, as well as certain visual and auditory processes are domains that are shown to be deficient in individuals with dyslexia. The variability of behavioral manifestations led to a suspicion that dyslexia is not a homogenous phenomenon and can be described in terms of several subtypes (Démonet et al., 2004; Ramus et al., 2003; Shaywitz & Shaywitz, 2005; Jednorog et al., 2014). Nevertheless, consistently the most described and the one that will be the most relevant for the current dissertation is the phonological awareness deficit. Phonological awareness is the ability to understand and manipulate (e.g. delete a phoneme from a word, produce a word rhyming with the target) the structure of spoken words. It is hypothesized that children with dyslexia have deficient phonological representations or the mechanisms that enable access to these representations (Snowling, 1981). Children with problems in phonological processing are more prone to difficulties in learning letter-speech sound associations, as fragmenting a stream of speech is a challenge for them (Snowling, 1981; Brady and Shankweiler, 1991, Jednoróg et al., 2010). Letter-speech sound correspondences acquisition is on the other hand crucial for efficient decoding of print.

Though neural correlates of difficulties in reading are diverse too (Ramus et al., 2003), dyslexia is considered to have a neurobiological basis (Habib, 2000 and Ramus, 2004). What is more, having a parent or a sibling diagnosed with dyslexia increases the risk of suffering from this disorder too up to 33 - 66 percent (Fisher & Francks, 2006; van Bergen et al., 2014), which suggests genetic components in dyslexia etiology (Smith et al., 1998). Accordingly, reading difficulties are more common in monozygotic twins (84–100%) than in dizygotic twins (20- 35 percent; Pennington & Olson, 2005). Familial history of dyslexia is thus an important risk factor. The Adult Reading History Questionnaire (ARHQ) is a common measure of familial risk of dyslexia (Lefly & Pennington, 2000) as a self-reported questionnaire measuring parents' lifetime reading experiences. ARHQ was used in studies that show that children with familial

risk of dyslexia often have lower performance on phonological and other early literacy measures than children without such risk (Dandache et al., 2014). It is important to mention that fortunately not all children with familial risk will develop dyslexia. Orthographic transparency may influence the importance of the familial risk factor. Children learning to read in more opaque orthographies are the most endangered with reading difficulties (Dębska et al., 2016). At-risk Polish-speaking children only had lower scores in the orthographic awareness test, while English-speaking pre-schoolers performed worse in various phonological (Kovelman et al., 2012; Pennington & Lefly, 2001; Raschle et al., 2012) and reading-related tests (Gallagher et al., 2000).

Neuronal deficits in dyslexia

Richlan et al., (2009 & 2011) conducted meta-analyses of reading-related dysfunctions in dyslexia and identified significant functional brain abnormalities in the left hemisphere brain areas. In these meta-analyses only studies in which reading or reading-related tasks were performed were taken into consideration. Lower activation in the left temporoparietal cortex, occipitotemporal cortex, and inferior frontal gyrus was typically observed in dyslexic readers compared to controls. Additionally, the left precentral gyrus consistently exhibited higher activation in dyslexics compared to controls (Richlan et al., 2009). In Chyl et al., (2019) it was shown that the left inferior frontal gyrus and ventral occipitotemporal cortex are less active during print processing in dyslexic readers than in the aged and reading matches controls. An additional meta-analysis focused on orthography-specific abnormalities (Martin et al., 2016) and found common underactivation in dyslexic readers of both transparent and opaque orthographies in the left occipitotemporal cortex including the visual word form area.

Findings on structural differences in grey matter are less clear (Jednoróg et al., 2015). Two meta-analyses (Linkersdörfer et al., 2012; Richlan et al., 2013) found that there was little consistency across investigations. The most frequently reported areas are: the left posterior temporal and tempo-parietal regions, where both increased and decreased grey matter volume (GMV) was found in dyslexic readers (Brambati et al., 2004; Hoeft et al., 2007; Silani et al., 2005; Steinbrink et al., 2008). GMV reduction was systematically reported in the left inferior frontal gyrus (Brown et al., 2001; Eckert et al., 2005), the occipito-temporal regions bilaterally (Eckert et al. 2005; Brambati et al., 2004; Kronbichler et al., 2008) and the cerebellum (Brown et al., 2001; Brambati et al., 2004; Eckert et al., 2005; Kronbichler et al., 2008). Finally, there are studies that found no discernible differences in GMV between the control and dyslexic readers groups (Pernet et al., 2009; Tamboer et al., 2015).

Chapter I.4. Braille reading

Letters presented visually, like in the Latin alphabet, are the most common signs we use to represent speech sounds in alphabetic languages. However, we cannot assume that phonetic representation is assigned only to the visual modality. People can also use somatosensory systems to transfer phonetic information, and Braille reading is a notable example. Braille letters - Braille's code consists of raised dots arranged in a cell that contains six possible dot positions, and each letter, like in the Latin alphabet, has a unique composition of dots. Louis Braille invented the Braille alphabet in 1824, and his inspiration was Barbier's dot-code system. The idea was to use the top four dots (1, 2, 4, 5) for the first ten letters. Then adding the dot number 3, he made subsequent ten letters and finally the dot number 6 for the last six letters. This rule is not applicable to the letter 'w' because at that time, in France the letter 'w' was not commonly used. This idea alone does not allow to include Polish letters such as *ą*, *ę*, or *ó*. As a result of extensive work done by Róża Czacka, most Polish letters are created by adding the dot number 6 to baseline letters. For example, 'a' is dot number 1 but 'ą' is dot number 1 and number 6, for 'e' dot number 1 and 5, and 'ę' dots number 1, 5, and 6. For the majority of alphabetic languages, the structure of Braille script is completely analogical to the print alphabet. One example of such a language is Polish, where every Braille symbol has its exact analogue in the Latin alphabet and the phoneme-grapheme mappings are conserved (i.e. uncontracted Braille).

In people with visual impairments the visual letters are possibly replaced with tactile Braille representations (Sadato et al., 1998). The brain may generate a phonetic representation in a second modality, such as visual or tactile, provided that the sound-symbol relationship is trustworthy (Sadato 2005). Blind Braille readers are on par with their sighted classmates in terms of phonological knowledge (Greaney & Reason 1999; Gillon & Young 2002). There is also proof that blind readers code Braille tactually and phonologically (Millar 1975; Pring 1982). As it was already mentioned, sighted, typical readers start literacy acquisition from the logographic stage and after the school entrance smoothly proceed to the alphabetic, and orthographic stage. Blind children do not have, or to be more specific, most of the children do not have any contact with the Braille alphabet before school. Some of the blind children start to recognize symbols, lines, and straightforward shapes in kindergarten, but, at least in Poland, they do not learn Braille letters. This is why the logographic stage is absent in the blind population. As it was mentioned in Chapter I.1, when children enter school, they learn that all the words are built from small units – phonemes - speech sounds. When this ability is fully automatized they move from serial to parallel reading. Braille readers use a more sequential, grapho-phonological strategy for reading (Daneman, 1988; Mommers, 1976;

Perea et al., 2015; Pring, 1982; Veispak et al., 2012a, 2012b; 2013). What is important, this strategy is also used by sighted readers but mainly at the early stages of reading development (Altani et al., 2018) or for reading unfamiliar words or pseudowords (Veispak et al., 2012b). Blind readers use this strategy constantly throughout all reading levels - from the beginning to the full automatization (Veispak et al., 2012b), though there is evidence that they read words faster than letters comprising them (Krueger, 1982). In blind Braille readers finger sensitivity, as measured with the grating orientation task (GOT), contributes to the accuracy of reading short pseudowords and to the reading speed of familiar longer words (Veispak et al., 2012a; 2013). There is no consensus about the blind's phonological awareness abilities as compared to the sighted (the blind better than the sighted: Greaney & Reason, 1999; the sighted better than the blind: Dodd & Conn, 2000; no differences: Veispak et al., 2012, 2013). These inconsistencies might be related to the tasks employed or to the participants' age and reading level.

Letter and speech sound association in blind Braille readers

The neural correlates underlying audiotactile phonetic processing have not been studied in the blind on a large scale. However, some hypotheses can be drawn from studies which investigated audio-tactile integration in the sighted (Fuxe et al., 2002) or vibrotactile and auditory stimuli (Schürmann et al., 2006; Beauchamp et al., 2008). In such studies, STC was found as a convergence area and with enhancement of activations for both conditions. Beauchamp et al., (2008) demonstrated visual, auditory, and tactile convergence in a subregion of posterior STS and verified that this region is involved in multisensory integration of tactile and audiovisual information. Later studies on multisensory object perception that used semantically corresponding audio-tactile stimuli reported concordant findings (Schneider et al., 2011; Kassuba et al., 2011, 2013). The implication that STC is the site of audiotactile integration is also supported by the electroencephalography studies (Fuxe et al., 2000; Gobbelé et al., 2003; Murray et al., 2005). There is only one study that investigated audiotactile phonetic processing in early-blind Braille readers (Pishnamazi et al., 2016). The task was to observe the appearing stimuli, spoken nonsense syllables, and corresponding tactile Braille syllables. Congruency effects were observed in the frontal lobe and in the cerebellum. The authors suggested that contrary to the sighted, blind subjects process letters and sounds separately due to the mal-development of multisensory neural circuits. It is important to mention that in this study bigger units – syllables were presented, the sample size was relatively small (N = 16) and there were no sighted controls, which greatly limits the merit of these findings

Part II: Original studies

Chapter II.1. Study aims

The overarching aim of the present thesis has been to examine the letter and speech sound integration in the Polish-speaking population. Firstly, I wanted to examine how this process develops in the Polish language. Thus, the first goal of this thesis was to reveal the time-course of LS acquisition and LS integration in Polish children (Chapter II.2, Experiment 1). I hypothesized that most children should master LS association at the end of the first year of formal education (similar to Dutch children; Blomert and Vaessen, 2009), while the reaction times of LS discrimination decisions should show a gradual decrease throughout the primary school as it was the case in Dutch children.

The second goal was to examine brain activation for letters and speech sounds in children with and without familial risk for dyslexia at the beginning of formal reading instruction and retrospectively assess which of the observed effects are present in children who developed dyslexia (Chapter II.3, Experiment 2). I hypothesized that if a different pattern of neural response for LS associations in the left STC is inherent to reading deficits, it should be already present at the beginning of literacy acquisition in children with familial risk, especially those who later develop DYS. If, however, it is a consequence of impoverished reading experience, at risk children should not differ from their peers in brain response to letters, speech sounds, and LS pairs.

The third aim was to check for developmental trajectories in the neural correlates subserving the processing of letters, speech sounds, and LS associations at different stages of reading development. (Chapter II.4 Experiment 3). Experiment 3 was designed to test our hypothesis directly, based on the findings from Experiment 2. i.e., whether higher incongruity effect in beginning readers reflected an early stage of LS integration that, with practice in reading, reversed into congruity effect. We compared changes in brain activation in typical and dyslexic readers after two years of reading education. Given the primordial role of phonological awareness in reading, insights into the neural correlates subserving the processing and integration of letters and speech sounds at different stages of reading development seem critical for understanding the emergence of reading difficulties in dyslexia.

Finally, the aim of Experiment 4 (Chapter II.5) was to explore whether the direction of the congruity effect and the brain areas involved in LS integration are the same or different for blind people. I hypothesized that tactility presented letters and auditory presented speech sounds should be integrated in STC, as in the sighted individuals.

Chapter II.2. Experiment 1

Research question

From studies based on different languages and teachers' observations, we know that typically developing children learn the associations between letters and speech sounds within months, most of them even before formal reading instruction (Blomert, 2011). However, data on the pace of learning letter and speech sound association in Polish has been missing and the current experiment aimed to test this phenomenon. I wanted to check how long it takes to automatize letter and speech sound associations and how this ability relates to letter knowledge, reading, phonological skills, and rapid naming.

Methods

Participants

We have tested 340 children from primary schools and kindergartens. We obtained ethical consent for this study from the Cardinal Stefan Wyszyński University in Warsaw Ethical Committee according to the Declaration of Helsinki. All children and their parents gave informed consent to the study. All children lived in Poland and followed formal education in Poland from the kindergarten level. We recruited children from the final grade of kindergarten to the 8th grade of the primary school, aged 5 to 16 years (mean age = 9.46, SD = 2.96). Because of technical problems, we excluded 15 children from the analyses.

Additionally, the pandemic situation in the world hindered gathering data at schools, which significantly reduced the sample of children attending the 6th grade (see Table II.2.1.). Therefore, for certain analyses we pooled participants attending the 6th or higher grades. Sanitary precautions (e.g., wearing masks) prevented gathering of some complimentary data. For example, it was not possible to conduct phonological or RAN tests with all the children. The numbers of the participants who underwent each examination are reported in Table II.2.1.

Table II.2.1. Grade distribution

Grade	Kindergarten	1st	2nd	3rd	4th	5th	6th	7th	8th	6th+
<i>N</i>	23	100	37	25	37	31	10	21	41	72

Note. *N* - number of students

Behavioral Measures

The recruited children performed a battery of reading and phonological tests. Letter knowledge test (containing upper and lower cases, Szczerbiński & Pelc-Pekala, 2013) was performed only with children from the kindergarten level to the 2nd grade because of the ceiling effect in later grades. Words and pseudowords reading test (score: the number of correctly read words or pseudowords in a minute), was conducted only with children who knew at least 30 letters (Szczerbiński & Pelc-Pekala, 2013). Two parts of the 'Nieznany język' test were used to measure phonological awareness (PA). The pseudowords comparison part (children had to judge if the pseudowords 'majk' and 'najk' were the same or different) was used with all the children. Children from the 3rd to 8th grade also took the differences detection part of the test (children had to judge if the pseudowords 'majk' and 'najk' were different and tell what the difference was; Bogdanowicz et al., 2009). For both parts of the test the outcome score was accuracy. Rapid automatized naming was examined with objects and letter naming subtests and the time to name the stimuli in each subtest was used as the outcome score. The letter naming subtest was conducted only with children who knew at least 30 letters (Bogdanowicz et al., 2009).

Additionally, to examine letter and speech sound association, all children performed a computer-based 'Phonemes to letters test.' A schematic view of the test is presented in Figure II.2.1. Children were presented with single letters on the screen and simultaneously with phonemes via headphones. The children were asked to press the green button if the letter and speech sound were congruent and the red button if the letter and speech sound were incongruent; accuracy and reaction time were measured as the score in this task.

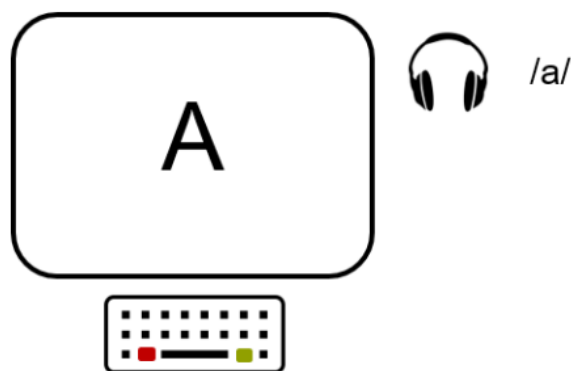


Figure II.2.1. A schematic representation of the screen from a computer-based 'Phonemes to letters test'.

Data analysis

We calculated accuracy and median reaction time for correct responses in the 'Phonemes to letters test'. Since several younger participants performed this test at chance level, we ran the analyses twice. First, for the whole group of children, and then again, excluding children with accuracy below 59%. Nineteen children had accuracy scores below chance level, but 47% of this group were kindergarten children. Since the results for both comparisons were almost identical, here we present only the results for the whole group of children.

We checked the normality distribution of the gathered data (see Table II.2.2.) and, based on the Kolmogorow-Smirnow test results, we applied the nonparametric tests. To examine differences between grades for RT time and accuracy we used the H Kruskal-Wallis test with post-hoc comparisons with Bonferroni correction. Spearman correlation coefficients were used to test the relation between accuracy and RT in 'Phonemes to letters test' and other behavioral measures.

Due to the fact that the age range in this study was 10 years we could not use the same behavioral sets of tests for all the participants (i.e. letter knowledge was tested only in children up to the second grade, while PA II in children from the third and higher grades). Therefore, we ran two separate regression tests examining whether the LS association is a significant predictor of word reading above and beyond other behavioral measures. The first regression was conducted for children from kindergarten to the second grade with letter knowledge, reaction time and accuracy in 'Phonem to letters test', PA I test and RAN letters and objects as predictors. This model included only children who could recognise at least 30 letters, so the word reading test had been performed (N = 142).

The second model included children from the third grade and included reaction time and accuracy in 'Phonem to letters test', PA I and II test, RAN letters and objects as predictors (N = 150). All the statistical analyses were conducted in SPSS Statistics ver. 27 for Macintosh.

Table II.2.2. Descriptive statistics of analyzed data and Kolmogorov-Smirnov test results

	N	M	Me	SD	Sk.	Kurt.	Min	Max	K-S	p
Accuracy in										
'Phonemes to letters test'	325	88.42	92.78	12.44	-2.34	6.45	12.37	100.	0.20	< 0.001
RT(median) in										
'Phonemes to letters test'	325	0.71	0.65	0.39	1.69	5.30	0.13	3	0.07	0.200
Letter knowledge	160	48.40	57.00	18.53	-1.20	0.09	1	64	0.26	< 0.001
Word reading	302	60.76	60.50	39.96	0.06	-1.39	0	137	0.21	< 0.001
Pseudoword reading	301	37.14	38.00	22.01	0.15	-0.87	0	90	0.14	0.042
PA test I -										
Pseudowords comparison	310	21.44	22.50	3.57	-1.50	1.95	6	25	0.20	< 0.001
PA test II -										
Pseudowords differences detection	155	13.32	14.00	4.03	-0.77	-0.30	2	18	0.53	< 0.001
RAN letters	291	31.08	28.00	13.22	1.95	5.12	11	93	0.12	0.103
RAN objects	318	52.24	47.00	33.61	10.15	145.96	21	545	0.11	0.186

Note. N – number of observations, Me – median, Sk. – skewness, Kurt – kurtosis, Min – minimal value, max – maximal value, K-S – Kolmogorov-Smirnov value, p - significance

Results

Accuracy in 'Phonemes to letters test' and letter knowledge by grades

Table II.2.3. presents the number of children with accuracy below or above 80% and 90% in 'Phonemes to letters test'. Most children from the first and higher grades performed above 80% correct. However, only from the third grade up the majority of children had the performance above 90% correct.

Table II.2.3. The number of children with scores below or above 80% and 90% for accuracy in 'Phonemes to letters test' in each grade.

Grade	Accuracy			
	< 80%	> 80%	< 90%	> 90%
Kindergarten	16 (69.6%)	7 (30.4%)	19 (82.6%)	4 (17.4%)
1st	18 (18%)	82 (82%)	57 (57%)	43 (43%)
2nd	9 (24.3%)	28 (75.7%)	17 (57%)	20 (43%)
3rd	1 (4%)	24 (96%)	3 (12%)	22 (88%)
4th	2 (5.4%)	35 (94.6%)	12 (32.4%)	25 (67.6%)
5th	1 (3.2%)	30 (96.8%)	3 (12%)	22 (88%)
6th	0 (0%)	10 (100%)	1 (10%)	9 (90%)
7th	0 (0%)	21 (100%)	3 (14.3%)	18 (85.7%)
8th	1 (2.4%)	40 (97.6%)	5 (12.2%)	36 (87.8%)

Between grades comparison

Next, we compared accuracy and RT in 'Phonemes to letters test' between the grades. The effect of grade was significant for both accuracy, $H = 102.08$, $p < 0.001$ and RT, $H = 162.02$, $p < 0.001$. Post-hoc comparisons are presented in Table II.2.4. for accuracy and in Table II.2.5. for RT. For accuracy, the kindergarten children had lower performance than children from all other grades (from the 1st and 2nd only on a trend level). Children in the 1st grade had lower performance than children from the 3rd to 6th+ grade.

For RT, children in kindergarten were slower at performing the task than children from the 3rd to 6th+ grade. Children in the 1st grade had higher RT than children from the 4th to 6th+ grade. Generally, children in the 6th+ grade had lower RT than all younger children except those in

the 5th grade. In addition, accuracy and reaction times are presented on scatter plots - Figure II.2.2. and Figure II.2.3.

Table II.2.4. P-values for post hoc comparisons for accuracy between children from different grades

Grade	Kindergarten	1st	2nd	3rd	4th	5th
1 st	0.088	-				
2 nd	0.097	1	-			
3 rd	< 0.001	< 0.001	0.005	-		
4 th	< 0.001	0.092	1	1	-	
5 th	< 0.001	0.065	0.747	1	1	-
6 ^{th+}	< 0.001	< 0.001	< 0.001	1	0.036	0.156

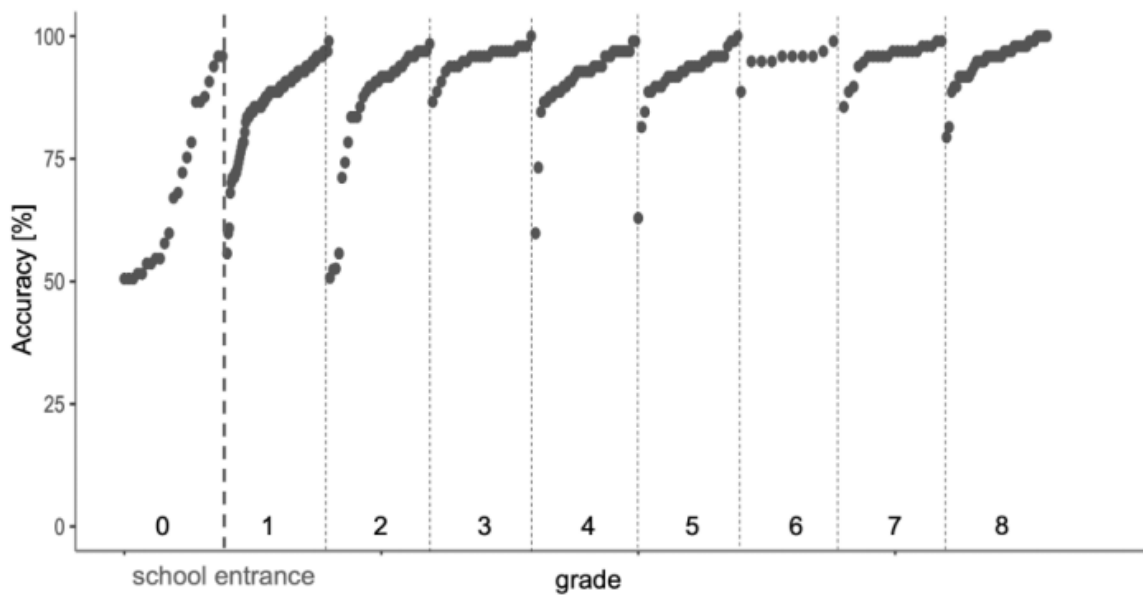


Figure II.2.2. Mean accuracy for different grades

There was a strong positive correlation between grade and accuracy in 'Phonemes to letters test', $\rho = 0.53$, $p < 0.001$. There was also a negative moderate correlation between grade and RT, $\rho = -0.31$, $p < 0.001$

Table II.2.5. P -values for post hoc comparisons for RT between children from different grades

Grade	Kindergarten	1st	2nd	3rd	4th	5th
1 st	0.639	-				
2 nd	0.042	1	-			
3 rd	0.056	1	0.005	-		
4 th	< 0.001	< 0.001	0.130	0.439	-	
5 th	< 0.001	<0.001	0.028	0.120	1	-
6 ^{th+}	< 0.001	< 0.001	< 0.001	<0.001	0.012	0.217

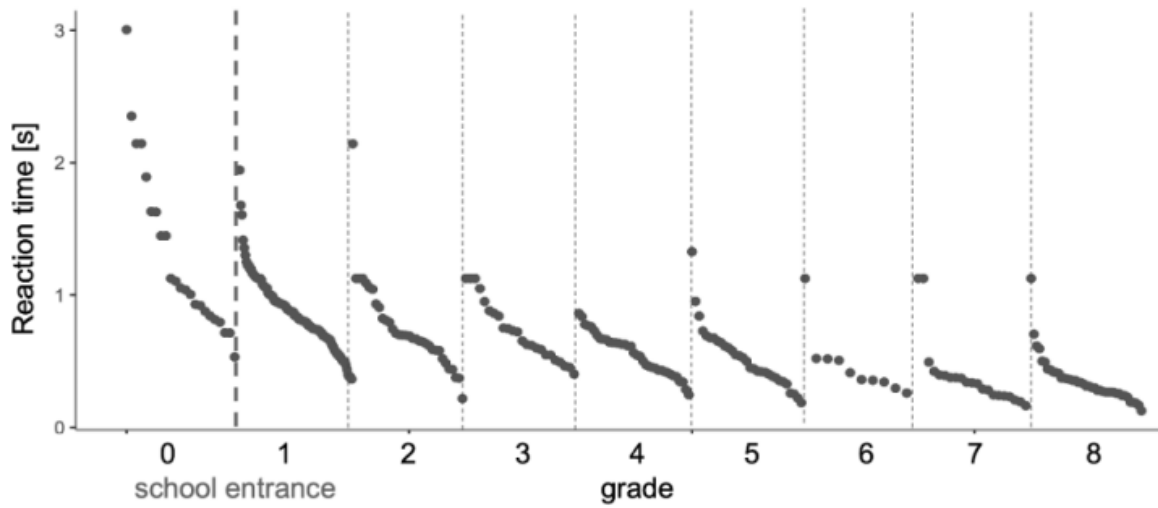


Figure II.2.3. Median RT for different grades

Correlations

All the correlation coefficients are presented in Table II.2.6. with p-values and also in Figure II.2.4. Moderate positive correlations were observed between accuracy in 'Phonemes to letters test' and letter knowledge, word and pseudoword reading, and PA test I (pseudoword comparison). Negative moderate correlations were found with the time needed to name letters and objects in the RAN test. For reaction times we observed a different direction of the correlations – positive with RAN tests and negative with word and pseudoword reading, and PA I and II test (pseudoword comparison and difference detection). Reaction time and accuracy in 'Phonemes to letters test' were weakly negatively correlated.

Table II.2.6. Correlations between accuracy and RT in 'Phonemes to letters test' and reading, RAN and phonological tests

	Accuracy		Reaction time (median)	
	Rho	p	Rho	p
Accuracy	-	-	-0.31	< 0.001
Reaction time (median)	-0.31	< 0.001	-	-
Letter knowledge	0.63	< 0.001	-0.163	0.075
Word reading	0.41	< 0.001	-0.60	< 0.001
Pseudoword reading	0.40	< 0.001	-0.58	< 0.001
PA test I - Pseudoword comparison	0.32	< 0.001	-0.27	< 0.001
PA test II- Pseudowords differences detection	0.29	<0.001	-0.57	< 0.001
RAN letters	-0.40	< 0.001	0.58	< 0.001
RAN objects	-0.43	< 0.001	0.62	< 0,001

Note. Rho - Spearman coefficient, p - significance

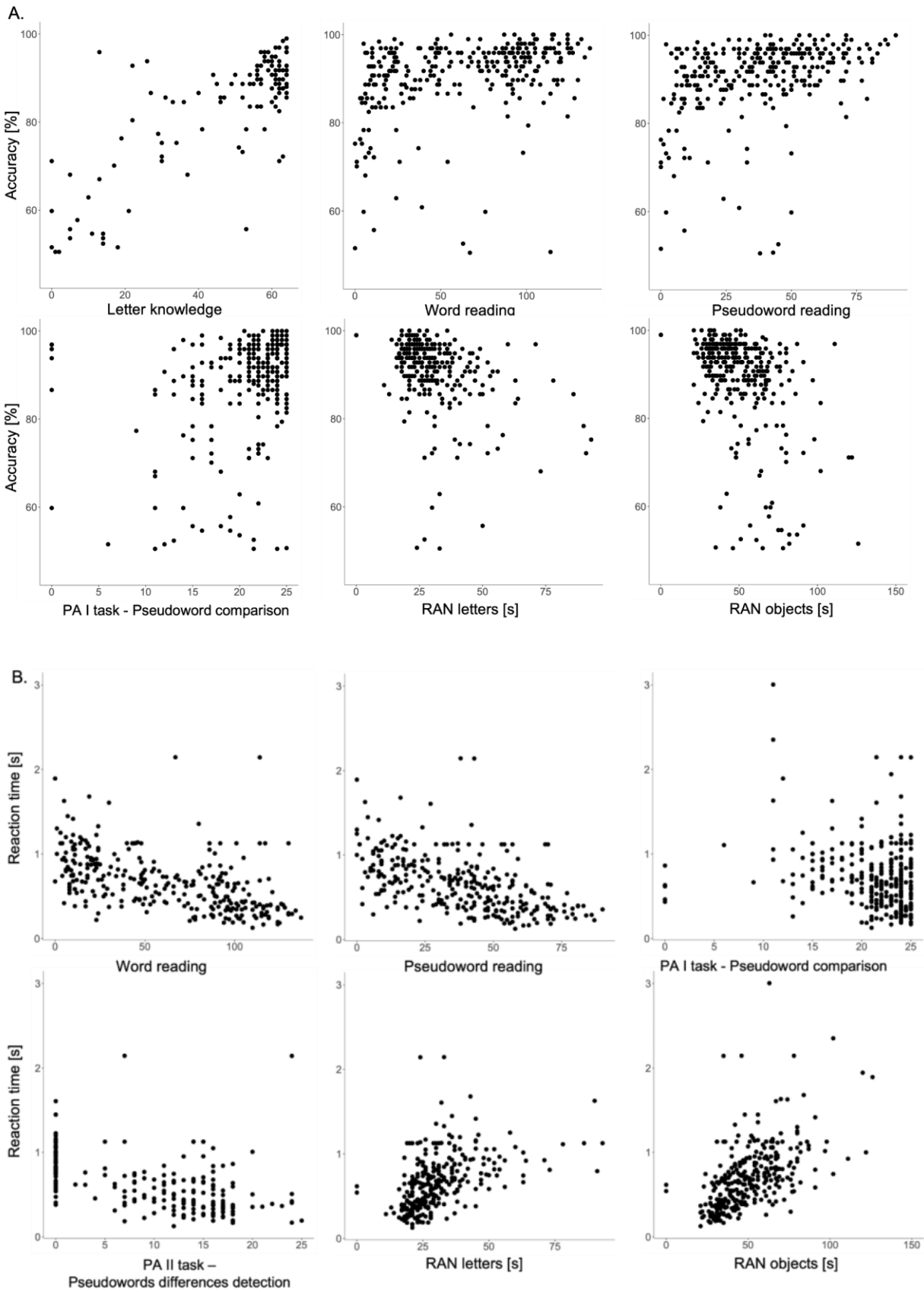


Figure II.2.4. Correlation with behavioral measures with accuracy (VI.4.A) and RT (VI.4.B)

Linear regression models

Model 1.

Model for younger children (0 - 2nd grade) concerning the simultaneous impact of accuracy and reaction time in “Phonemes to letter test”, letter knowledge, PA I task and RAN letters and objects on word reading demonstrated that letter knowledge and RAN letters were statistically significant and included in the model. The model fitted the data well, $F(6,142) = 12.22$, $p < 0.001$, and explained 44% of the variance.

Table II.2.7. Results of linear regressions for word reading for children from kindergarten to second grade

	<i>B</i>	<i>SE</i>	<i>Beta</i>	<i>t</i>	<i>p</i>	<i>95% CI</i>	
Constant	13.64	19.96		0.68	0.50	-26.07	53.36
Letter knowledge	0.56	0.21	0.29	2.63	0.01	0.14	0.99
Accuracy	-0.04	0.13	-0.03	-0.31	0.76	-0.30	0.22
Reaction time (median)	-6.08	5.61	-0.09	-1.08	0.28	-17.24	5.08
PA test I - Pseudowords comparison	0.82	0.54	0.14	1.53	0.13	-0.25	1.88
RAN letters	-0.39	0.17	-0.30	-2.34	0.02	-0.73	-0.06
RAN objects	-0.15	0.14	-0.12	-1.12	0.27	-0.43	0.12

Note. B - Unstandardized Coefficient, SE - standard error, Beta - Standardized Coefficient, t - value for t-test, p - significance, 95 % CI - 95 % Confidence Interval for B

Model 2.

Model for older children (from the 3rd to 8th grade) concerning the simultaneous impact of accuracy and reaction time in ‘Phonemes to letter test’, RAN letters and objects, and PA tasks on word reading demonstrated that PA test II - Pseudowords differences detection, RAN letters and RAN objects were statistically significant and included in the model. The model fitted the data well, $F(5,150) = 34.01$, $p < 0.001$, and explained 51% of the variance. It is important to mention that RAN object task is strongly related to RT in ‘Phonemes to letter test’ and cuts out the RT from the model, in addition, p-value for the RT is on a trend level ($p = 0,102$).

Table II.2.8. Results of linear regressions for word reading for children from third to eight grade

	<i>B</i>	<i>SE</i>	<i>Beta</i>	<i>t</i>	<i>p</i>	<i>95% CI</i>	
Constant	112.80	30.59		3.69	< 0.001	52.22	173.39
Accuracy	0.01	0.20	0.00	0.06	0.955	-0.38	0.40
Reaction time (median)	-12.96	7.87	-0.12	-1.65	0.102	-28.56	2.63
PA test I - Pseudoword comparison	0.96	1.07	0.07	0.90	0.371	-1.16	3.08
PA test II- Pseudowords differences detection	1.61	0.41	0.31	3.91	< 0.001	0.80	2.42
RAN letters	-1.11	0.38	-0.22	-2.89	0.005	-1.87	-0.35
RAN objects	-0.92	0.25	-0.31	-3.74	< 0.001	-1.41	-0.43

Note. B - Unstandardized Coefficient, SE - standard error, Beta - Standardized Coefficient, t - value for t-test, p - significance, 95 % CI - 95 % Confidence Interval for B

Discussion

This experiment aimed at examining when Polish-speaking children master letter and speech sound associations. Results from the 'Phonemes to letters test' showed that a relatively simple ability to distinguish between correctly and incorrectly associated letters and speech sounds pairs differs between children in different grades along with different reading experiences. What is essential to note is that formal phonics-based reading instruction in Poland begins in the first grade. However, some literacy experience could be present even before school onset. The Polish language has a relatively transparent orthography with grapheme to phoneme correspondence higher for reading than for spelling (Schüppert et al., 2017).

During the examination of children in schools, it was found that most children know the Polish alphabet quite well in the first grade. Already, in the first grade around 80% of children reached 80% accuracy in deciding whether individual letters matched specific speech sounds. Generally, there was a strong correlation between letter knowledge and accuracy in 'Phonemes to letters test' ($r = -0.63$, $p < 0.001$). These results can be related to previous findings in other languages. In Dutch, a relatively transparent language, most children master letter–speech sound associations within one year of reading instruction (Wentink & Verhoeven, 2003; Vaessen et al., 2009). Even in English, with its opaque orthography, letter and speech sound associations should be established within a few years of reading instruction (Siegel & Faux, 1989; Snowling, 1980; Hardy et al., 1972). In an English study, around 80 % of children obtained maximum scores (the task contained 33 representations of letters) within a year of undergoing reading instruction when they were asked to choose whether letters paired with speech sounds (Hardy et al., 1972). We can say that learning the letter and speech sound correspondence is a relatively straightforward process to acquire which children master in the first year of reading instruction irrespective of the differences in language transparency. Despite the fact that in the 3rd grade, we can observe a ceiling effect in accuracy (the majority of children reach performance above 90%) in the 'Phonemes to letters test', the RT still shows gradual decrease until 6+ grade. These findings show that automatization of letter and speech sound correspondence takes longer and may have important implications for potential interventions. Since this skill is still developing, there might be a wider window for intervention than previously thought.

Both accuracy and reaction times from the 'Phonemes to letters test' correlated with letter knowledge, reading words and pseudowords, phonological awareness, and RAN tasks. Letter knowledge was found to be an important predictor of both accuracy and fluency of forming LS associations, and it is recognized as an important predictor of reading readiness

(Snow et al., 1998).

Our findings, in line with previous longitudinal study on English speaking children (Clayton et al., 2020), show that LS associations are established early, but do not predict variations in the reading skill over and above other language skills. As regards early reading skills in younger children, letter knowledge and RAN letters were strong independent predictors of reading skill. This result is in line with previous studies stating that letter knowledge (Foulin, 2005) or letter knowledge, together with phonological awareness and alphanumeric RAN (Clayton et al., 2020) are the best predictors for reading skill. Similarly, for older children neither accuracy nor RT in 'Phonemes to letters test' were among the unique predictors of reading skill. Instead, phonological awareness (PA II task) and RAN letters and objects were found to be significant predictors of reading. These findings suggest that at later stages of reading development more explicit phonological awareness appears to be linked to reading efficiency together with fluency RAN measures. Most probably, in younger children letter knowledge and accuracy in 'Phonemes to letters test', and RAN objects and RT in older children co-develop and explain the similar level of variance in reading skill, as shown by strong correlations between these measures. Importantly, reading proficiency has been linked to positive academic, career, economic, and social consequences (Irwin et al., 2007). Struggling readers are more likely to experience anxiety and sadness since reading difficulties have been related to social-emotional and mental health issues (Dahle & Knivsberg, 2014; Hendren et al., 2018). Intervention studies showed that training letter and speech association could enhance reading skills in typical reading development (Hulme et al., 2012) as well as in developmental dyslexia (Fraga González et al., 2015). However, the studies emphasize that the most efficient training should start in the first grade or even before children start to read.

At the same time, in many countries, including Poland, we face the “dyslexia paradox”, which refers to the fact that dyslexia diagnoses are frequently made after the best window for intervention has passed (Ozernov-Palchik & Gabb, 2016). It has been shown that dyslexic children need more time to learn letter and speech sound association or even fail to automatize letter and speech sound association (Blomert, 2011; Blomert & Froyen, 2010; van Atteveldt & Ansari, 2014). We cannot exclude the possibility that children with bad scores in the 'Phonemes to letters test' in that experiment may have had dyslexia, which could be reflected also in low reading skills and PA performance. Worldwide, studies show that training with digital Graphogame (based on LS associations, through syllables and rhyme units) implemented in classrooms with high adult interaction have a positive effect on reading, however only few studies presented transfer from letter training to efficiency in word reading (see McTigue et al., 2020 for meta-analysis). A study on the effectiveness of Graphogame in Polish first graders showed that children with low initial level of letter knowledge improved on letter knowledge, but the training did not improve children's word reading speed (Kamykowska

et al., 2013). Future research should examine the efficacy of training letter sound correspondence but with a phonological awareness part, for readers of Polish beyond early grades.

Chapter II.3. Experiment 2.

Research question

Previous fMRI studies examined LS association in adults or children with at least three years of reading experience. Therefore, it remains unclear how the brain activation to letter and speech sound association differs between typically reading children and children at risk of/with dyslexia at the beginning of reading instruction. Also, as mentioned in the introduction, orthographic transparency, as well as presence of reading difficulties can influence the nature of the brain response to multisensory LS pairs. The congruency effects are broadly considered to be a marker of successful and automatized letter-speech sound integration, independently of the language of reading instruction and reading proficiency. However, the direction of this effect (congruent > incongruent vs incongruent > congruent) may depend on the aforementioned factors.

Methods

Participants

One hundred and twenty children were recruited for the longitudinal study on dyslexia from kindergarten and the first grade of primary school. The first graders had received formal reading instruction for 3.62 months on average (SD=2.01, range 1.20 – 7.80). Inclusion requirements included having a typical IQ (below the 25th percentile on Raven's Colored Progressive Matrices), being born at term (37 weeks), speaking Polish as their native language, being right-handed, being monolingual, having normal (or corrected to normal) vision and hearing, having no history of neurological disorders or brain damage, and not exhibiting any signs of ADHD. The Warsaw University Ethical Committee approved the study, and all of the children and their parents provided informed consent.

Thirty-five children were removed from the analysis due to excessive motion during the fMRI scan (n = 20), some did not finish two runs (n = 6) or left the study before the diagnosis of dyslexia (n = 9). Therefore, 85 children were included in the analyses: 35 without familial history of dyslexia (FHD-, 21 girls and 14 boys; mean age: 6.89 years; range: 5.93 to 8.04); and 50 with familial history of dyslexia (FHD+, 30 girls and 20 boys; mean age: 6.92 years; range: 5.52 to 8.06). In FHD+ group, the children had at least one first degree relative with a dyslexia diagnosis (65.6%), or at least one parent who scored greater than forty points on the Adult Reading History Questionnaire (ARHQ, Lefly and Pennington, 2000) as specified in previous studies (Maurer et al., 2003; Black et al., 2012).

Raven's Colored Progressive Matrices were used to control nonverbal IQ (Szustrowa & Jaworowska, 2003). Hollingshead's (1975) indicator of social standing based on parental education and occupation was used to determine parental socioeconomic status (SES); two households did not respond to the SES questionnaire. Four children's fathers could not be reached, making it impossible to estimate their ARHQ scores. Age, sex, grade, IQ, and parental SES did not differ between the two groups (for details see Table II.3.1.).

Table II.3.1. Demographic characteristics of FHD- and FHD+ participants, as well as DYS and TR children together with group differences. Mean (SD) are depicted.

	FHD+ n = 50	FHD- n = 35	Test statistics FHD+ vs. FHD-	DYS n = 17	TR n = 68	Test statistics DYS vs. TR
Gender	20 B, 30 G	14 B, 21 G	Chi(1) = 0, p = 1	8 B, 9 G	26 B, 42 G	Chi(1) = 0.441, p = .507
Grade	12 K, 38 FG	9 K, 26 FG	Chi(1) = 0.033, p = 0.857	6 K, 11 FG	14 K, 54 FG	Chi(1) = 1.635, p = 0.202
Age (years)	6.92 (0.58)	6.89 (0.57)	t(83) = -.189, p = 0.851	6.74 (0.56)	6.96 (0.57)	p ^b = 0.176
SES	46.86 (12.20)	50.17 (8.00)	t(81) = 1.513, p = 0.134	42.63 (11.35)	49.74 (9.89)	p ^b = .016*
ARHQ mother	37.66 (13.50)	22.14 (7.76)	t(83) = -6.700, p < 0.001*	34.24 (16.85)	30.94 (12.58)	p ^b = 0.322
ARHQ father	41.63 (14.30)	25.46 (7.21)	t(79) = -6.641, p < 0.001*	37.67 (11.77)	33.94 (14.63)	p ^b = 0.281
IQ (sten)	7.46 (1.42)	7.60 (1.24)	t(83) = .471, p = 0.639	7.06 (1.59)	7.60 (1.25)	p ^b = 0.106

B: boys; G: girls; K: kindergarten; FG: first grade of elementary school; ^b bootstrap statistics

We performed a formal dyslexia diagnosis two years after the fMRI experiment using a set of tests that allowed us to retrospectively select the dyslexic (DYS) group (Bogdanowicz et al., 2009). Seventeen kids from the current sample were given the diagnosis of dyslexia based on the standardized tests (DYS; N = 17, mean age = 6.74, 9 girls, 8 boys). Five children belonged to the FHD- group, whereas twelve were in the FHD+ group. The remaining 68 kids were classified as typical readers (TR group, mean age = 6.96, 38 FHD+, 42 girls, 26 boys). Thus, in the studied sample, the proportion of dyslexic children was comparable across the FHD- (16.7 percent) and FHD+ (24 percent) groups, Chi²(1) = 1.21, p = 0.27. In contrast, it substantially differed and was higher for the at risk group in the case of 109 children who participated in the longitudinal study: FHD+ (31.3%) and FHD- (11.9%), Chi²(1) = 5.37, p = 0.02). There were no differences between DYS and TR children in terms of age, sex, grade, IQ, or parental ARHQ; however, TR kids had greater parental SES (see Table II.3.1.).

Behavioral measures and analysis

All children underwent behavioral testing prior to the fMRI experiment (46 days on average and no more than four months). The Decoding Test (Szczerbiński & Pelc-Pkala, 2013) was applied to evaluate phonological awareness and early reading abilities. It comprised of letter recognition (upper and lower case), reading sight words and pseudowords (score: number of words or pseudowords correctly read in a minute), solving phoneme elision problems (score: number of problems successfully answered in a minute), and phoneme analysis (score: the number of correctly solved items). Since our sample also included kindergarteners and psychometric norms were only available for first graders, raw scores were used. Young readers' orthographic knowledge was also tested with a task in which they had to select a letter string that exists in Polish (for example, the DAG trigraph exists while DGA does not exist in Polish spelling) (Awramiuk & Krasowicz-Kupis, 2014). The total number of correctly assigned trigraphs served as the outcome metric.

The Picture Vocabulary Test: Comprehension (Haman et al., 2012) was used to test children's passive vocabulary. Each child was asked to choose one of four pictures that best represented a given word. Raw scores were utilized in the analyses because the test was normalized for children between the ages of 2 and 6 years. Subtests for the naming of items and colors were used to measure rapid automatized naming (RAN, Fecenec et al., 2013). The average amount of time (in seconds) required to name every stimulus in two subtests served as the outcome measure.

Children who received low scores (equal to or lower than the third sten) on at least two of the four reading subtests (sight word reading, pseudoword reading, text reading, and lexical decision task) were classified as dyslexics in a formal diagnosis of dyslexia (Bogdanowicz et al., 2009).

The differences in behavioral performance between the FHD+ and FHD- groups were examined using parametric t tests. We used bootstrap technique to evaluate which behavioral variables significantly differed between DYS and TR due to the uneven group sizes. The actual between-group difference for each variable was first calculated. One data set was created by combining the results from the two groups. Next, two subsets were created using a replacement from this data set with sizes equal to those of the real groups (i.e., DYS = 17, TR = 68) and the difference between the means of the subsets was determined. The distributions of the computed mean differences were represented on histograms after that step was performed 10,000 times. We counted the instances where the genuine between-group difference was greater than the absolute value of differences from the distribution. In order to estimate the two-tailed p-value, the resulting number was divided by the number of drawings (i.e. 10000).

fMRI task and scan

There were two runs in the experiment, each with 12 blocks of stimulation and 12 periods of fixation. One block (15.6 sec) was divided into three mini-blocks (5.2 sec each), each of which contained four stimuli and was repeated twice, giving rise to 48 stimuli for each condition. Pseudorandomization was used to arrange the blocks in such a way that two of the same kind were not shown consecutively. This procedure was based on van Atteveldt et al., (2004) study. Using Presentation software (Neurobehavioral Systems), stimuli from one of six conditions were presented in each block. There were two control conditions: symbols (Greek letters unfamiliar to children) and speech sounds converted into noise-vocoded speech using an in-house script in Praat (Boersma & Weenink, 2001). The experimental conditions included unisensory visual letters and speech sounds corresponding to selected Polish single letters (consonants: B, C, D, G, H, J, K, L, M, N, P, R, S, T, W, Z; and vowels: A, E, I, O, U. Children were told to pay close attention to the stimuli. We used the same task as Blau et al., (2010) to make sure the kids were paying attention to the stimuli. Each block contained a single presentation of a line drawing of a cat, a voice saying "cat," or a mix of the two in the multisensory blocks. Every time they noticed such stimuli, kids were asked to click a button on a response pad with their left thumb.

fMRI data acquisition

Before the start of the experimental session, all participants were made comfortable with the MRI setting and protocol in a mock scanner. Scans were acquired using 3T Siemens Trio MR system (Siemens AG, Munich, Germany) with sparse design sequence. By presenting the stimuli during a silent volume acquisition delay, we were able to limit the impact of scanning noise on experimental activation (van Atteveldt et al., 2004). A T2* - sensitive, gradient echo planar imaging sequence covering the whole-brain (29 slices, slice thickness: 4 mm, 3 x 3 in-plane resolution, TR = 5.2 s (1.5 s of volume acquisition followed by 3.7 s delay), TE = 25ms, matrix size: 64 x 64) was applied. There were two runs, each lasting 6 minutes and 17 seconds (73 volumes). Anatomical data were acquired using a T1 weighted sequence (176 slices, slice-thickness 1 mm, TR = 2.53 s, TE = 3.32 ms, flip angle = 7°, matrix size: 256 x 256, voxel size 1 x 1 x 1 mm).

fMRI data preprocessing

The fMRI data were analyzed with BrainVoyager QX 2.2.0 (Brain Innovation, Maastricht, the Netherlands; Goebel et al., 2006). Functional data were first preprocessed to correct for 3D motion artifacts (trilinear interpolation), linear drifts, and low-frequency non-linear drifts (high pass filter ≤ 3 cycles/time course). Then all images were co-registered to the anatomical image. The anatomical image was then transformed into Talairach stereotaxic space (Talairach & Tournoux, 1988), and this transformation was applied to the aligned fMRI data. Next, the functional images were spatially smoothed with a FWHM 6-mm Gaussian kernel. Finally, to detect motion-affected functional volumes ART toolbox (http://www.nitrc.org/projects/artifact_detect) was used (thresholds were adapted from Raschle et al., (2012): movement threshold: 3mm, rotation threshold: 0.05 mm). If the number of motion-affected volumes was higher than 20%, the participant was excluded from the analysis.

Whole brain statistical analyses

Both experimental and control conditions were modeled in single subjects' design matrix together with motion parameters and separate regressors for each artifactual volume that was identified by ART toolbox. Second level statistical analyses were performed using the general linear model (GLM) approach based on Blau et al., (2010) study. The first analysis was a single factor model including four experimental conditions (i.e., letters, speech sounds, congruent LS pairs and incongruent LS pairs) as separate predictors, and was used to identify the brain regions involved in the experimental tasks for the whole sample of children. The statistical map from this analysis (all four experimental conditions vs. baseline contrast) was used as a mask (thresholded at $p = 0.05$) for subsequent GLMs. Subsequently, two separate GLMs (GLM1 and GLM2) were computed to evaluate the spatial pattern of activation for letters and speech sounds in FHD- and FHD+ children separately (corrected for multiple comparisons using false-discovery rate, $q(\text{FDR}) < 0.01$).

Direct between-group comparisons for letters and speech sounds were performed in GLM3. GLM 4 was a 2 x 2 factorial model including FHD status and multimodal conditions – congruent and incongruent LS pairs. The congruency effect – the difference between congruent and incongruent LS pair – calculated in the GLM4 was used to identify multisensory integration sites (van Atteveldt et al., 2007). We applied an identical statistical threshold as in the previous study on dyslexic children (Blau et al., 2010), i.e. voxel-wise threshold of $p < 0.01$, corrected for multiple comparisons using cluster extent threshold of $p < 0.05$ (Forman et. al., 1995; Goebel et. al., 2006). The clusters are reported in the Talairach space and displayed on the average brain from all participants.

fMRI ROI analysis

To further explore the differences between the groups in regions previously reported to differ between dyslexic and control subjects in unisensory and multisensory conditions, ROI analyses were performed. Seven ROIs: left and right fusiform gyrus (for letter condition), left and right anterior superior temporal gyrus (aSTG) (for speech sound condition) as well as left and right STS and left planum temporale/Heschl's sulcus (PT/HS) (for multisensory conditions) were tested by creating 4 mm spheres around the peak coordinates taken from Blau et al., (2010) study. The percent signal change in these ROIs was compared between FHD+ and FHD- children. The statistical threshold was corrected for the number of ROIs using Bonferroni correction with $p < 0.025$ for letters and speech sounds, and $p < 0.016$ for multisensory conditions.

Next, similarly as for behavioral variables, we retrospectively analyzed brain activity differences between DYS and TR groups by the means of bootstrap analysis in ROIs taken from Blau et al., (2010) study as well as in regions showing significant differences between FHD- and FHD+ children in the whole brain analysis.

Additionally, we calculated Pearson's correlations between the scores on reading-related tests (word reading, orthographic awareness, phoneme analysis and elision) and the strength of the fMRI congruency effect (i.e. congruent - incongruent). The correlations were performed in regions showing a significant group x congruency interaction in the current study and in Blau et al., (2010) study (i.e. left and right STS and left PT/HS) in FHD+ and FHD- children, and in TR and DYS groups separately. The statistical threshold was corrected for the number of ROIs and behavioral measures ($p < 0.007$).

Results

Behavioral results

With regard to performance on early reading, phonological awareness, or orthographic awareness tests, FHD+ children did not substantially differ from the FHD- group (for details see Table II.3.2.).

On the other hand, the bootstrap analyses showed that children who were later diagnosed as DYS had poorer scores at the beginning of reading acquisition in letter knowledge, word and pseudoword reading, phoneme analysis, elision, RAN, and orthographic awareness than TR children (for detailed scores see Table II.3.2.). Yet, there were no significant group differences in the children's passive vocabulary.

Table II.3.2. The results from behavioral tests in FHD+ and FHD- groups, as well as DYS and TR groups.

	FHD+ n = 50	FHD- n = 35	Test statistics FHD+ vs. FHD-	DYS n = 17	TR n = 68	Test statistics DYS vs. TR
Letter knowledge (upper & lower case, max. 64)	46.92 ±18.41 (0 - 64)	47.40 ±18.07 (0 - 64)	t(83) = 0.12, p = 0.905	31.76 ±20.00 (0 - 59)	51.26 ±15.28 (4 - 64)	p ^b < .001*
Words read per minute	15.18 ±15.96 (0 - 52)	18.43 ±21.01 (0 - 69)	t(83) = 0.81, p = 0.420	4.65 ±5.13 (0 - 16)	19.69 ±18.84 (0 - 69)	p ^b = .003*
Pseudowords read per minute	13.97 ±13.40 (0 - 47)	12.96 ±13.61 (0 - 40)	t(82) = 0.336, p = 0.738	4.00 ±5.03 (0 - 15)	15.90 ±13.74 (0 - 47)	p ^b < .001*
Phoneme analysis (solved items, max. 12)	6.60 ±4.44 (0 - 12)	7.77 ±4.05 (0 - 12)	t(83) = 1.241, p = 0.218	3.59 ±3.48 (0 - 10)	8.04 ±4.02 (0 - 12)	p ^b < .001*
Phoneme elision (solved items per minute)	4.10 ±4.23 (0 - 13)	4.26 ±4.52 (0 - 15)	t(83) = 0.164, p = 0.870	1.47 ±2.28 (0 - 7)	4.88 ±4.42 (0 - 15)	p ^b = .004*
RAN object & color subtests (seconds)	127.04 ±29.49 (77 - 203)	135.43 ±35.41 (91 - 268)	t(83) = 1.188, p = 0.238	152.12 ±40.69 (113 - 268)	125.16 ±26.66 (77 - 196)	p ^b = .003*
Orthographic awareness (solved items, max. 30)	18.45 ±4.74 (8 - 29)	20.06 ±4.42 (13 - 29)	t(83) = 1.563, p = 0.122	15.38 ±3.92 (8 - 25)	20.03 ±4.31 (11 - 29)	p ^b < .001*
Vocabulary (max. 88)	79.48 ±5.40 (64 - 87)	77.20 ±7.29 (57 - 88)	t(83) = -1.657, p = 0.101	76.59 ±6.14 (64 - 85)	79.25 ±6.04 (57 - 88)	p ^b = .145
Sight word reading* (sten)	5.82 ±2.04 (1 - 10)	6.09 ±1.98 (2 - 10)	t(83) = 0.598, p = 0.552	3.65 ±1.50 (1 - 6)	6.51 ±1.69 (4 - 10)	p ^b < .001*
Pseudo-word reading* (sten)	4.94 ±1.89 (1 - 10)	5.24 ±1.69 (1 - 8)	t(83) = 0.734, p = .465	2.88 ±1.41 (1 - 6)	5.61 ±1.45 (3 - 10)	p ^b < .001*
Text reading ^d (sten)	4.63 ±2.08 (1 - 9)	5.27 ±2.60 (1 - 10)	t(81) = 1.235, p = 0.221	2.12 ±0.86 (1 - 3)	5.62 ±1.99 (2 - 10)	p ^b < .001*
Lexical decision task ^d (sten)	5.16 ±2.21 (1 - 10)	5.91 ±2.17 (2 - 10)	t(83) = 1.544, p = 0.126	2.41 ±0.87 (1 - 4)	6.24 ±1.72 (3 - 10)	p ^b < .001*

Note. Means ±SD together with range in parentheses are presented, ^dbattery of tests used for dyslexia diagnosis; ^b bootstrap statistics; * Remains significant after Bonferroni-Holm correction for multiple comparisons

fMRI results

Whole brain results

Figure II.3.1. shows the overlapping of brain activity in response to unisensory presented letters and speech sounds for FHD- and FHD+ children (GLMs 1 and 2).

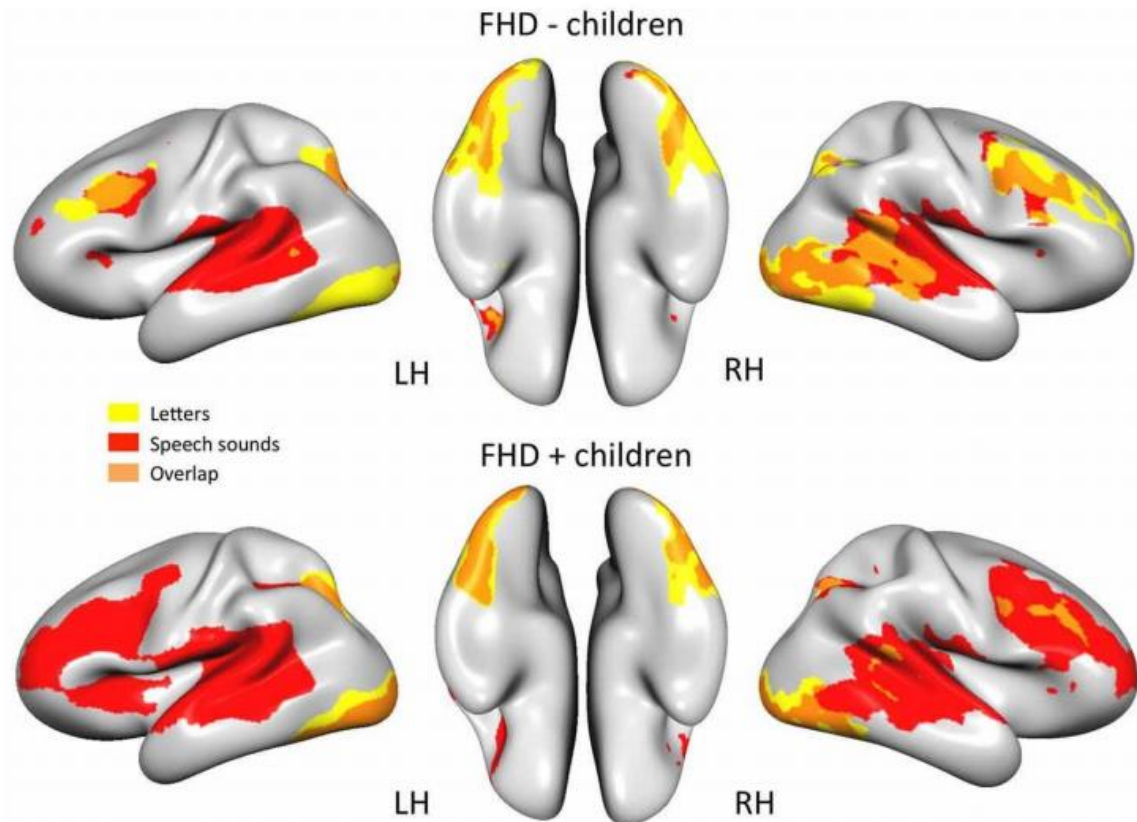


Figure II.3.1. Brain areas involved in processing letters (yellow), speech sounds (red) or both unisensory conditions (orange) in children with (FHD+) and without (FHD-) family history of dyslexia.

Significant differences in brain activity were only found for speech sounds when the two groups' responses to each unisensory condition were directly examined (GLM3). Children with FHD+ demonstrated more activity for speech sounds in the right middle and inferior frontal gyri than their FHD- counterparts (see Figure II.3.2. and Table II.3.3.). There were no significant differences in letter processing between the groups.

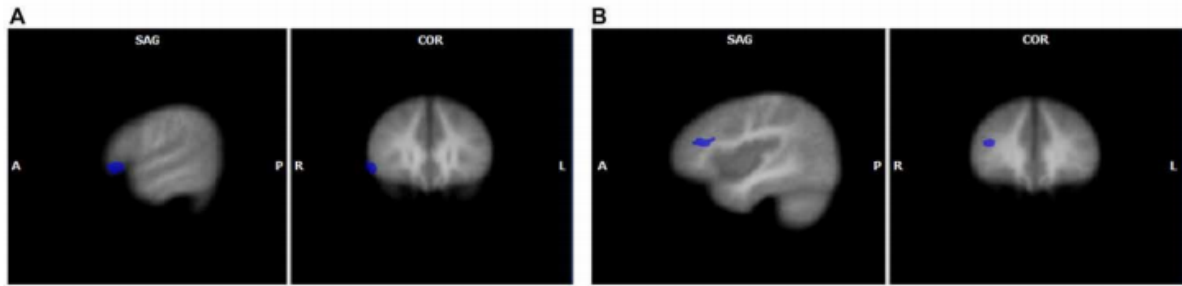


Figure II.3.2. Unisensory group effects for speech sounds with increased activation in FHD+ compared to FHD- children in the right inferior frontal gyrus (A) and in the right middle frontal gyrus (B). The clusters are displayed on the average brain from all participants at voxel-wise threshold of $p < 0.01$, corrected for multiple comparisons using cluster extent threshold of $p < 0.05$.

Table II.3.3. Group differences in response to speech sounds and for interaction between group and multisensory conditions

Brain region	Hemisphere	x	y	z	t / F	Voxels
Speech sounds: FHD+ > FHD-						
Inferior Frontal Gyrus	R	54	39	-2	-4.01	910
Middle Frontal Gyrus	R	39	32	22	-3.20	715
Congruency effect x FHD group interaction						
Inferior Temporal Gyrus	R	54	-49	-23	17.62	648
Planum Temporale, Superior temporal gyrus	L	-42	-16	19	13.77	1700

The right inferior temporal gyrus (ITG) and left planum temporale (PT/STG) also showed a significant interaction between group and multisensory conditions (GLM4, for details see Table II.3.3. and Figure II.3.3.). In the left PT/STG it was driven by a reversed pattern (greater activity for congruent pairs) in FHD+ children ($p = 0.037$) compared to FHD- children (increased activation for incongruent pairs). The groups differed with respect to the incongruent condition (FHD- > FHD+; $p = 0.029$), but there was no difference for the congruent condition. In the right ITG, the pattern was reversed; congruent LS pair activation was higher in FHD- children compared to incongruent pair activation ($p = 0.004$), but the opposite effect (increased activity for incongruent pair activation) was observed in FHD+ children ($p = 0.024$). In this cluster, the groups did not differ for the incongruent condition but for the congruent condition (FHD- > FHD+; $p = 0.008$).

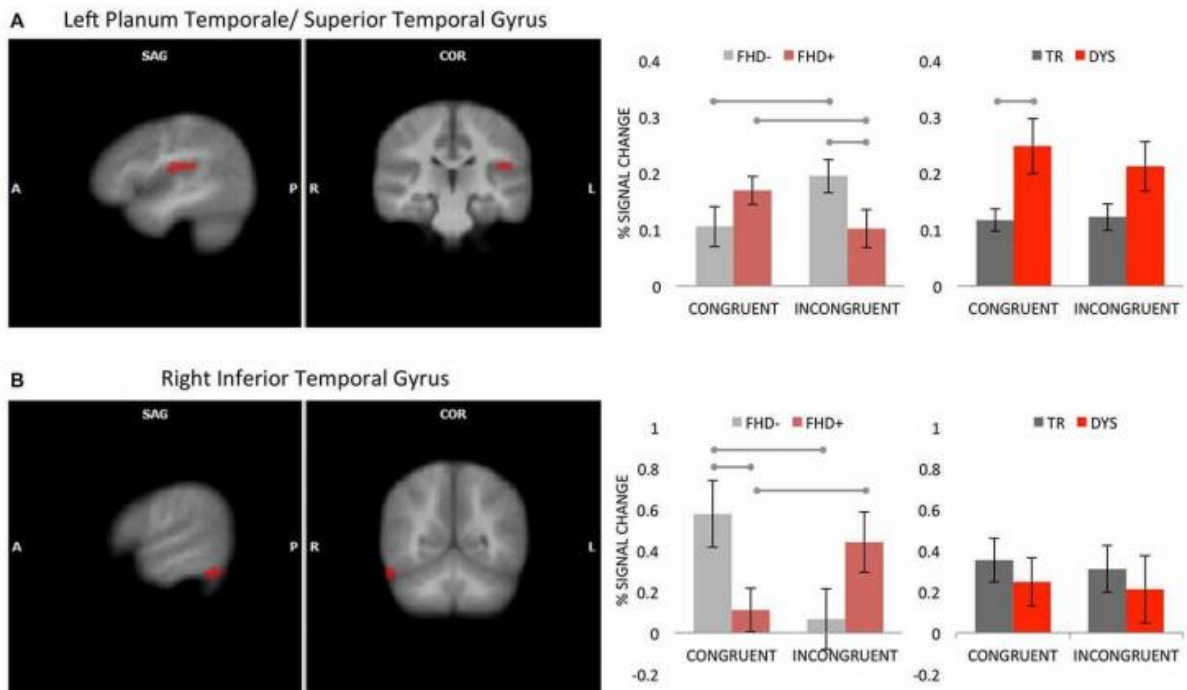


Figure II.3.3. Interaction effect between group and multisensory conditions (congruent, incongruent) in the left planum temporale/superior temporal gyrus (PT/STG) (A) and in the right inferior temporal gyrus (B). The clusters are displayed on the average brain from all participants at voxel-wise threshold of $p < 0.01$, corrected for multiple comparisons using cluster extent threshold of $p < 0.05$. Bar graphs illustrate the percent signal change with SEM for multisensory conditions in FHD- and FHD+ (horizontal lines illustrate significant *post hoc* tests) as well as in DYS and typical reading (TR) children (horizontal line illustrates significant bootstrap statistics).

ROI analyses results

Analysis of ROIs based on regions distinguishing between dyslexic and control children in Blau et al., (2010) revealed a trend for lower activation in FHD+ compared to FHD- children in the left fusiform gyrus for letter processing ($x = -36, y = -51, z = -17; t = 1.95, p = 0.056$). In the left PT/HS ($x = -42, y = -28, z = 13$) we found a significant interaction between group and multisensory conditions ($F(1,83)=6.22, p=0.012$). The groups differed only in the incongruent condition ($p = 0.009$), where FHD- children had higher activation than FHD+ children. FHD+ children presented higher activation for congruent compared to incongruent LS pairs ($p = 0.029$), while there were no differences between the conditions in FHD- children. We did not find any FHD effects in the other ROIs.

Bootstrap analyses (comparisons between retrospective TR and DYS groups)

For ROIs taken from Blau et al., (2010), a trend for differences appeared in left PT/HS - DYS children had higher activity than TR group for congruent LS pairs ($p = 0.039$). Additionally, in the right aSTG in response to speech sounds DYS group had significantly higher activity than TR group ($p = 0.022$). We did not find any dyslexia effects in the other ROIs taken from Blau et al., (2010). Furthermore, in the left PT/STG, an ROI showing significant interaction between familiar risk and congruency in the whole brain analysis, DYS children had higher activation than TR group for congruent LS pairs ($p = 0.006$, see Figure II.3.4.).

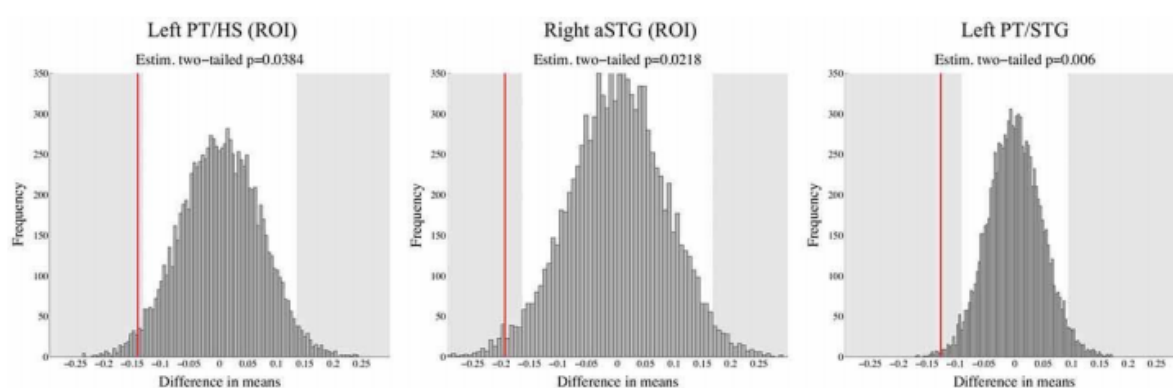


Figure II.3.4. Results obtained using bootstrap analysis based on percent signal change data in two ROIs from Blau et al., (2010) and in the left PT/STG cluster from the whole brain analysis of FHD+ and FHD- children. Red line represents the actual observed value of difference in means between TR and DYS children, whereas shaded gray areas depict significant differences (two-tailed $p < 0.05$). DYS compared to TR showed higher brain response to congruent letter-sound (LS) pairs in left PT/HS and in left PT/STG as well as higher brain response to speech sounds in right anterior STG (aSTG).

Correlations with behavioral variables

In the left STS ROI several significant negative correlations were observed between congruency effect (i.e. congruent - incongruent LS pairs) and early reading skills in FHD- children (word reading $r = -0.59$, $p < 0.001$; orthographic awareness $r = -0.60$, $p < 0.001$; phoneme analysis $r = -0.52$, $p = 0.001$; phoneme elision $r = -0.55$, $p = 0.001$, see Figure II.3.5.). None of the above correlations were significant in FHD+ group. There were no significant correlations for the clusters showing significant FHD effects on the whole brain level.

When retrospectively splitting the sample into TR and DYS, negative correlations in TR between congruency effect in the left STS and word reading ($r = -0.34$, $p = 0.005$) were found, while correlations with phoneme analysis ($r = -0.30$, $p = 0.012$) and elision ($r = -0.27$, $p = 0.027$) did not survive the correction for multiple comparisons. None of the correlations were significant in the DYS group.

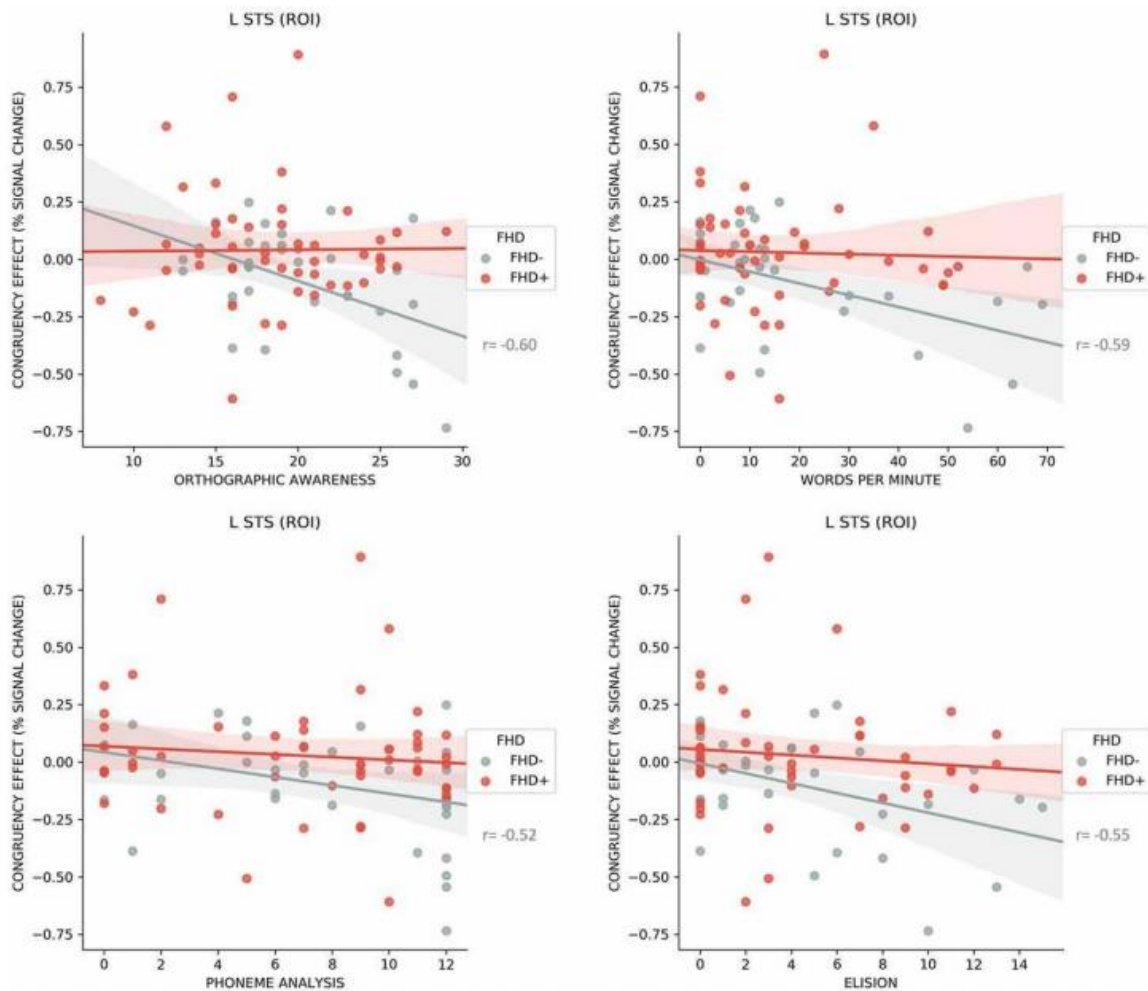


Figure II.3.5. Correlations for FHD- and FHD+ children between the neural response to congruent vs. incongruent letter speech sound pairs (fMRI congruency effect) in the left superior temporal sulcus (STS) and orthographic awareness, word reading, phoneme analysis and elision along with 95% confidence intervals. Correlations are significant only in FHD- children.

To test the relation between reading instruction, behavioral performance and brain activity, we correlated months of reading instruction that the first-grade children ($n = 66$) had received with congruency effects in ROIs taken from the whole brain analysis of FHD status and from Blau et al., (2010). These correlations were performed in the whole sample of first graders and separately in each group: FHD- ($n = 28$), FHD+ ($n = 38$) and TR children ($n = 56$). We did not test for correlations in DYS ($n = 10$) because the number of subjects was too small. What is important to note, there were no differences in months of reading instruction between FHD- and FHD+ children or between TR and DYS children. The length of reading instruction was weakly positively correlated with word and pseudoword reading in the whole sample ($r = 0.25$, $p = 0.047$ and $r = 0.32$, $p = 0.009$), in FHD+ children ($r = 0.33$, $p = 0.04$ and $r = 0.36$, $p = 0.025$) and in TR (only pseudoword reading, $r = 0.34$, $p = 0.011$), however these correlations did not survive the correction for multiple comparisons (seven behavioral measures were tested). On the neural level only in the whole sample of first graders and in

FHD- children a weak negative correlation was found between congruency effect in right STS and months of reading instruction ($r = -0.31$, $p = 0.012$ and $r = -0.46$, $p = 0.015$ for the whole sample and FHD- f respectively). Again, these correlations were not significant after correction for multiple comparisons (five ROIs were tested).

Discussion

The aim of Experiment 2 has been to examine brain response to letter, speech-sounds and LS pairs in emerging readers with and without familial risk of dyslexia. In addition, we have retrospectively assessed which of the observed effects are present in children who have developed dyslexia.

Similarly to Specht et al. 2009 FHD+ children did not differ from the FHD- group on the behavioral level with respect to early reading, phonological awareness and orthographic skills. This is typical for transparent orthographies. The prevalence of dyslexia was also similar between these groups. On the other hand, children retrospectively diagnosed with dyslexia had lower early reading skills than typically reading peers.

Differences between the FHD- and FHD+ groups were present on the neural level for both unisensory and multisensory conditions. When processing speech sounds, FHD+ children showed increased brain response compared to the FHD- group in the right inferior and middle frontal gyri, possibly reflecting more effortful speech comprehension in the FHD+ group (Monzalvo & Dehaene-Lambertz, 2013). In addition, in the right aSTG ROI from Blau et al., (2010) children who developed dyslexia had higher activation to speech sounds than typically reading children. This result is in contrast to Blau et al., (2010) who found a reversed pattern, but is in line with study on literate and illiterate subjects. Literate relative to illiterate participants had lower response to speech in bilateral STG (Dehaene et al., 2010).

We found an interaction between FHD group and LS congruency in the left STC and in the right inferior temporal cortex. The cluster in the left STC was in close proximity to the left PT/HS cluster where weaker congruency effect in DYS children was found in the previous study (Blau et al., 2010) but the effect was in opposite direction. Namely, FHD- children had higher activation to incongruent compared to congruent LS pairs, while FHD+ children presented the congruency effect (higher activation for congruent compared to incongruent condition). The reversed direction of the congruency effect was further confirmed in the ROI analysis. Brain activity in the left PT/HS for incongruent condition was significantly higher in the FHD- than FHD+ group, while there were no group differences for the congruent condition.

There might be several explanations for the reversed congruency effects in the left STC observed in the current experiment. First, the effect could be related to differences in

orthographic transparency. The direction of congruency effect in Polish children is more comparable to the results obtained from English and Swiss-German (Holloway et al., 2015; Kronschnabel et al., 2014). This is counterintuitive as Polish and German were recently showed to be more transparent than Dutch which in turn was more transparent than English (Schüppert et al., 2017). Thus, we do not think that current results can be explained by differences in orthographic transparency.

Conversely, developmental stage of reading skill or even effects related to processing effort could affect the directionality of the congruency effect as the studied sample was younger and had less reading experience than previously studied samples. The observed pattern could reflect an early stage in the process of LS integration in the FHD- group, where the brain actively responds to the conflicting LS pairs. Perhaps, only after automatization, incongruent pairs could be suppressed. FHD+ children do not show the increased response to conflicting pairs, but instead – higher activation to congruent ones (especially those children who later develop dyslexia), which might later lead to failures in suppressing the incongruent information. Such an explanation would be consistent with research showing that the automatization in LS integration develops relatively slowly (Foryen et al. 2009, Experiment 1) and with the result showing that children who developed dyslexia retrospectively had significantly higher response than the typically reading group in the left STC (left PT/STG and the left PT/HS ROIs) for congruent LS pairs.

Stronger activation to incongruent LS pairs (relative to congruent pairs) in the left STS ROI was positively related to early reading skills in FHD- children and (retrospectively) in typical readers. This effect was missing from previously reported PT/HS ROIs (Blau et al. 2010) The congruency effect was not related to behavioral measures neither in FHD+ nor in DYS children. Nevertheless, the lack of correlation in children with dyslexia could be explained by both smaller sample and more restricted range of behavioral performance in the lower end of the continuum.

The discrepancy in the localization of the effects related to reading efficiency can be explained by the methodology used by Blau et al. 2010. The significant relations with congruency effect in the left STS and PT/HS were driven by group differences and were no longer significant when the group factor was controlled for. Additionally, the PT/HS and the surrounding STG are regions sensitive to acoustic features, and the former does not distinguish between speech and non-speech (Price, 2012). The STS on the other hand, is more involved in speech than non-speech, is sensitive to phonological information (Vaden et al., 2010), while bilateral lesions of the STS are often associated with word deafness (Stefanatos, 2008). Activation in the left STS in response to both print and speech was found to be related to reading abilities in emerging readers (Chyl et al., 2018). That is why enhanced activation to congruent vs. incongruent LS pairs in the left HS and PT was putatively attributed

to feedback from STS and STG (van Atteveldt et al., 2004). Perhaps in typical beginning readers the more efficient the reading skills the more effective the feedback from STS to auditory cortex, resulting in higher incongruency effect as compared to children at risk of dyslexia.

Rather unexpectedly, in the right inferior temporal cortex, we found a congruency effect in FHD- children and an opposite effect (incongruency effect) in the FHD+ group. The two groups differed only with respect to the congruent condition in this brain area. As no significant differences were found between children who developed dyslexia and typical readers in any multisensory condition, we suggest that the effects observed in the right inferior temporal cortex reflect early reading strategies based mostly on perceptual analysis of text and non-lexical form recognition systems, which might be altered in FHD+ children. It was shown that due to greater exposure to text in the course of reading acquisition, children shift away from those strategies as reflected by progressive disengagement of the right ventral cortex (Turkeltaub et al., 2003).

To conclude, we suggest that the incongruency effect observed in the left STC in beginning readers in the present experiment reflects an early stage of LS integration, which could reverse into the congruency effect observed in previous studies (Blau et al., 2009, 2010) with increasing reading experience. The incongruency effect is behaviorally relevant — in FHD- children or those who become typical readers the higher the incongruency effect in the left STS the better the reading and reading-related skills. FHD+ children show diminished incongruency effect, which is atypical for beginning readers. Higher familial risk of dyslexia was correlated with diminished incongruency effect and children with a very high familial risk presented a congruency effect.

Chapter II.4. Experiment 3

Research question

Using a longitudinal voxel-wise analysis, we have investigated how the neural basis of letters, speech sounds, and LS association processing changes with time and reading experience in typical reading development. We hypothesized that the incongruity effect observed in the left STC in beginning readers (Plewko et al., 2018) would reverse into a congruency effect with increasing reading experience. Furthermore, we looked for specific alterations in dyslexic readers. Using a region of interest approach based on Blau et al., 's (2010) findings, we examined the differences in the left STC response to multisensory information between dyslexic and typical readers, after two years of school education from Experiment 2.

Methods

Participants

As for Experiment 2, 120 children from kindergarten and the 1st grade of primary school were recruited for the longitudinal study on dyslexia, approved by the Warsaw University Ethical Committee. The study consisted of three time points, a year apart from each other. The first time point (TP1 - results described in Experiment 2) and the third time point (TP3) involved both behavioral and fMRI sessions, while the second one (TP2) – only a behavioral session. All children and their parents gave informed consent to the study. Out of 120 children, 85 participants had usable fMRI data from TP1 and were included in Experiment 2 (Plewko et al., 2018). In the current experiment, out of 85 children, 18 were excluded from the analyses, either due to excessive motion (see fMRI data preprocessing) in the second fMRI session (9 children), failure to complete two runs (2 children), or dropping out from the study (7 children). The final sample in Experiment 3 included 67 children (42 girls and 25 boys). The choice to include only the participants with sufficient quality data at both time points was made in order to obtain a truly longitudinal sample. Complete cases analysis (listwise deletion) as a strategy for handling incomplete data is the most popular choice in developmental neuroscience (see Chyl et al., 2021) due to its simplicity and the fact that the currently available software packages for imagining data require each subject to have complete data at all time points (Telzer et al., 2018).

At TP3, the formal diagnosis of dyslexia was conducted using a standardized battery of tests for dyslexia diagnosis in Poland (Bogdanowicz et al., 2009), and 14 out of 67 children were diagnosed with dyslexia (DYS, TP1: mean age = 6.81, SD = 0.53, range: 6.11 - 7.56;

TP3: mean age = 8.79, SD = 0.53, range: 8.06 - 9.54), while 53 developed typical reading skills (TR, TP1: mean age = 6.93, SD = 0.53, range: 5.93 - 8.04; TP3: mean age = 8.92, SD = 0.55, range: 7.91 - 10.04). Children were classified as dyslexic when at TP3 they achieved low scores (equal or lower than the 3rd sten, i.e. at least 1 SD below the population mean, which corresponds to below 16 percentile) in at least two reading subtests (out of four: single-word reading, pseudoword reading, reading with lexical decision, and text reading). Children who had a low score in no more than one reading subtest were assigned to the typically reading group. Children assessed as dyslexic readers achieved low scores in 3.15 tests (out of four; SD = 0.69) on average, and children assessed as typical readers scored low in 0.23 tests (out of four; SD = 0.42) on average. No normalized tests measuring reading and reading-related skills in Polish were available for children, when they were tested at TP1 and TP2. However, children selected to the DYS group performed lower than TR on reading tests (word and pseudoword reading per minute) at each TP (all $p < 0.001$, see Table II.4.1.). To relate to previous literature on LS integration deficits in dyslexia, including Experiment 2 (Plewko et al., 2018) we decided to employ a categorical approach to dyslexia instead of a continuous one.

Behavioral measures and analysis

At each TP, participants completed behavioral tests. Reading and phonological abilities were assessed using the test battery consisting of several tests: letter knowledge (lower- and uppercase letters), word and pseudoword reading (items read correctly per minute), phoneme deletion, and phoneme analysis (Szczerbiński & Pelc-Pękala, 2013). All these tests were applied at all TPs. Rapid automatized naming (RAN) was tested with subtests of object and color naming (at all TPs) while letter and digit naming subtests were added to TP2 and TP3 (Ferenc et al., 2013). Additionally, TP1 language skills were measured with the Picture Vocabulary Test: Comprehension (receptive vocabulary assessment; Haman et al., 2012), and non-verbal intelligence was measured with Raven's Colored Progressive Matrices (Szustrowa & Jaworowska, 2003). At TP3 standardized battery of tests for dyslexia diagnosis was used (Bogdanowicz et al., 2009). Parents of children who participated in our study completed questionnaires regarding their reading history (Adult Reading History Questionnaire (ARHQ, Lefly and Pennington, 2000). Information on education and profession was used to estimate socioeconomic status (SES) based on Hollingshead's (1975) index.

To investigate behavioral performance differences between the time points for TR and DYS separately, we performed repeated measure ANOVAs. Behavioral performance was compared at each time point between DYS and TR groups with the use of bootstrap analyses with 10000 permutations.

fMRI task and scan

Each time before the fMRI scan, all the children were familiarized with the stimuli and procedure in the mock scanner. The task was exactly the same as in Experiment 2. As a continuation of Experiment 2, (Plewko et al., 2018), this study focuses on the four experimental conditions.

fMRI data acquisition

Both scans took place in the 3T Siemens Trio MRI system using the same sparse design sequence, in which the stimuli were presented during a silent delay of volume acquisition (see description of the T2* - sensitive and T1 weighted sequences in Experiment 2).

fMRI data preprocessing

The imaging data were analyzed with BrainVoyager QX 22.0 (Brain Innovation, Maastricht, the Netherlands; Goebel et al., 2006) using standard preprocessing steps. fMRI data were preprocessed to correct for 3D motion artifacts (trilinear interpolation), linear drifts, and low-frequency non-linear drifts (high pass filter 3 cycles/time course). Functional images from each TP were co-registered to the corresponding anatomical images. The anatomical images were then transformed into Talairach stereotaxic space with a manual approach (Talairach and Tournoux, 1988), and this transformation was applied to the aligned functional data. The functional images were spatially smoothed with a FWHM 6-mm Gaussian kernel. To detect motion-affected functional volumes we calculated framewise displacement (FD). To calculate FD we used Power et al., 2012 approach. Volumes affected by excessive scan-to-scan head motion higher than $FD = 1,5$ mm, were used as nuisance regressors in the first level General Linear Model (as in Whitfield-Gabrieli et al., 2020). This threshold was chosen based on recent studies performed on children populations of similar age (e.g. Achterberg & van der Meulen, 2019; Yu et al., 2018; Romanovska et al., 2021). Participants were included in the analyses only when having less than 20% of motion affected volumes at both TPs. For TR, on average 2.50 volumes were removed at TP1 and 2.71 at TP3; artefactual volumes did not differ between the timepoints ($t(52) = 0.42$; $p = 0.515$). For DYS, 3.5 volumes were removed at TP1 and 2.01 at TP3 ($t(13) = 0.33$, $p = 0.564$). There was also no difference between groups in the number of artefactual volumes ($F(1,65) = 0.82$, $p = 0.369$).

fMRI data analysis

Longitudinal voxel-wise analyses were performed in a predefined task positive mask in typical readers and in children who developed dyslexia separately, because of largely unequal sample sizes (DYS = 14; TR = 53), making heterogeneity of variance a problem. Longitudinal voxel-wise analyses in the DYS group should be treated with caution, given the

relatively low sample size. The supported ANOVA models in currently available software packages (including BrainVoyager) assume equal sample sizes for the groups (balanced studies). While tolerating slightly different numbers of subjects in different groups, inferences for unbalanced data with fixed and random factors require more complex procedures (e.g. maximum likelihood approach), which are not currently available. For this reason, we did not compute voxel-wise group analyses of LS integration development over time between DYS and TR. For the group comparisons at TP3 (see Experiment 2 for comparison at TP1), we chose a region of interest (ROI) approach, which is better suited for unbalanced data than voxel-wise analysis, and performed bootstrap analyses to test for dyslexia effects relative to the normal variation in a total sample of typically reading children.

For dyslexic and typically reading children, both experimental and control conditions were modeled in single subjects' design matrix together with motion parameters and separate regressors for each volume identified as motion-affected by FD analysis. To combine statistical maps from both TPs, we used a dummy coding approach via Predictor Analysis – Predictor tool in BrainVoyager software. The idea behind this tool is to build a statistical design based on dummy-coded random effects GLM. This method allows comparison of activation from both TPs, taking into account that both scans come from the same person.

In order to delineate regions activated by the experimental tasks in both TR and DYS, a model with TP (TP1 and TP3) and experimental conditions (letters, speech sounds, congruent and incongruent LS pairs) as factors was created.

The GLM approach was used for the second level analyses. All group level results were intersected with a mask based on positive activations to avoid the effects produced by de-activations (Blau et al., 2009, 2010; Plewko et al., 2018) of which biological bases remain unknown (Frankenstein et al. 2005). The clusters are reported in the Talairach space and displayed on the default TAL brain. For all comparisons, we applied statistical voxel-threshold of $p < 0.005$ corrected for multiple comparisons using ClusterThresh Plugin with Monte Carlo simulation with 1000 iterations for each contrast map (a cluster-size threshold corresponding to $p < 0.05$; reducing Type I errors while enabling the detection of true activations; Forman et al., 1995, Goebel et al., 2006). We performed several contrasts to investigate: (1) the spatial pattern of activation for letters and speech sounds at each TP (corrected for multiple comparisons using voxel-wise false-discovery rate, $q(\text{FDR}) < 0.01$); (2) direct between-time points comparisons for unisensory conditions – letters (TP3 letters vs. TP1 letters) and speech sounds (TP3 speech sounds vs. TP1 speech sounds); (3) relaxed criterion for super-additive effect i.e. congruent $> (\text{letters} + \text{speech sounds})/2$; (4) direct between-time points comparisons for multisensory conditions - congruent and incongruent pairs of letters and speech sounds and TPs (repeated measures ANOVA including multimodal conditions at both TPs).

Following previous studies based on similar groups of participants (Kronshabel et al. 2014), the relaxed criterion for testing super- and sub-additive effect was used. This means that the multisensory congruent condition compared to the mean of the unisensory conditions: (letters + speech sounds)/2. This approach was shown to be more reliable than the max criterion which compares the multisensory congruent condition to the sum of unisensory conditions: letters + speech sounds (Hocking & Price, 2008). If a significant interaction of TP and multisensory condition turned out significant in a cluster on the whole-brain level a post-hoc analysis was done. The post-hoc analysis was conducted on the betas extracted from the significant interaction cluster. Moreover, correlation analyses between the activations for the letter and speech sound conditions, as well as between the incongruent > congruent contrast-related betas and word reading level were conducted on the full sample (67 children).

ROI analysis

The left STC was selected to be the ROI for the analyses comparing TR and DYS groups. This choice was dictated by a great consistency between numerous studies that have shown this region to be involved in audio-visual integration for language (grapheme-speech sounds associations), regardless of task, age range and orthographies. What is more, the left STC was the site of group differences between typical readers and readers with dyslexia in previous literature (Blau et al., 2009, 2010; Kronshabel et al., 2014; Plewko et al., 2018; but see study on adult sample (Holloway et al., 2015)). Two left STC subregions were considered for the analysis: the left superior temporal sulcus (STS) and left planum temporale/Heschl's sulcus (PT/HS). The DYS and TR groups percent signal change from multisensory conditions at TP3 were compared (see Experiment 2 for comparison at TP1). ROIs were defined as 4 mm spheres around the peak coordinates reported by Blau et al., (2010) for group differences in multisensory conditions (left STS: $x = -56$, $y = -33$, $z = 4$ and left PT/HS: $x = -42$, $y = -28$, $z = 13$). Bootstrap approach was used to compare the groups (for details see Experiment 2).

Results

Behavioral results

Behavioral performance was analysed with a parametric repeated measure ANOVAs with TP as factor (TP1, TP2, TP3 or TP1 vs TP2). Significant differences were found between all TPs, indicating significant improvement for all of the reading and phonological skills measures (see Table II.4.1.). The differences were present in both TR and DYS groups.

Table II.4.1. Progress and group differences in behavioral tests applied at different time points in typical (TR) and dyslexic (DYS) readers.

Behavioral measure	Time point	TR (n = 53)	Progress	DYS (n = 14)	Progress	Group Difference
Letter knowledge (upper and lower case)	TP1	50.23 (15.92)	t(52) = 6.22, p < 0.001*	32.36 (20)	t(52) = 5.77, p < 0.001*	p < 0.001*
	TP2	63.08 (2.66)		59.93 (7.93)		p = 0.166
Word reading (items read/minute)	TP1	19.13 (19.02)	F(2,51) = 228.01, p < 0.001*	5.07 (5.69)	F(2,12) = 95.12, p < 0.001*	p < 0.001*
	TP2	48.49 (21.51)		22.64 (9.47)		p < 0.001*
Pseudoword reading (items read/minute)	TP3	71.02 (21.22)	F(2,51) = 129.20, p < 0.001*	36.21 (8.46)	F(2,12) = 64.70, p < 0.001*	p < 0.001*
	TP1	15.21 (13.53)		4.57 (5.50)		p < 0.001*
	TP2	33 (10.65)		18.64 (7.52)		p < 0.001*
Phoneme analysis (items solved)	TP3	42.06 (9.87)	F(2,51) = 19.59, p < 0.001*	26.93 (6.68)	F(2,12) = 34.49, p < 0.001*	p < 0.001*
	TP1	7.77 (4.04)		3.43 (3.55)		p < 0.001*
	TP2	10.21 (2.72)		9.07 (2.84)		p = 0.206
Phoneme deletion (items solved)	TP3	10.89 (2.04)	F(2,51) = 140.18, p < 0.001*	10.79 (1.37)	F(2,12) = 24.51, p < 0.001*	p = 0.825
	TP1	4.75 (4.48)		1.29 (2.02)		p < 0.001*
	TP2	9.96 (3.62)		5.43 (4.42)		p = 0.001*
Rapid naming colors and objects (seconds)	TP3	13.57 (4.06)	F(2,51) = 76.04, p < 0.001*	9.07 (4.71)	F(2,12) = 12.49, p = 0.001*	p = 0.002*
	TP1	127.62 (28.11)		150.14 (43.53)		p = 0.063
	TP2	108.43 (20.27)		119.71 (21.99)		p = 0.048
Rapid naming letters and digits (seconds)	TP3	93.43 (17.00)	t(52) = 6.67, p < 0.001*	113.64 (24.36)	t(52) = 10.19, p = 0.009*	p = 0.003*
	TP2	62.06 (13.45)		84.08 (26.72)		p = 0.047
	TP3	51.70 (9.19)		64.36 (13.23)		p = 0.007*

Note. Behavioral measures for TR and DYS are reported with mean and standard deviation. The statistical test used to check progress between TP is repeated measures ANOVA or paired t-test (in case of measures with only two TP). For group differences, bootstrap analysis was used.* Remains significant after Bonferroni-Holm correction for multiple comparisons

fMRI results - Typical readers

Voxel-wise longitudinal analyses

In the typical readers, the longitudinal analyses results indicated a decrease in the spatial extent of the overlap between the letters and speech sounds processing related activations (Figure II.4.1., marked in orange) between TP1 and TP3.

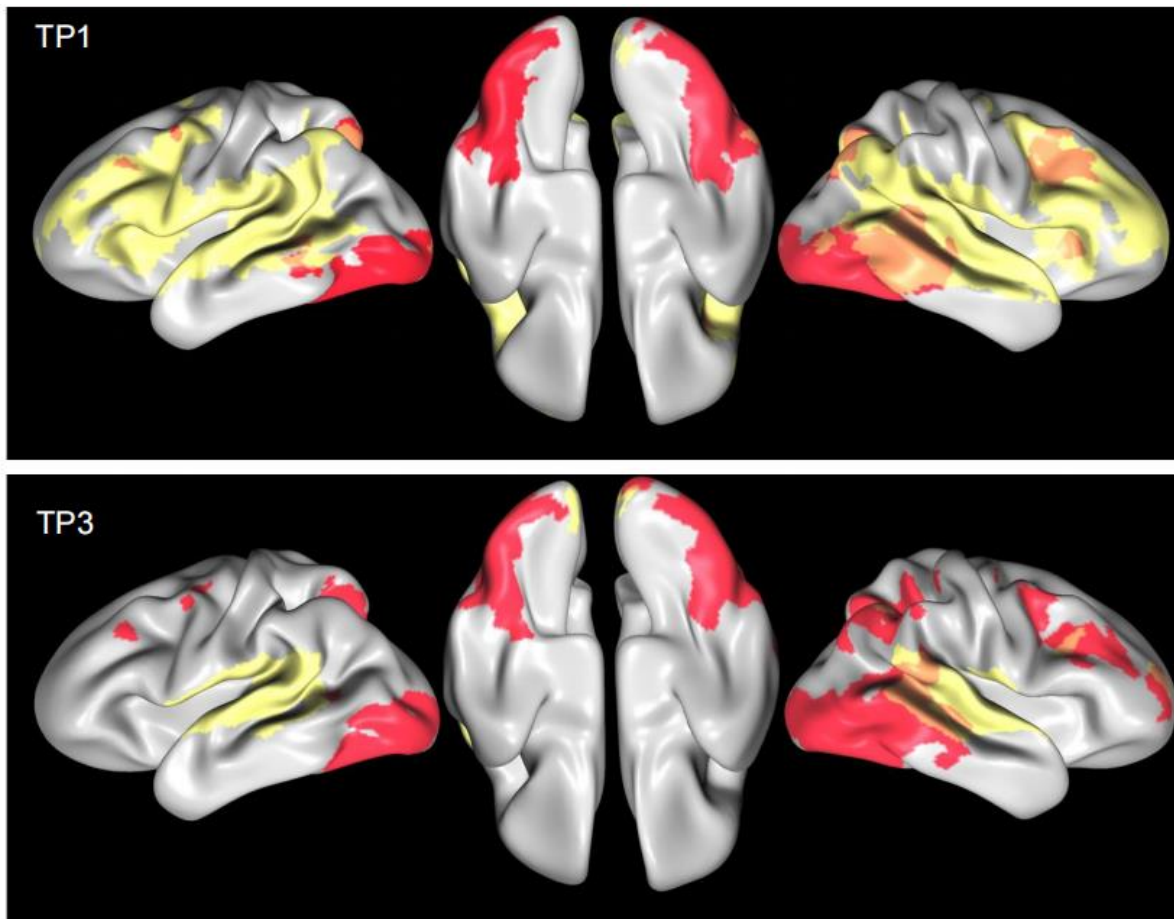


Figure II.4.1. Brain activity in typical readers group in a predefined task positive mask in response to unisensory presented letters (in red) and speech sounds (in yellow) as well as the overlap of brain activity for both conditions (in orange) at both time-points (TP1 - at the beginning of schooling, TP3 - after 2 years of schooling).

The overlap was analysed using the logical AND conjunction approach. The overlap was present in more brain areas and was larger in TP1. At TP1 typical readers presented overlap in the right frontal, parietal, and bilateral temporal cortex, which at TP3 was less extensive and included only the right temporal cortex (see Table II.4.2.).

Table II.4.2. Logical conjunction (co-activation) between letters and speech sounds at TP1 and TP3 in typical readers.

Brain region	Hemisphere	x	y	z	Stat (t)	Cluster size
Letters & speech in TP1						
Middle temporal gyrus	R	60	-31	-2	7.07	16166
Middle frontal gyrus	R	48	17	37	5.52	3763
Superior parietal lobule	L	-33	-58	43	5.27	3189
Middle temporal gyrus	L	-60	-40	4	5.09	722
Inferior frontal gyrus	R	30	23	4	4.78	377
Letters & speech in TP3						
Superior temporal gyrus	R	57	-43	16	6.32	2548

We found that brain activation during processing of unimodal presented visual letters and speech sounds significantly changed between time points in typical readers. For letters, decreased activation at TP3 compared to TP1 was observed in the left Fusiform gyrus (Figure II.4.2. and Table II.4.3.). For speech sounds there was also decreased activation at TP3 found in bilateral frontal and temporal cortex, right declive and left precuneus (Figure II.4.3. and Table II.4.3.)

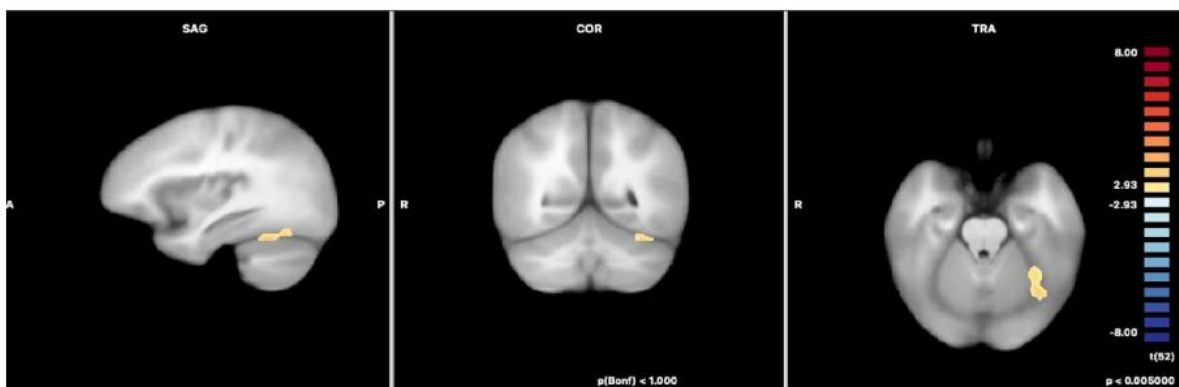


Figure II.4.2. Time effect for unisensory presented letters (in a predefined task positive mask) for typical readers - in yellow areas with higher activation at TP3 compared to TP1

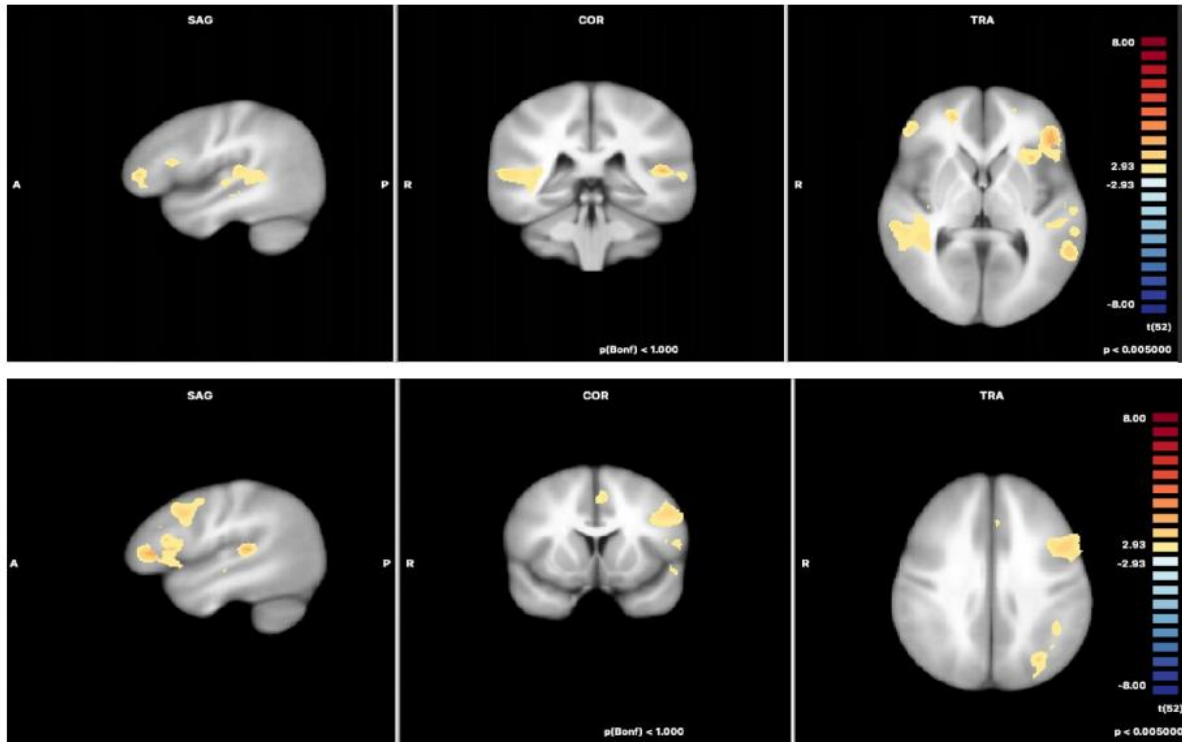


Figure II.4.3. Time effect for unisensory presented speech sounds for typical readers in a predefined task positive mask - in yellow areas with higher activation at TP3 compared to TP1

Table II.4.3. Effect of time - differences between time points in the processing of unimodally presented letters and speech sounds in typical reading development

Brain region	Hemisphere	x	y	z	Stat (t)	Cluster size
Letters TP1 > TP3						
Fusiform gyrus	L	-33	-46	-23	5.47	887
Speech TP1 > TP3						
Inferior frontal gyrus	L	-45	32	4	4.40	8883
Middle frontal gyrus	L	-45	11	34	4.46	3483
Superior temporal gyrus	L	-48	-28	10	4.46	2959
Superior frontal gyrus	R	6	20	58	4.03	3997
Middle temporal gyrus	R	39	-40	4	4.02	6319
Middle temporal gyrus	L	-57	-49	7	3.97	1265
Inferior & middle frontal gyrus	R	21	38	-2	3.93	1262
Middle frontal gyrus	R	45	41	7	3.84	3406
Precuneus	L	-34	-70	37	3.79	1937
Declive	R	6	-67	-14	3.76	1014

Super-additivity effect

At TP1 we found the super-additivity effect in the left fusiform gyrus and in the superior temporal gyrus/planum temporale bilaterally. At TP3 super-additivity effect was more extensive and included bilateral frontal, superior temporal, and fusiform gyri (Figure II.4.4. and Table II.4.4.)

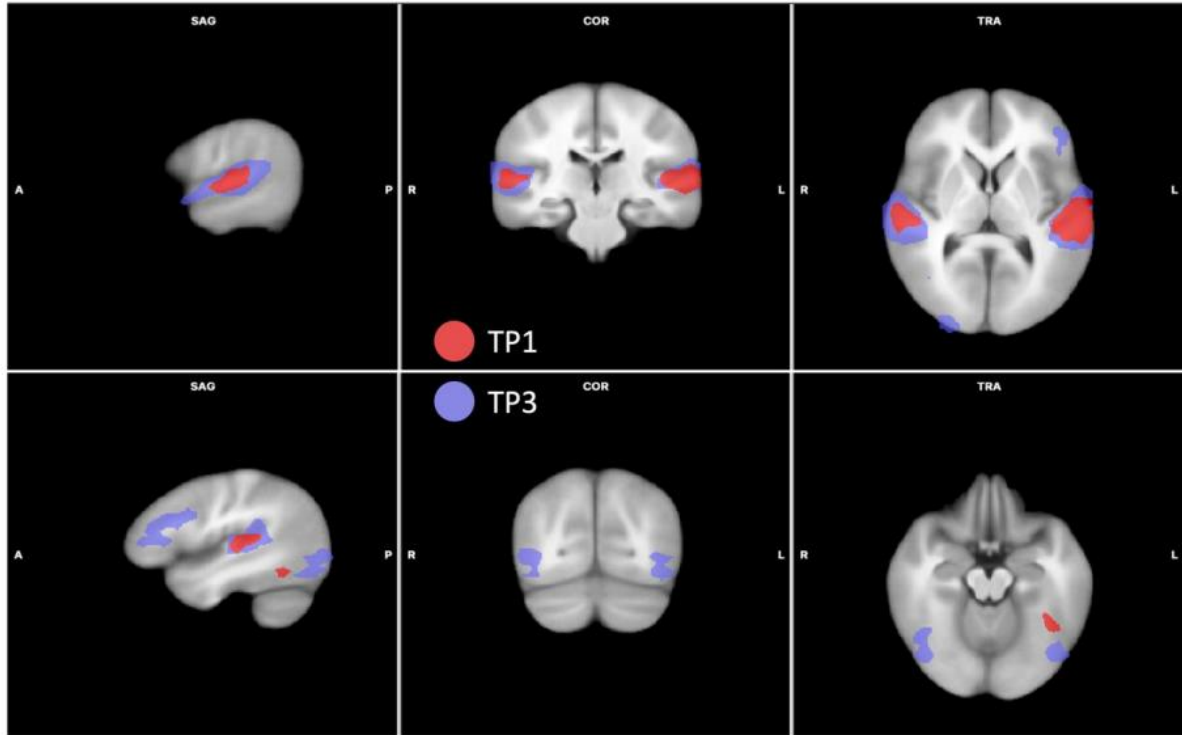


Figure II.4.4. Brain activity in typical readers group in a predefined task positive mask for super-additivity effect, in red for TP1 - at the beginning of schooling, and in violet in TP3 - after 2 years of schooling.

Table II.4.4. Regions of relaxed criterion for super-additivity effect in TP1 and TP3, in typical readers

Brain region	Hemisphere	x	y	z	Stat (t)	Cluster size
TP1: congruent > (letters + speech)/2						
Superior temporal gyrus	L	-57	-16	4	6.10	10688
Superior temporal gyrus	R	60	-19	7	5.38	3724
Fusiform gyrus	L	-42	-49	-14	3.80	842
Middle frontal gyrus	L	-54	23	28	3.75	683
TP3: congruent > (letters + speech)/2						
Superior temporal gyrus	L	-57	-25	10	12.07	18554
Superior temporal gyrus	R	60	-28	10	8.77	18134
Fusiform gyrus	L	-42	-70	-11	6.38	4566
Middle frontal gyrus	L	-36	23	22	4.57	5013

Fusiform gyrus	R	45	-58	-17	4.47	2881
Middle occipital gyrus	R	24	-94	7	4.17	1310
Middle frontal gyrus	R	36	17	28	4.03	1813

Congruency effect

We did not find any significant time effects for the congruency effect. The comparisons between multisensory conditions (congruent vs. incongruent) at each time point produced no suprathreshold activations.

fMRI results - Dyslexic readers

Voxel-wise longitudinal analyses

Figure II.4.5. depicts brain activity in DYS children at the beginning of literacy education (TP1) and two years later (TP3) in response to unisensory presented letters and speech sounds as well as the overlap of brain activity for both conditions. Only at TP1 we can see small regions which show an overlap between letters and speech sounds (depicted in orange).

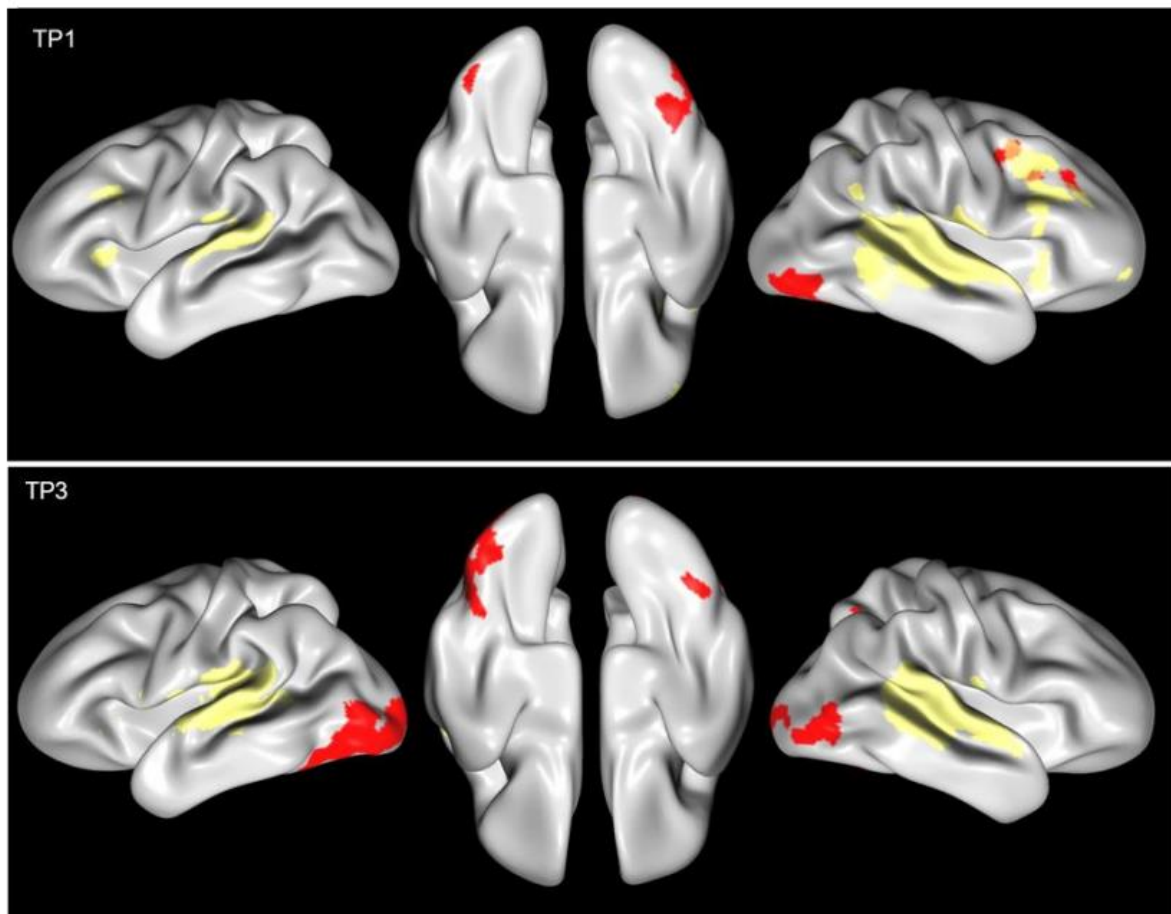


Figure II.4.5. Brain activity in DYS readers' group in a predefined task positive mask in response to unisensory presented letters (in red) and speech sounds (in yellow) as well as the overlap of brain activity for both conditions (in orange) at both time-points (TP1 - at the beginning of schooling, TP3 - after 2 years of schooling).

We examined the overlap (coactivation) between brain activation to unisensory presented letters and speech sounds by means of logical AND conjunctions separately for TP1 and TP3. At TP1 DYS readers presented an overlap in the right frontal cortex, which was no longer observed at TP3 (see Table II.4.5.).

Table II.4.5. Logical conjunction (co-activation) between letters and speech sounds at TP1 DYS readers.

Brain region	Hemisphere	x	y	z	Stat (t)	Cluster size
Letters & speech in TP1						
Middle frontal & precentral gyrus	R	42	8	37	6.17	2190

We did not find any differences in brain activation during processing of unimodally presented visual letters between time points. Activation for speech sounds significantly changed between time points in DYS readers. For speech sounds there was also decreased activation at TP3 found in the left Inferior parietal lobule (Figure II.4.6. and Table II.4.6.)

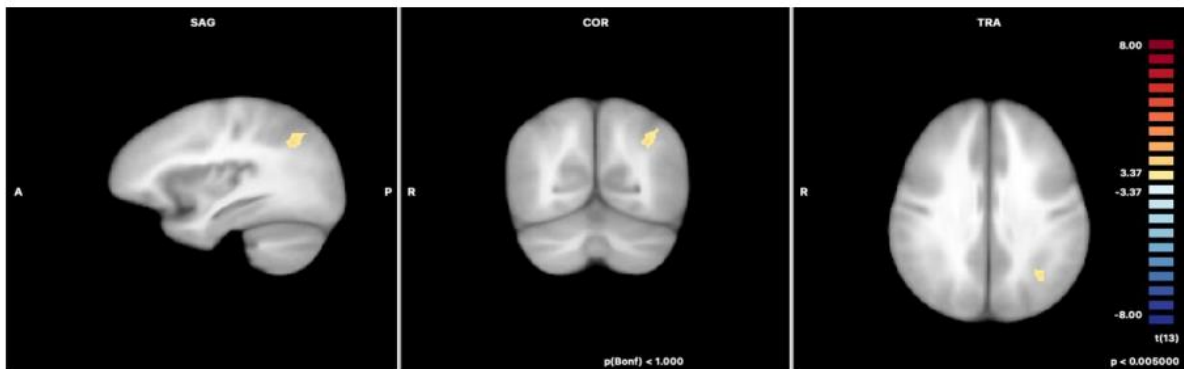


Figure II.4.6. Time effect for unisensory presented speech sounds in readers with dyslexia in a predefined task positive mask - in yellow areas with higher activation at TP3 compared to TP1

Table II.4.6. Effect of time - differences between time points in the processing of unimodally presented letters and speech sounds in readers with dyslexia

Brain region	Hemisphere	x	y	z	Stat (t)	Cluster size
Speech TP1 > TP3						
Inferior parietal lobule	L	-36	-58	41	2.49	680

Super-additivity effect (relaxed criterion)

At TP1, the super-additivity effect was present in bilateral temporal areas, left lingual gyrus and right fusiform gyrus. At TP3, similarly as in typical readers, the super-additivity effect was presented in bilateral temporal areas, occipital areas and left fusiform (Figure II.4.7. and Table II.4.7.)

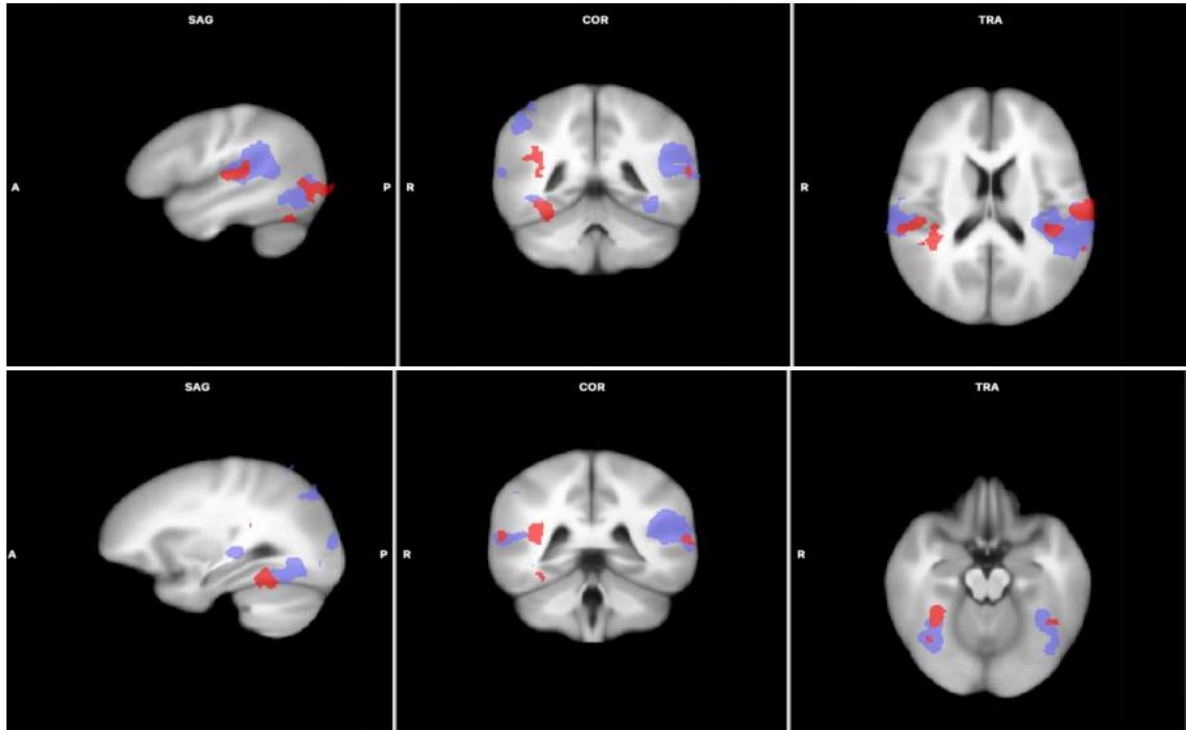


Figure II.4.7. Brain activity in the DYS group in a predefined task positive mask for relaxed criterion for super-additivity effect, in red for TP1 - at the beginning of schooling, and in violet in TP3 - after two years of schooling.

Table II.4.7. Regions active for relaxed criterion for super-additivity effect in TP1 and TP3, in dyslexic readers

Brain region	Hemisphere	x	y	z	Stat (t)	Cluster size
TP1: 2 x congruent > letters + speech						
Superior temporal gyrus	R	51	-25	13	8.10	5974
Middle temporal gyrus	L	-67	-31	7	8.06	9605
Lingual gyrus	L	-18	-97	-5	6.30	1846
Inferior temporal gyrus	L	-55	-70	-2	6.11	3272
Fusiform gyrus	R	33	-40	-20	5.60	2282
Inferior temporal gyrus	R	48	-64	-2	5.14	1188

TP3: 2 x congruent > letters + speech

Insula, Inferior parietal lobule, Middle & Superior temporal gyrus, Postcentral gyrus	L	-51 -31 13	13.95	20840
Fusiform gyrus, Inferior & Superior temporal gyrus, Lingual gyrus, Middle occipital gyrus	R	45 -70 1	8.03	10836
Postcentral gyrus, Superior temporal gyrus	R	63 -10 13	7.57	12129
Fusiform gyrus, Inferior & Middle occipital gyrus	L	-33 -85 -2	7.29	9410
Inferior parietal lobule	R	45 -52 52	7.21	9589
Thalamus	R	27 -22 1	6.57	1160
Angular gyrus	L	-27 -58 37	5.35	2544

Congruency effect

No time effects were observed for the congruency effect. The comparisons between multisensory conditions (congruent vs. incongruent) at each time point produced no suprathreshold activations.

ROI analyses - comparison typical and dyslexic readers at TP3

To examine differences in brain activation between TR and DYS (despite unequal group size), we ran a bootstrap analysis on the percent signal change in the left STS and left PT/HS for multisensory conditions.

DYS had higher activation than TR for congruent LS pairs at TP1 ($p = 0.02$) and at TP3 ($p = 0.003$) in PT/HS, see: Figure II.4.8. There were no significant group differences for L STS.

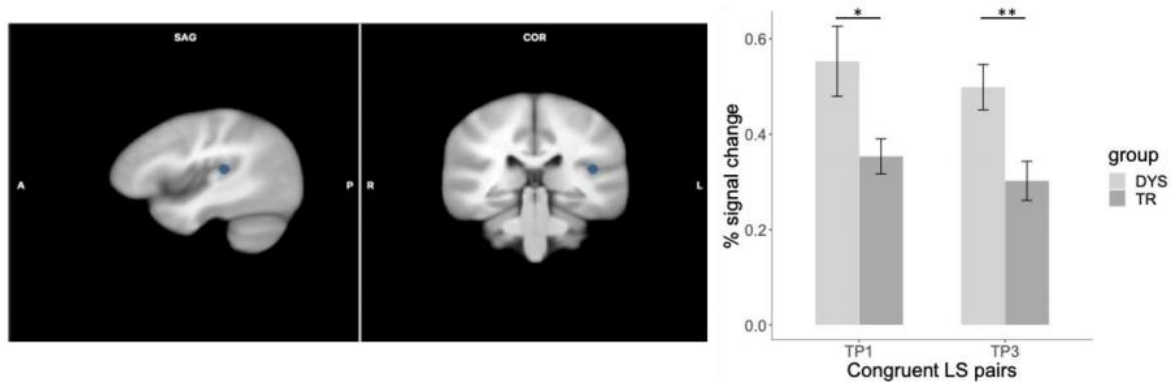


Figure II.4.8 Activation for congruent LS pairs condition at TP1 and TP3 for TR and DYS groups, error bars represent standard error of the mean.

Whole – brain correlations with reading

To check if word reading is correlated with activation for letters, speech, and incongruent vs. congruent LS pairs (i.e. incongruency effect), we ran whole-brain correlations for typical and dyslexic readers as one cohort.

We did not find any correlations for letters (neither at TP1 nor TP3), but we found several regions showing positive correlations between word reading and brain response to speech sounds (Figure II.4.9., Figure II.4.10., and Table II.4.8.), including bilateral frontal and parietal regions at TP1 and TP3 and additionally temporal and occipital regions at TP3. For incongruent vs. congruent LS comparison, we found positive correlation in the left anterior STG and the left fusiform gyrus at TP1 as well as the left superior parietal lobule and the right precuneus at TP3 (Figure II.4.11., Figure II.4.12., and Table II.4.9.).

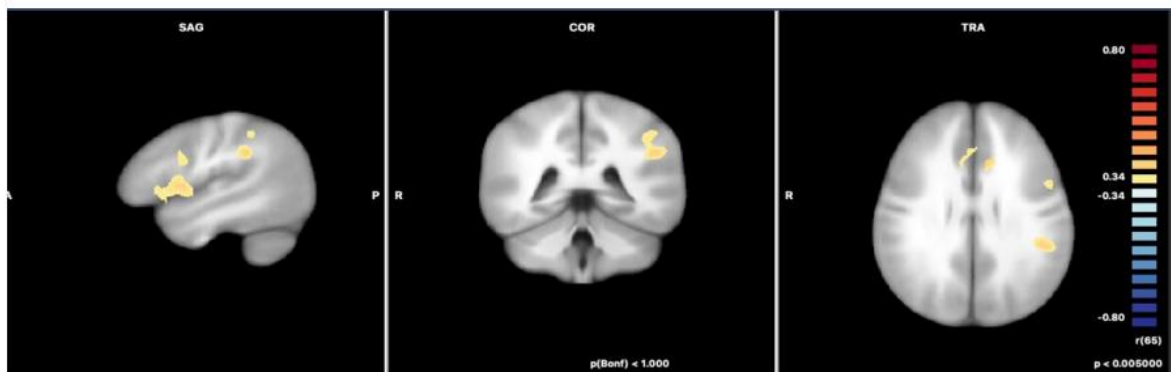


Figure II.4.9. Positive correlations between word reading (words per minute) and activation for speech sounds at TP1.

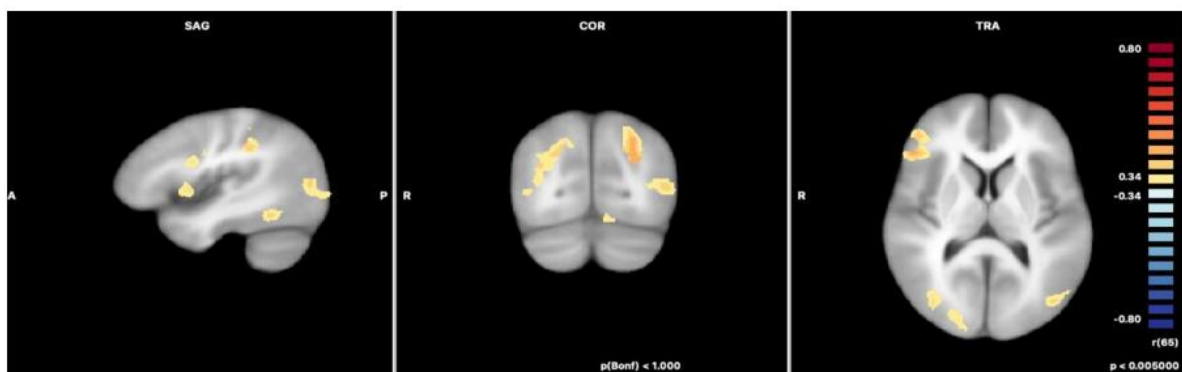


Figure II.4.10. Positive correlations between word reading (words per minute) and activation for speech sounds at TP3.

Table II.4.8. Areas showing positive correlation between word reading and speech sounds in TP1 and TP3

Brain region	Hemisphere	x	y	z	r	Stat (t)	Cluster size
Speech sounds x word reading TP1							
Cingulate gyrus	L	-12	17	37	0.49	< 0.001	2301
Clastrum	L	-27	2	13	0.49	< 0.001	904
Precentral gyrus	L	-45	5	4	0.47	< 0.001	2588
Inferior parietal lobule	L	-45	-34	28	0.47	< 0.001	1351
Middle frontal gyrus	R	24	14	43	0.43	< 0.001	779
Inferior frontal gyrus	R	51	26	13	0.42	< 0.001	1053
Inferior frontal gyrus	L	-51	8	25	0.42	< 0.001	608
Speech sounds x word reading TP3							
Inferior frontal gyrus	R	48	30	13	0.49	< 0.001	3575
Precuneus	L	-27	-67	34	0.49	< 0.001	3490
Cingulate gyrus	L	-8	23	28	0.49	< 0.001	1654
Lingual gyrus	R	18	-88	4	0.46	< 0.001	8848
Middle frontal gyrus	R	27	38	31	0.46	< 0.001	1451
Inferior parietal lobule	L	-48	-34	31	0.46	< 0.001	1304
Precentral gyrus	R	48	2	37	0.45	< 0.001	3199
Superior temporal gyrus	L	-51	14	-5	0.44	< 0.001	1098
Fusiform gyrus	L	-36	-40	-20	0.43	< 0.001	1570
Declive	L	-6	-61	-14	0.43	< 0.001	1077
Middle temporal gyrus	L	-42	-73	10	0.42	< 0.001	2123
Precentral gyrus	L	-36	-1	28	0.41	< 0.001	835
Lingual gyrus	L	-9	-91	-1	0.38	< 0.001	598

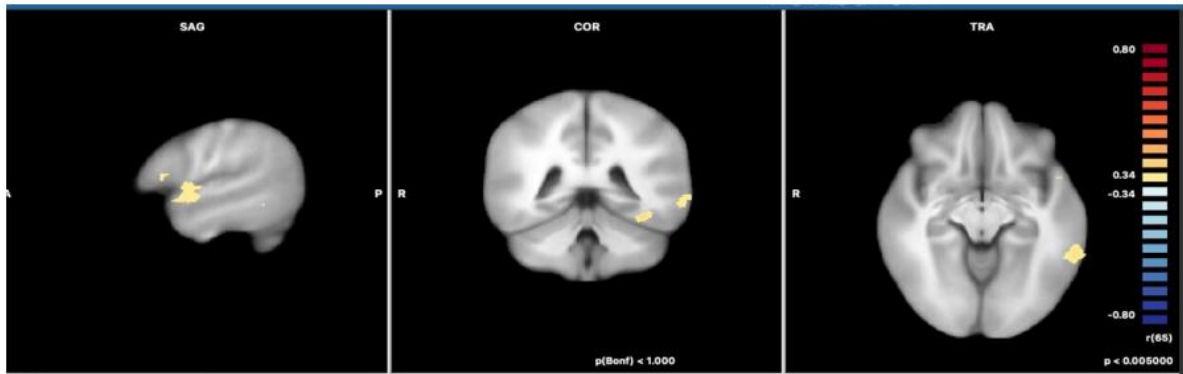


Figure II.4.11. Positive correlations between word reading and brain activation for incongruent > congruent LS contrast at TP1

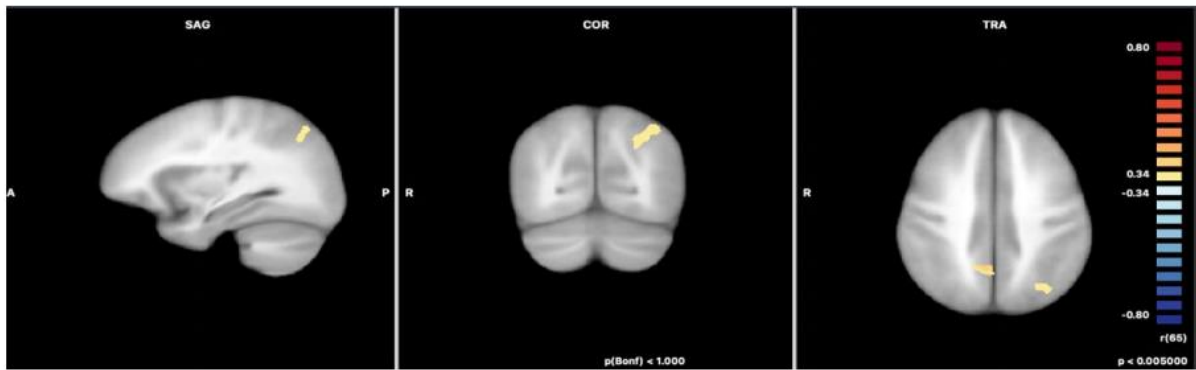


Figure II.4.12. Positive correlations between word reading and brain activation results for incongruent > congruent LS contrast at TP3

Table II.4.9. Areas showing positive correlations between word reading and incongruent vs. congruent LS contrast at TP1 and TP3.

Brain region	Hemisphere	x	y	z	r	Stat (t)	Cluster size
Incongruent > congruent LS TP1 x word reading TP1							
Fusiform gyrus	L	-36	-37	-17	0.46	< 0.001	1487
Superior temporal gyrus	L	-57	5	13	0.42	< 0.001	2577
Incongruent > congruent LS TP3 x word reading TP3							
Precuneus	R	9	-52	37	0.50	< 0.001	594
Superior parietal lobule	L	-36	-71	43	0.45	< 0.001	834

Discussion

In Experiment 3, we used a longitudinal design in a large group of beginning readers to examine how the neural basis of LS processing changes with reading experience in typical reading development. We also tested for differences between typical and dyslexic readers in the left STC response to multisensory information. Typical reading development was characterized by a decrease in brain response to unimodal stimuli (letters and speech sounds) over time. Additionally, we found that reading is positively related to the incongruity effect in the left fusiform gyrus and anterior STG at TP1, but two years later, the correlation was observed only in the parietal cortex. For group comparison, we found that children with dyslexia presented increased activation to congruent LS pairs compared to typical readers in the left PT/HS at both time points (in line with findings from Experiment 2 on an extended sample).

When we take a closer look at unimodal conditions, in typical readers, we observe decreased activation in the left fusiform gyrus for visually presented letters, while no time differences are observed in the dyslexic group. Interestingly, these findings are in contrast to the results on an overlapping sample of typical readers where increased activation in the left fusiform gyrus for processing printed words was found between the two time points (Chyl et al., 2019). This difference could be related to the fact that whole-word reading is a more complex ability than letter processing and with time and reading instruction, the left fusiform gyrus becomes a storage of orthographic representation responsible for whole word recognition (Lerma-Usabiaga et al., 2018, Dehaene et al., 2002).

We did not find any correlations between brain activation in response to letters with word reading skill at both timepoints. EEG studies (Brem et al., 2013; Maurer et al., 2007, 2011) suggest that the developmental trajectory of the left ventral occipito-temporal cortex (including the fusiform gyrus) activation to print could be described by an inverted U-shaped function, with growing specialization at the shift from the pre-reading to the reading stage which levels off with higher expertise (for review see Chyl et al., 2021). Since processing of single letters is less demanding than processing of letter strings, the specialization occurs earlier and within a narrower time frame and thus at TP3 the fusiform activation could be already leveled off resulting in a lower level of activity at TP3 (conducted in the second or third grade) compared to TP1 (kindergarten/first grade). This is in agreement with a recent EEG study following children from kindergarten to the fifth grade showing that activation in vOT in preschool is low and at the same level for letters and words, then in the first grade the activation for letters is higher whereas with the second grade, activation to letters drops. At this time conversion occurs and activation is higher for words than for letters until the fifth

grade (Fraga-Gonzalez et al., 2021). We did not observe correlations with word reading and activation to letters at both TP1 and TP3 in whole brain analyses. Such correlation was previously found in one study on older, nine years old Dutch children in left fusiform gyrus ROI (Blau et al., 2010).

For speech sounds, we can observe a decrease in the activation over time in bilateral fronto-temporal regions in typical readers and in the left inferior parietal lobule for dyslexic readers. Despite significant decreases in activation to speech sounds with time, bilateral fronto-parietal activation was positively related to reading skill at both time points, with additional clusters in the left temporal and ventral occipito-temporal cortex (including the fusiform gyrus) at TP3. Data from the same cohort of children, but from a different task showed that typical readers without the risk of dyslexia activated structures responsible for auditory phonological processing already at the beginning of literacy, and later presented decreased brain activation over time, which is argued as automatization of phonological skills (Łuniewska et al., 2019). It is also possible that speech sound processing in the brain shows a similar trajectory. Even though the neural circuitry involved in speech sound processing becomes more specialized, it is still relevant for word reading skills.

Although activation to unisensory stimuli decreased with time and reading experience in typical readers, we found evidence for enhanced multisensory LS processing. While examining the overlap to unisensory presented letters and speech sounds, we could observe that at TP3 it was less extensive than at TP1. However, when the super-additivity effect was tested in typical readers at both TPs, the reversed pattern was noted. Namely, in addition to bilateral STG and left fusiform at TP1, bilateral frontal and right ventral occipito-temporal regions showed super-additivity effect at TP3. A similar pattern, though less pronounced, was observed in readers with dyslexia. Super-additivity effect in bilateral STG had been previously reported in both typical and dyslexic adolescents (Kronshabel et al., 2014), displaying no significant group differences. Super-additivity effect in the fusiform gyrus might be in line with the findings of increased left fusiform activation during audio-visual exposure to letters and ambiguous speech sounds (Romanovska et al., 2021). Our finding could also be in agreement with a report of audiovisual integration in the left fusiform gyrus during a rhyming task, which additionally showed a positive relation to reading level (McNorgan & Booth, 2015). It also supports a hypothesis proposed by Pattamadilok et al., (2019) that spoken and written language is repeatedly associated in the left ventral occipito-temporal cortex during reading acquisition. Decrease of modality specific activation together with an increase of multimodal audiovisual processing might be explained by the interactive specialization model of neurocognitive development (Johnson, 2011), which posits that the refinement of task-related functional networks is driven by a shared history of co-activation between cortical regions.

We did not find any differences for congruent vs. incongruent LS pairs in both groups,

nor any changes of the congruency effect with time. The congruency effect in the literature is linked to the higher-level associative (orthographic and phonological) aspects of letter and speech sound integration and was mainly associated with STC activity (including our results in Experiment 2). There are several reasons why we did not replicate this finding (i.e. incongruency effect). Here, we did not take into account the family history of dyslexia and focused only on typical or dyslexic readers. Both groups included FHD+ and FHD- children, and while family history of dyslexia might have influenced the congruency effect (as shown in Experiment 2), the sample size was too low to afford splitting groups by FHD status. Secondly, in Experiment 3, in line with current statistical standards of fMRI analyses (Eklund et al., 2016), we applied stricter voxelwise threshold in the whole brain analyses than in Experiment 2. We managed to replicate the group effects in the ROI analyses with dyslexic readers having higher activation for congruent LS pairs than typical readers in the left PT/HS, in line with the results of Experiment 2 and in contrast to Blau et al., (2010) findings, where an opposite pattern (higher activation in typical readers than dyslexic readers) was observed in this region. As it was established and summed up by Richlan (2019), these differences can be driven by language transparency or age (the sample is relatively younger than those from previous studies (Blau et al., 2009, 2010, Froyen et al., 2009, Kronschnabel et al., 2014)). However, a recent longitudinal study with an approach similar to ours (three time points from kindergarten to the second grade, Karipidis et al., 2021) on German speaking-children showed that early audiovisual integration was characterized by higher activation for incongruent than for congruent letter-speech sound pairs in the inferior frontal gyrus and ventral occipitotemporal cortex (for mean activation in all the time points). Furthermore, the findings in the left STG/PT were mainly visible when TP1 (kindergarten) was compared to TP2 (first grade). In Wang et al., 2020 study on German-speaking children, differences for congruent vs. incongruent print-speech conditions were not present until the middle of the second grade. In the second grade, an incongruency effect emerged in the bilateral fronto-temporal regions. Difference between multimodal conditions was found in T2 but not in T1 (T1: middle of 1st grade, TP2: middle of 2nd grade).

Unfortunately, we did not scan children at TP2, which can be the reason why we did not observe any time differences in the congruency effect. This explanation could be further supported by findings, from the behavioral study (Experiment 1), showing that Polish children learn the letter the speech sound association within one year of reading instruction (at least this is the period of the most pronounced changes). Therefore, one could expect that functional brain reorganization should take place within this time period. Contrary to our expectations, the incongruency effect did not reverse into the congruency effect with increasing reading experience, as was hypothesized in Experiment 2. We stated that the higher incongruency effect observed in left STC in beginning readers likely reflects an early stage of LS association,

which could reverse into a congruency effect (as in previous studies - Blau et al., 2009, 2010) with increasing reading experience. However, the results of recent studies including longitudinal ones (Wang et al., 2020; Karipidis et al., 2021;) suggest that typical beginning readers are more likely to present an incongruency effect which increases over time.

Finally, behaviorally, for both groups, we can observe significant progress in all measured abilities: letter knowledge, word and pseudoword reading, phoneme analysis, phoneme deletion, and rapid naming. When we compare typical readers to dyslexic readers, we can notice that typical readers outperform dyslexic readers in almost all tests except RAN at TP1. The groups differ only for reading and phoneme deletion at TP2. In the last time point, after two years of formal reading instruction, the groups also differ in RAN. These findings are in line with previous findings on behavioral changes during first years of formal education, based mostly on studies in English or other opaque orthographies (for meta-analysis see Melby-Lervåg et al., 2012). In addition, there is mounting evidence that phonological awareness and RAN share a reciprocal relationship with reading, such that they develop in tandem with the development of reading (Clayton et al., 2020; Perfetti et al., 1987; Peterson et al., 2017; Wolff, 2014). Therefore, these deficits in dyslexia may be partially a consequence of reading failure, especially in the case of more transparent orthographies.

There are a few limitations of the current experiment. Conclusions from the results obtained for dyslexic readers in the current experiment should be drawn with caution due to the fact that a small number of children were diagnosed with dyslexia and thus the results cannot be properly extended to the entire population. Unfortunately, to our best knowledge, it is not possible to compare quantitatively the t-maps obtained for super-additivity effects between time points. In the case of subject-specific beta values, the beta values can represent either specific conditions or differences between conditions, which is not the approach one follows when calculating the super-additivity effect. Therefore, we only compare the maps qualitatively to check for consistency or inconsistency of the effects between timepoints.

In conclusion, these results advance our understanding of the initial steps of reading acquisition, specifically focusing on the association between letters and speech sounds, one of the building blocks in the formation of the reading network in alphabetic languages. The first two years of formal reading development are associated with changes in multisensory LS processing and with growing responses to letter and speech sounds pairs and at the same time reducing activation for letters and speech sounds in time, which may reflect entering a higher level of specialization in the association of the letters and speech sounds.

Chapter II.5. Experiment 4

Research question

In the previous experiments, we have examined when the LS association is learned by children and how it is represented in the brain of sighted print readers. In this experiment, we wanted to compare the neural basis of LS integration between blind Braille readers and sighted print readers. So far, there have been no studies examining how the process of LS association looks like in different languages, let alone different reading modalities. The reading network of the blind shows both similarities (i.e., engagement of the left ventral occipitotemporal cortex, Reich et al., 2011; Dzięgiel-Fivet et al., 2021) and differences (i.e., disengagement of the superior temporal cortex, Dzięgiel-Fivet et al., 2021). Therefore, we were interested if audio-tactile LS integration in the blind shares similarities to audio-visual LS integration in the sighted. As no studies tackled this question before, we treated these analyses as exploratory.

Methods

Participants

Forty-two blind (mean age = 24.90, age range: 9 to 60, SD = 10.52, male = 16, female = 27) and 47 sighted (mean age = 24.24, age range: 9 to 60, SD = 9.79, male = 18, female = 29) subjects participated in the study. Most of the blind subjects were congenitally blind (only two subjects had lost sight before they were 3) and had at most minimal light perception (measured by a questionnaire). The blind subjects began to learn Braille in the first grade of their primary school (between the ages of 6 and 9) and assessed their ability to read Braille as average, exemplary, or very good. None of the participants had any history of neurological illness or brain damage (other than the cause of blindness). Fourteen Braille readers used their right hand for reading, but only one subject was left-handed (the same as in the sighted group). Ethical consent for this study was provided by Jagiellonian University Ethical Committee. Following the Declaration of Helsinki, all adult subjects and parents of minor participants signed an informed consent form.

Behavioral measures and analysis

During the behavioral testing sessions, the participants completed several different reading and language-related measures:

Word Reading: There were eight lists of six words each in this test. Every subsequent list increased in word length which ranged from 2 to 11 letters. High-frequency words with various grammatical forms were used (declined nouns and adjectives, infinitive or conjugated

verbs, adverbs) and the structure was the same for the blind and the sighted. For each list, accuracy and time were measured. The average of the accuracy/time ratios for each list was used as the outcome variable (the number of words correctly read per minute).

Pseudowords Reading - There were eight lists of six pseudowords each in this test. Every subsequent list increased in word length which ranged from 2 to 11 letters. The pseudowords were created by changing or transposing letters or entire syllables in high-frequency real words (different from those used in the Single Word Reading test). They were roughly equal in terms of length, CVC structure, and orthographic complexity to the ones used in the Word Reading test. For each list, accuracy and time were measured. The average of the accuracy/time ratios for each list was used as the outcome variable (the number of words correctly read per minute).

Vowel Replacement task - participants were instructed to substitute the vowel /a/ for the vowel /u/ in words uttered by the experimenter. Three training items were given to the participants before test items. The first 8 stimuli contained only one vowel (/a/; example: rak), next 8 test items featured two vowels (/a/; example: rama). In all phases of the task, accuracy and time were recorded. The outcome variable was the time (in seconds) used to complete the task.

Phoneme Deletion - participants were instructed to say a word that the experimenter had provided without the phoneme that was specified (for example, krowa [cow] without 'r'). The participants were familiarized with the task with six training examples and then solved 26 test items. The outcome variable was the time (in seconds) used to complete the task.

Rapid Naming Letters (RAN Letters) - two test lists and one training list of single letters were given to the subjects. The training list had five distinct letters that were repeatedly shown in pseudorandom sequence in two lines, five letters per line; the test lists had the same five letters but were presented in four lines, six letters per line. All of the letters were to be named by the participants as quickly as they could. The blind subjects performed the task tacitly and the test included Braille letters: a, l g, m, and t. The letters a, e, k, m, and s were presented to the sighted subjects, who completed the task visually. In order to maximize the perceptual distinctiveness of the used objects in both groups, the letters shown to the blind and the sighted individuals were different. The outcome variable was the time (in seconds) used to complete the task.

Rapid Naming Textures (RAN Textures) - the participants were shown two test boards and one training board of five materials with various textures. The test boards had four lines with six items in each line, whereas the training board had two lines with five items each. The participants practiced naming the five textures (glass, cardboard, sponge, net, and velcro) on a training board before being asked to name every item on the test boards as quickly as they could. This task was performed tacitly by both the sighted and the blind with the sighted

subjects blindfolded. The outcome variable was the time (in seconds) used to complete the task.

The computer-based letter and speech sounds association task named: 'Phonemes to letters test' was presented to the participants with simultaneously presented letters on the braille display/or screen and speech sounds in headphones.

Behavioral analysis was performed in SPSS Statistics 27. Because most of the analyzed behavioral data did not have normal distribution, for group comparison U Mann-Whitney tests were used and Spearman rho for correlations. To test differences between correlation coefficients in groups we used an approach from Hinkle et al., 1988, implemented in the online calculator MedCalc Software Ltd. Bonferroni-Holm correction for multiple comparisons was used and alpha was set as 0.95 in behavioral analysis in this study.

fMRI task and scan

The experiment was divided into two runs, each having 12 stimulation blocks and 12 fixation periods. In each block stimuli from one of 4 conditions were presented using Presentation software (Neurobehavioral Systems). Auditory stimuli were presented via headphones, visual stimuli were displayed on an LCD monitor, while tactile stimuli via NeuroDevice Tacti™ Braille display.

Conditions contained unisensory visual letters (1) and speech sounds (2) corresponding to selected Polish single letters (consonants: B, C, D, G, H, J, K, L, M, N, P, R, S, T, W, Z; and vowels: A, E, I, O, U), multisensory congruent (3) and incongruent (4) LS pairs. Each block (15.6 sec) consisted of 3 mini-blocks (5.2 sec) with 12 stimuli (4 per mini-block) and was repeated twice per run, resulting in 48 stimuli per condition. The order of the blocks was pseudorandomized with no more than two blocks of the same kind displayed in a row. To ensure that participants paid attention to the stimuli, we asked them to press a button on a response-pad with left thumb every time they detect target stimuli, similarly to Blau et al., (2010). Target stimuli were “#” on the screen for the sighted, six dot signs for the blind or a recording of white-noise in the unisensory auditory blocks, and a combination of the two in the multisensory blocks. The targets were presented once per block and the participants were familiarized with the target before the task.

The scan took place in the 3T Siemens Trio MRI system using sparse design sequence, in which the stimuli were presented during silent delay of volume acquisition. fMRI data were acquired using a T2* - sensitive, gradient echo planar imaging sequence covering the whole-brain (29 slices, slice thickness: 4 mm, 3 x 3 in-plane resolution, TR = 5.2 s (1.5 s of volume acquisition followed by 3.7 s delay), TE = 25ms, matrix size: 64 x 64). The task was presented in two fMRI runs, each lasting for 6 minutes and 17 seconds (73 volumes), which in total gave 12 minutes and 34 seconds (146 volumes). Anatomical data were acquired using

a T1 weighted sequence (176 slices, slice-thickness 1 mm, TR = 2.53 s, TE = 3.32 ms, flip angle = 7°, matrix size: 256 × 256, voxel size 1 x 1 x 1 mm). The timing of letters presentation on the Braille display was checked behaviourally for Braille readers on young and older volunteers to ensure that it is long enough for blind participants to correctly encode the letter.

fMRI data preprocessing

The imaging data were analyzed with BrainVoyager QX 2.2.0 (Brain Innovation, Maastricht, the Netherlands; Goebel et al., 2006). fMRI data were preprocessed to correct for 3D motion artifacts (trilinear interpolation), linear drifts, and low-frequency non-linear drifts (high pass filter 3 cycles/time course). Functional images were co-registered to the corresponding anatomical images. The anatomical images were then transformed into Talairach stereotaxic space (Talairach and Tournoux, 1988), and this transformation was applied to the aligned functional data. Because of the differences in the quality and heterogeneity of BOLD signal between the blind and the sighted groups, ICA was used to clean the data. The ICA was run for 20 components. The exclusion criteria were the correlation of each component with the experiment condition higher than 0.25.

fMRI data analysis

Whole brain analyses for the blind and the sighted groups experimental conditions were modeled in single subjects design matrix together with ICA components. Second level analyses were performed using the GLM approach. The first level analysis was a single factor model including four experimental conditions (i.e., letters, speech sounds, congruent LS pairs and incongruent LS pairs) as separate predictors and was used to determine brain regions involved during the experimental tasks for the whole sample. For both groups, the statistical map from this analysis (all experimental conditions vs. baseline (rest period) contrast) was used as a mask (thresholded at $p = 0.05$) for all subsequent analyses, following previous studies (Blau et al., 2009, 2010; Plewko et al., 2018).

On the group level, several analyses were conducted. Firstly, the regions activated by unimodal letter and speech sound conditions were delineated in both groups (corrected for multiple comparisons using false-discovery rate, $q(\text{FDR}) < 0.01$). Additionally, super-additivity effect with relaxed criterion was tested in each group. Subsequently, activation during letters and speech sound processing was compared between the groups. Finally, a 2 x 2 factorial model with group (Blind and Sighted) and multimodal conditions (congruent and incongruent LS pairs) as factors was specified. In a post-hoc manner the direction of the congruency effect (congruent > incongruent vs incongruent > congruent) was studied in each group as the age range of participants was broader than in Experiments 2 and 3. The results of the whole-brain analyses are reported in the Talaraich space. Results were significant at $p < 0.005$ at voxel-

level, corrected for multiple comparisons using ClusterThresh Plugin with Monte Carlo simulation with 1000 iterations (Forman et al. 1995, Goebel et al. 2006).

Results

Behavioral results

Between groups differences

Blind and sighted groups differed significantly in word and pseudoword reading (sighted > blind), as well as for time in RAN textures (blind > sighted). Differences in other measures did not survive the correction for multiple comparisons (Table II.5.1.). The RT in 'Phonemes to letters' test correlated significantly with age and most of the behavioral measures only in the sighted group. All of the correlations were insignificant in the blind group, however, only for the correlation with age and the phoneme deletion test the differences between the groups were significant (Table II.5.2. and Figure II.5.1.).

Table II.5.1. Behavioral data statistics and group differences

Measurement	Group		Statistics
	Blind	Sighted	
Word reading (per min)	48,48 (22,45)	106,76 (27,8)	Z = -6,8 , p < 0,001*
Pseudoword reading (per min)	33,09 (15,35)	71,96 (22,68)	Z = -6,52 , p < 0,001*
Vowel replacement (time in sec)	27,16 (6,17)	31,98 (13,08)	Z = -0,84 , p = 0,4
RAN letters (time in sec)	28,79 (12,09)	22,38 (6,22)	Z = 2,63 , p = 0,01
RAN textures (time in sec)	68,37 (39,25)	92,92 (27,06)	Z = -4,44 , p < 0,001*
Phoneme deletion (time in sec)	115,18 (38,24)	146,29 (51,73)	Z = -2,74 , p = 0,01
RT in 'Phonemes to letters test' (sec)	170,73 (50,54)	163,11 (30,78)	Z = 1,95 , p = 0,05
Accuracy in 'Phonemes to letters test' (%)	93,88 (3,87)	95,61 (2,57)	Z = -0,14 , p = 0,89

Note. * Remains significant after Bonferroni-Holm correction for multiple comparisons

Correlations with RT and accuracy in 'Phonemes to letters test.'

Table II.5.2. Correlation between RT in 'Phonemes to letters test.' and behavioral measures and age for both groups

Measurements	Blind	Sighted	Statistics
Age (years)	Rho = -0.29, p = 0.107	Rho = -0.64 , p < 0.001*	Z = 2.09, p = 0.037*
Word reading (per min)	Rho = -0.39, p = 0.027	Rho = -0.54, p < 0.001*	Z = 0.88, p = 0.282
Pseudoword reading (per min)	Rho = -0.33, p = 0.059	Rho = -0.57, p < 0.001*	Z = 1.39, p = 0.166
Vowel replacement (time in sec)	Rho = -0.2, p = 0.272	Rho = -0.54 , p < 0.001*	Z = - 1.82, p = 0.068
RAN letters (time in sec)	Rho = 0.35, p = 0.043	Rho = 0.32 , p = 0.059	Z = 0.15, p = 0.878
RAN materials (time in sec)	Rho = 0.27, p = 0.125	Rho = 0.5, p = 0.003*	Z = 1.24, p = 0.215
Phoneme deletion (time in sec)	Rho = -0.14, p = 0.467	Rho = 0.47 , p = 0.004*	Z = -2.96, p = 0.003*

Note. * Remains significant after Bonferroni-Holm correction for multiple comparisons

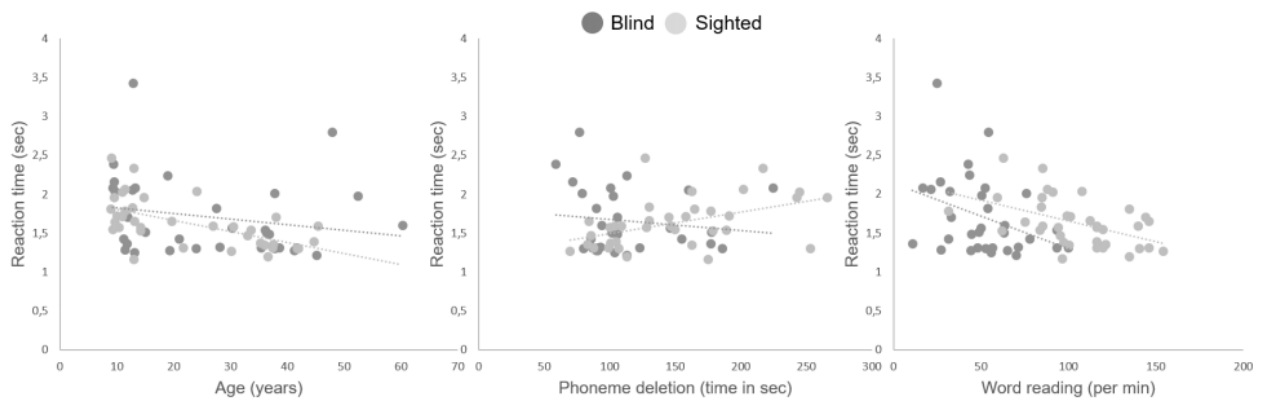


Figure II.5.1. Correlation coefficient for RT and behavioral measures and age for both groups

fMRI results

Voxel-wise analyses

Figure II.5.2. depicts brain activity in the blind (A) and the sighted (B) in response to unisensory presented letters and speech sounds as well as the overlap of brain activity for both conditions. We can observe that more brain regions show an overlap between letters and speech sounds (depicted in orange) in the blind group than in the sighted.

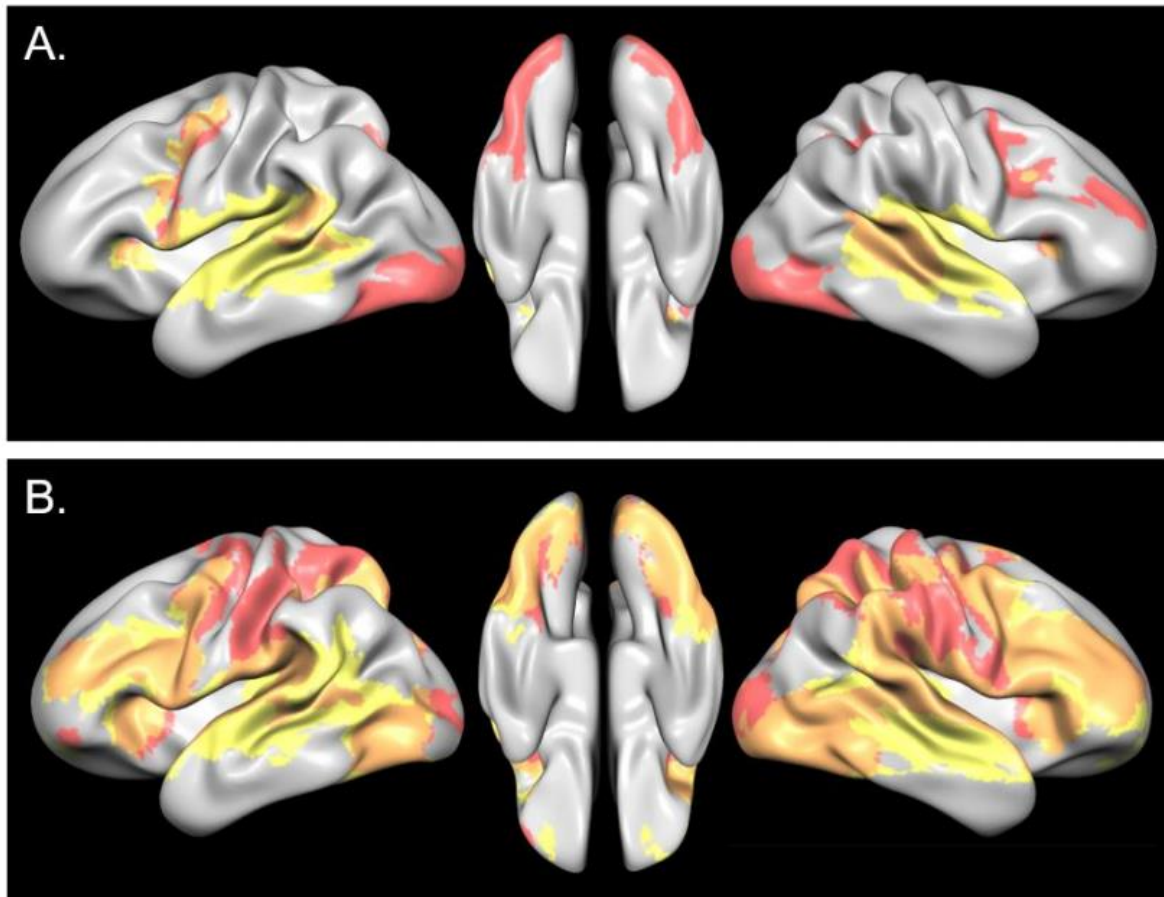


Figure II.5.2. Brain activity in the blind (A) and the sighted (B) in a predefined task positive mask in response to unisensory presented letters (in red) and speech sounds (in yellow) as well as the overlap of brain activity for both conditions (in orange)

The overlap (coactivation) in brain activation to unisensory presented letters and speech sounds was examined by the means of logical conjunctions separately for blind and sighted. The blind group presented an overlap in the bilateral frontal, temporal, parietal and occipital regions. For sighted the overlap was less extensive and included bilateral superior temporal cortex and left frontal areas (see Table II.5.3.).

Table II.5.3. Logical conjunction (co-activation) between letters and speech sounds for blind and sighted

Brain region	Hemisphere	x	y	z	Stat (t)	Cluster size
Letters & speech for blind						
Cuneus, Culmen, Declive, Superior Temporal Gyrus, Insula, Middle Temporal Gyrus, Superior Temporal gyrus, Inferior Parietal Lobule, Precuneus, Inferior Frontal Gyrus, Middle Frontal Gyrus, Superior Frontal Gyrus	R	57	-19	19	8.47	135198*
Cuneus, Declive, Middle Occipital Gyrus, Precuneus, Inferior Parietal Lobule, Middle Occipital Gyrus, Middle Temporal Gyrus, Insula, Superior Temporal Gyrus, Lingual Gyrus	L					
Middle Frontal Gyrus	L	-33	47	19	6.14	16826
Superior Frontal Gyrus	R	3	8	49	5.71	4125
Letters & speech for sighted						
Superior Temporal Gyrus	L	-51	-37	16	7.38	11207
Superior Temporal Gyrus	R	45	-37	13	6.80	17905
Precentral Gyrus	L	-42	-4	46	6.59	5252
Medial Frontal Gyrus	L	-6	-4	61	5.04	1509
Culmen	R	27	-55	-26	5.01	2125
Culmen	L	-30	-55	-23	4.83	2869
Inferior Parietal Lobule	L	-30	-52	37	4.25	1270
Inferior Frontal Gyrus	R	42	8	28	4.17	1973

* cluster contains a lot of different areas in left and right hemisphere

For unimodal presented letters we found that the blind group had more robust activation mainly in sensorimotor cortex bilaterally whereas the sighted presented higher activation in the visual cortex in agreement with what could be expected based on the differences in processing modality (see Figure II.5.3. and Table II.5.4.).

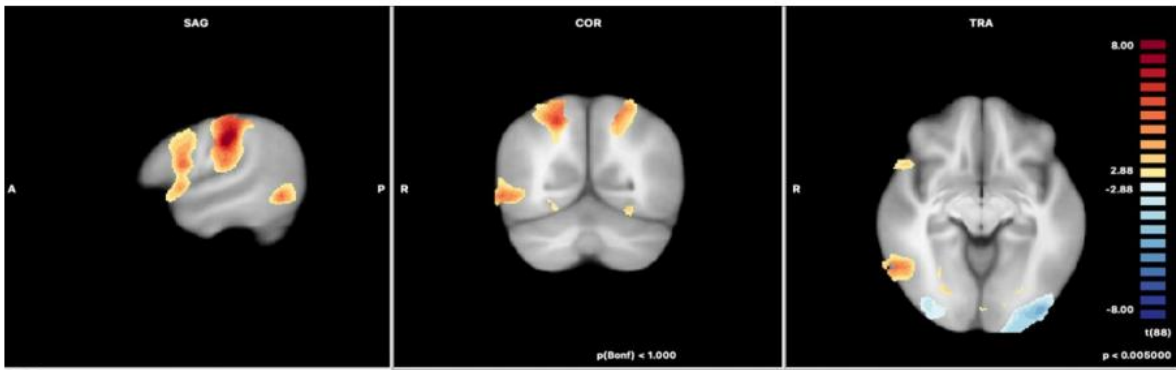


Figure II.5.3 Differences in brain activation for letters between the blind and the sighted, orange clusters are those in which the blind always have higher activation for speech than the sighted, and the blue ones are those with higher activation for the sighted.

Table II.5.4 Differences between groups in the processing of unimodally presented letters.

Brain region	Hemisphere	x	y	z	Stat (t)	Cluster size
Letters: Blind > Sighted						
Cuneus, Inferior parietal lobule, Precentral Gyrus, Precuneus, Postcentral gyrus, Superior parietal lobule,	R	51	-19	34	9.08	44222
Postcentral gyrus	L	-54	-22	40	8.79	27184
Inferior frontal gyrus	R	61	11	22	5.79	8731
Inferior & Middle temporal gyrus	R	57	-54	-5	6.19	2980
Inferior frontal gyrus	L	-51	5	31	4.93	1644
Fusiform gyrus	L	-24	-61	-13	4.21	1440
Superior & Medial frontal gyrus	R	3	8	49	4.81	1266
Declive	R	20	-64	-14	4.30	957
Precentral gyrus	R	30	-10	58	3.65	759
Letters: Sighted > Blind						
Inferior occipital gyrus	L	-39	-85	-8	-5.74	6462
Middle occipital gyrus	R	27	-85	-2	-5.21	2460

We found that brain activation during processing of unimodally presented speech sounds, despite involving similar auditory modality, significantly differed between the groups. The blind participants had higher activation for speech sounds in temporal, frontal and ventral occipito-temporal areas (see Figure II.5.4. and Table II.5.5.).

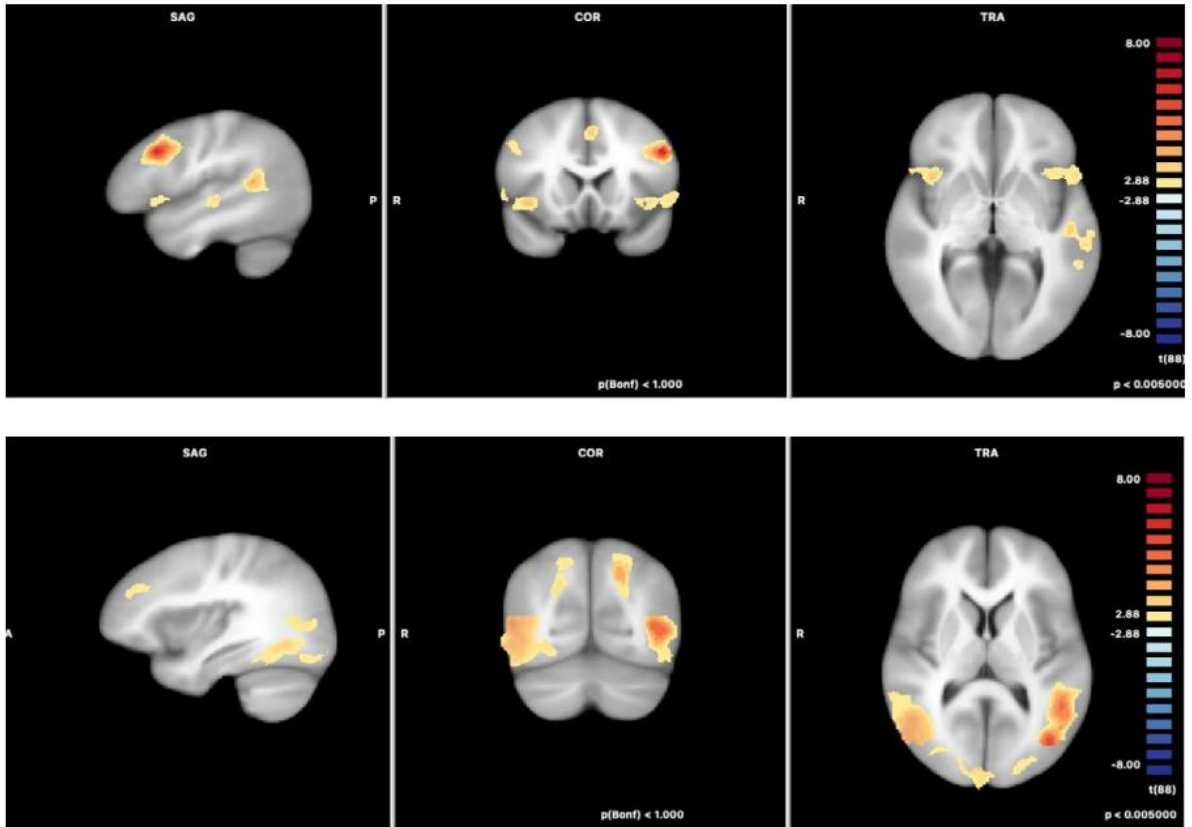


Figure II.5.4. Differences in brain activation for speech between the blind and the sighted, with the blind always displaying higher activation for speech than the sighted.

Table II.5.5. Differences between groups in the processing of unimodally presented speech sounds.

Brain region	Hemisphere	x	y	z	Stat (t)	Cluster size
Speech sounds: Blind > Sighted						
Fusiform gyrus, Middle & inferior occipital gyrus, Middle, Inferior & Superior temporal gyrus, Precuneus	R	51	-64	7	7.15	38528
Cuneus, Fusiform gyrus, Middle, Inferior & Superior temporal gyrus, Middle occipital gyrus	L	-42	-70	7	6.59	17722
Precuneus	L	-18	-64	37	4.60	4810
Inferior frontal gyrus	R	42	11	22	3.72	833
Superior frontal gyrus	R	30	44	28	3.48	805

Super - & sub additivity effect

We found super-additive effects in both groups bilaterally in the superior temporal cortex/planum temporale and in the visual cortex. In the sighted subjects, super-additive effects were also present in the ventral occipito-temporal cortex, whereas in the blind in the somatosensory cortex bilaterally. Only in the blind population, we found sub-additivity effect (letters + speech sounds > 2 congruent LS) in the left inferior frontal gyrus (see Figure II.5.5., Table II.5.6.).

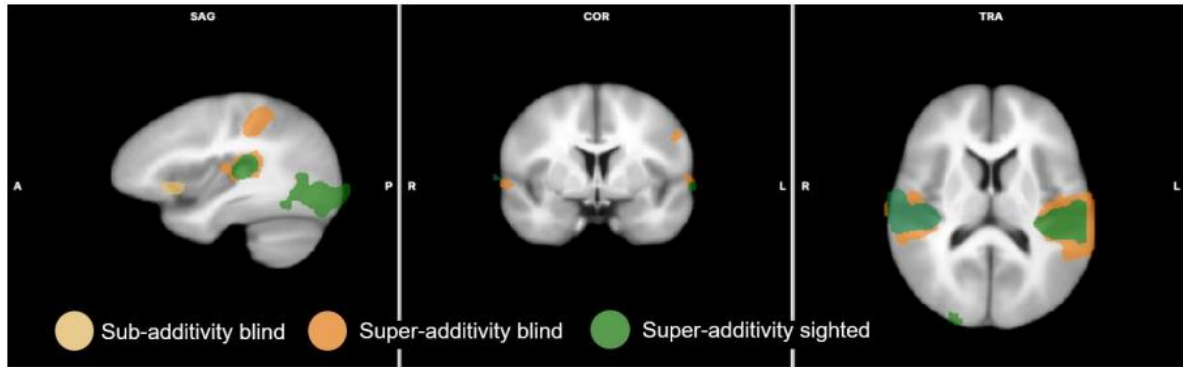


Figure II.5.5. Brain activity for relaxed super-additivity effect in the sighted is depicted in green, super-additivity effect in orange and sub-additivity effect in the blind is depicted in yellow.

Table II.5.6. Regions of relaxed criterion super- and sub-additivity effect in the blind and the sighted

Brain region	Hemisphere	x	y	z	Stat (t)	Cluster size
Blind: congruent > letters + speech sounds (super-additivity effect)						
Superior temporal gyrus	R	60	-22	7	8.07	25211
Superior temporal gyrus, postcentral gyrus	L	-39	-28	13	7.53	41184
Inferior parietal lobule	R	33	-48	43	4.57	3792
Blind: letters + speech sounds > congruent (sub-additivity effect)						
Inferior frontal gyrus	L	-33	13	-2	-2.61	1772
Sighted: congruent > letters + speech sounds (super-additivity effect)						
Superior temporal gyrus	R	60	-22	7	8.07	13741
Middle & Inferior occipital gyrus	R	36	-82	-5	7.73	18352
Inferior occipital gyrus	L	-45	-70	-8	7.68	15898
Superior temporal gyrus	L	-39	-28	13	7.53	13974

Additionally, when we compared super-additive contrast between groups we found that groups differ in occipital cortex bilaterally (super-additive effect for sighted) and in the left somatosensory cortex (super-additive effect for blind, Figure II.5.6., Table II.5.7.).

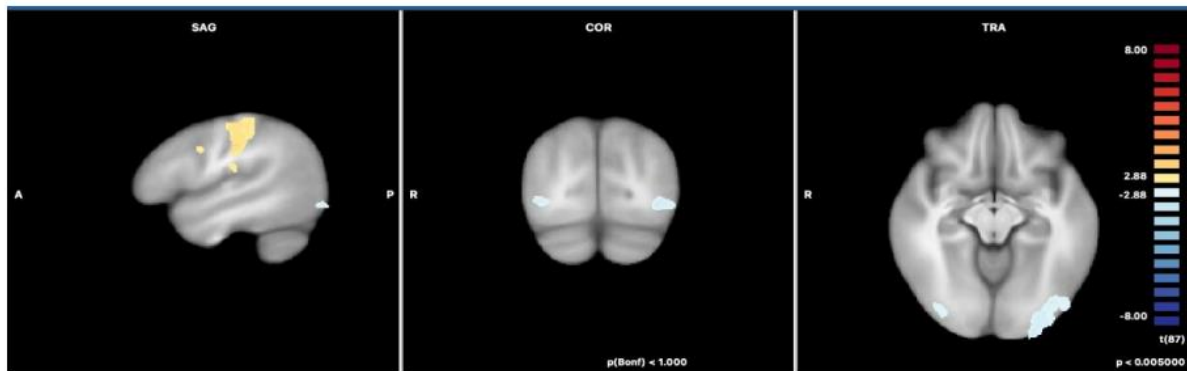


Figure II.5.6 Differences in brain activation for super-additivity contrast between the blind and the sighted, orange clusters are those in which the blind have higher activation than the sighted, and the blue ones are those with higher activation for the sighted.

Table II.5.7. Regions of relaxed criterion super- and sub-additivity effect between the blind and the sighted

Brain region	Hemisphere	x	y	z	Stat (t)	Cluster size
Super-additivity effect : Blind > Sighted						
Postcentral gyrus	L	-54	-19	-5	5.37	7555
Super-additivity effect : Sighted > Blind						
Inferior occipital gyrus	L	-33	-91	-5	-4.79	3650
Inferior occipital gyrus	R	33	-85	-5	-4.70	3853

Congruency effect

We found a significant interaction between multisensory stimuli and groups in the bilateral STG. Namely, the blind group presented a congruency effect in the right superior temporal gyrus, and the sighted group presented an incongruency effect in bilateral superior temporal gyri (Figure II.5.7 and 8., Table II.5.8.)

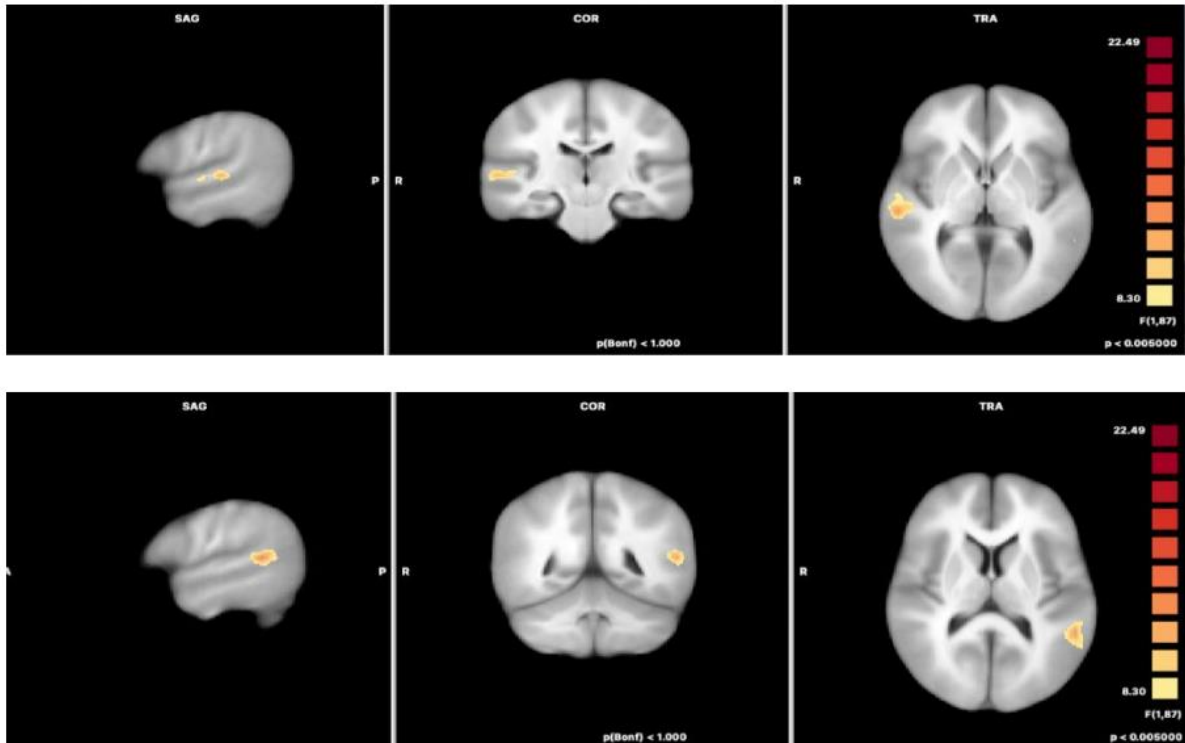


Figure II.5.7. Regions of interaction between multisensory stimuli and groups

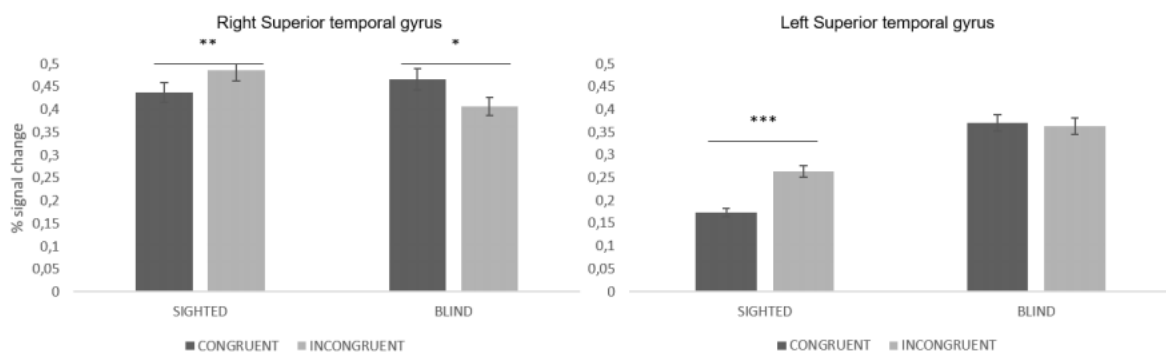


Figure II.5.8. Percentage signal change in regions showing interaction between multisensory stimuli and groups.

Table II.5.8. Differences for congruency effect between groups

Brain region	Hemisphere	x	y	z	Stat (t)	Cluster size
Superior temporal gyrus	L	-54	-43	10	21.48	1020
Superior temporal gyrus	R	57	-22	4	19.27	740

Congruency effect in the sighted group

We examined the direction of congruency effect in the sighted group to relate it to the results from Experiments 2 and 3, which included younger beginning readers. We found higher activation for incongruent than for congruent LS pairs in several regions including bilateral frontal, left parietal and left superior temporal areas (Figure II.5.9. and Table II.5.9.).

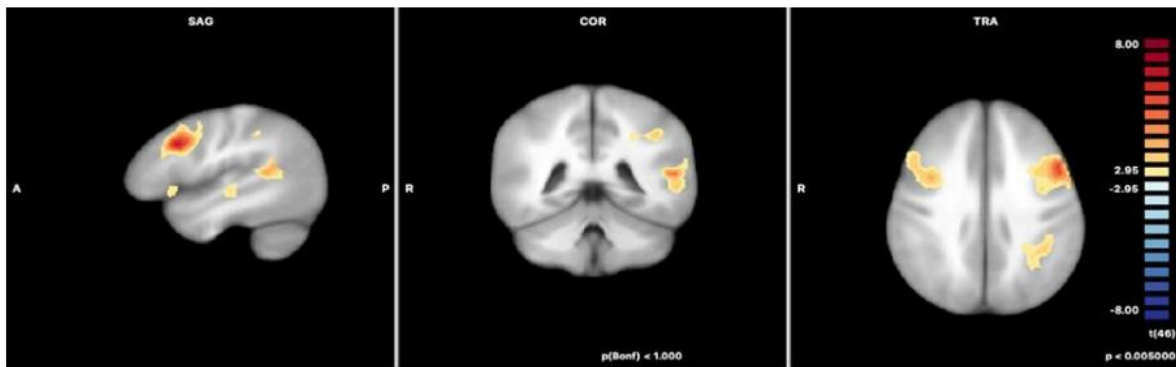


Figure II.5.9. Regions with incongruency effect in the sighted

Table II.5.9. Regions with incongruency effect in the sighted

Brain region	Hemisphere	x	y	z	Stat (t)	Cluster size
Middle & inferior frontal gyrus	L	-48	17	31	7.43	8079
Superior temporal gyrus	L	-51	-46	13	6.10	7458
Medial frontal gyrus	R	-3	14	46	4.85	1061
Precentral gyrus	R	36	8	34	4.83	3624
Inferior frontal gyrus	R	-54	17	4	4.60	1320
Superior parietal lobule	L	-30	-49	40	4.57	2871
Insula	R	36	20	-3	3.74	825

Discussion

This experiment aimed to examine LS integration in the blind and sighted Polish readers using a relatively large sample size compared to previous studies on blind individuals. We also focused on the differences between blind Braille and sighted print readers related to different reading modalities on a behavioral and neural level. Since no previous studies had examined these issues, we treated the analyses as exploratory. The only previous study testing the neural underpinnings of audiotactile phonetic processing used nonsense syllables and corresponding tactile Braille letter pairs and found the congruency effect in the frontal lobe and cerebellum in 16 blind participants but did not include a control group of sighted subjects (Pishmanazi et al.2016). They concluded that blind readers most likely process letters and sounds independently, which may be caused by poor multimodal brain circuit development in blind people or by fundamental distinctions between Braille and print reading mechanisms. Our findings paint a different picture.

The results from Experiment 4 show that during multimodal LS processing, the blind differ from the sighted in the most cited and explored area of multisensory integration - the superior temporal cortex (Beauchamp et al., 2004; Macaluso et al., 2004). The blind group showed a congruency effect in the right STG, while an opposite pattern was present in the sighted group. Namely, the sighted individuals presented higher activation to incongruent than to congruent LS pairs (incongruency effect) in STG bilaterally. The first conclusion that can be drawn is that audio-tactile LS integration occurs in the superior temporal cortex of the brains of blind people. However, the mechanism appears to be different from that of sighted people, perhaps connected to different reading modality. Blind braille readers have slower reading speeds and use different decoding strategies compared to sighted readers. The necessity for excellent orthographic representations is weakened by Braille reading's reliance on a grapheme-to-phoneme translation. In order to successfully implement the parallel processing in reading (or lexical route), high-quality orthographic representations are essential (Moll & Landerl, 2009). The quality of orthographic representations may be inferior in the blind, because tactile Braille reading is based on sequential grapho-phonological strategy. Additionally, blind Braille readers have reduced exposure to reading compared to sighted print readers - blind people read less in everyday life than the sighted (Barlow–Brown & Connelly, 2002). Therefore, they resemble to some extent dyslexic readers, who do not develop high-quality orthographic representations and because they struggle with reading they have lower exposure to print (Bergen et al., 2021). Furthermore, both groups might present a higher level of perceptual noise during reading - either related to tactile modality of reading in the case of the blind or to mirror confusion with letters (Corballis, 2018). The brain activation during multisensory LS processing also seems to be similar, as both blind readers and sighted dyslexic readers (Experiment 2 and 3) presented higher activation to congruent than

incongruent LS pairs in superior temporal cortex. We hypothesize that the more efficient the reading skills, the more effective the feedback from STS to the auditory cortex, resulting in a higher incongruency effect in sighted typical readers.

When we look at the lower level of LS integration, we can observe that both blind and sighted readers showed a super-additivity effect in bilateral temporal regions and areas involved in letter processing - in the blind - the somatosensory cortex and in the sighted - the occipital cortex. Super-additive effects in the superior temporal cortex including planum temporale are in line with previous findings in the blind (Pishnamazi et al., 2016) and sighted individuals (Calvert et al., 2000; van Atteveldt et al., 2004; 2007). Super-additivity effect in the fusiform gyrus for the sighted is in agreement with our findings in sighted children (Experiment 3) and increased activation of left fusiform during audio-visual exposure to letters and ambiguous speech sounds (Romanovska et al., 2021). Therefore, analogous super-additivity effects in the somatosensory regions for the blind is not surprising.

For unimodal conditions, we observed that overall there was more activation for the blind group. For letters, the blind activated the frontal and temporal areas and the premotor cortex more. The sighted had more activation in occipital areas. For speech sounds the blind activated several areas more than the sighted (including the occipital cortex (with fusiform gyrus)). This sensitivity in the occipital cortex is in line with our previous findings in this sample in a different task (Dzięgiel-Fivet et al., 2021) and previous literature (Bedny et al., 2011, 2015, Burton et al., 2003). Burton et al., 2003 stated that blind people's visual cortex may participate in language as a consequence of Braille acquisition. This assertion may be founded on the fact that blind persons must learn Braille by extensive practice connecting the feel of the Braille fields to phonics. The visual cortex can receive tactile and auditory information related to Braille and speech through multimodal regions with connections to somatosensory, auditory, and visual cortical areas. Visual deprivation may cause a reverse flow of information from multimodal regions to visual areas, one strategy for activating the visual cortex (Falchier et al., 2002). Alternatively, findings of occipital cortex activation for speech sounds in the blind population can be discussed in terms of the pluripotent cortex hypothesis. This hypothesis states that we are born with a cognitively pluripotent cortex, while the cortical area's ability to represent and process cognitive information depends on the information it gets while developing, based on its connectivity (Bedny, 2017). Our findings are in line with the results showing that the visual cortex in the blind is involved in higher-cognitive functions, including language (Kim et al., 2017).

Furthermore, when we look at the overlap of activation for letters and speech sounds, we see a higher number of overlapping areas in the blind than in the sighted, which may be caused by the fact that letter and speech sound perception processes are far less automated in the blind population.

On a behavioral level, the blind group outperform the sighted in RAN textures/materials and phoneme deletion (though the latter difference does not survive correction for multiple comparisons). In contrast, sighted readers score better than blind readers in words and pseudowords reading efficiency. The fact that visual reading is faster than tactile reading is a significant factor in these results - showing that the sighted were faster than the blind. These results are consistent with behavioral research conducted in the past (Carreiras & Álvarez, 1999; Mommers, 1976; Veispak et al., 2012a, 2012b; 2013). On the other hand, tactile reading requires better haptic and phonological skills. RAN with naming materials was less complicated for the blind group since they were more accustomed to recognizing objects by touch and to read in order - avoiding losing any item while touching and generally having more practice in tactile domain (Wong et al., 2011). With respect to phonological awareness, previous studies found mixed evidence, either showing that blind readers outperform the sighted in phoneme deletion tasks (in line with Greaney & Reason, 1999) or perform similarly to the sighted (Veispak et al., 2012, 2013). Reaction times in the "Phonemes to Letters Test" correlated with age and phonological awareness in the sighted group more than in the blind. In general, in the blind group LS automatization, measured with RTs in "Phonemes to Letters Test" was relatively little related to reading and reading-related skills, unlike in the sighted where strong correlations with reading and phonological skills were found.

In conclusion, we can see that the letter and speech sound integration process takes place in the blind, but its brain mechanism seems to be different and it is less automated than in the sighted group. The activation pattern in response to multimodal stimuli resembles, to some extent, young dyslexic readers of Polish. At the same time, letter and speech sound integration seems less important for Braille than print reading.

Chapter II.6. General Discussion

The current dissertation contained four unique experiments aimed at examining the process of letter and speech sound integration in Polish readers spanning preliterate children from kindergarten to skilled adults, including a population of blind Braille readers. We showed that children acquire the association between letters and speech sounds in the first year of reading instruction, but mastering this process takes longer (Experiment 1). Brain networks related to letter and speech sound association differ between children with and without familial risk of dyslexia, even at the beginning of reading acquisition (Experiment 2) and are further refined by growing reading experience (Experiment 3). Finally, we found both similarities and differences between letters and speech sound integration in blind and sighted readers related to different reading modalities (Experiment 4).

Behavioral measurement of LS association

As it was mentioned in the introduction to this thesis, we know that most children can master LS associations within the first years of school education, and this process is strongly connected to language transparency. The results cannot be simply transferred from one language to another. Studies show that children from most European countries become accurate in basic-level reading before the end of the first year of formal reading instruction (Seymour et al., 2003, Blomert and Vaessen, 2009). This rule, however, does not apply to less transparent languages like French, Portuguese, Danish, and English.

So far, there is only one study showing that reaction times of LS matching steadily decreased throughout the entire primary school reading instruction in Dutch children (Froyen et al., 2009), which shows slow and steady automatization of this process. Furthermore, it has been convincingly shown that the development of automated LS integration is essential for developing fluent reading abilities. According to research by Caravolas et al., (2012) and Schatschneider et al., (2004), the capacity to efficiently generate LS associations strongly predicts later reading skills across a wide range of languages. Consequently, the lack of automatic LS integration could decrease reading fluency (Blomert, 2011), which convinced us to conduct more studies on LS integration in Polish-speaking children.

In this thesis, I put substantial effort into examining the behavioral aspects of the letters and speech sound association process and its possible connection to further reading outcomes. When we try to combine the obtained results, we can say that, in the case of the Polish language, in order to accurately learn letter and speech sound association children need one year, but to master the process, they need two more years (Experiment 1).

What is more, accuracy and reaction time in the task where participants were asked to choose whether letters paired with speech sounds correlated with letter knowledge, reading words and pseudowords, phonological awareness, and RAN tasks (in children: Experiment 1, and in sighted children and adults: Experiment 4). These findings are in line with previous studies in other languages (Seymour et al., 2003, Blomert & Vaessen, 2009, Froyen et al., 2009). We proved that in Polish, the letter and speech sound association is strongly connected to different reading and phonological skills in sighted children and adults. Most probably due to this strong relationship LS integration does not predict variations in reading skill over and above other language skills.

In the case of atypical readers, we have shown that children with reading difficulties need more time to learn letters than their typically reading peers, as the groups differed in letter knowledge in kindergarten/first grade but not a year later (Experiment 2). Unfortunately, we did not conduct the 'Phonemes to letters' task for readers with dyslexia. With respect to blind Braille readers, we did not obtain similar correlations between reaction time in 'Phonemes to letters' task with age, reading and phonological skills in blind children and adults (Experiment 4) as in the sighted group, which suggests that LS integration is less important for Braille reading than print reading. This is a novel finding as no previous study has examined LS integration in the blind.

These findings can be discussed in terms of early reading intervention programs. Intervention studies revealed that training letter and speech associations (together with phonological awareness) could improve reading abilities in both developmental dyslexia and typical reading development (Hulme et al., 2012; Fraga-González et al., 2015). Research highlights that the best instruction should begin in the first grade or even before kids learn to read. To overcome the "dyslexia paradox", children from kindergarten and the first grade with low letter knowledge and phonological awareness (especially phoneme analysis) should be selected for training, as these are the skills (besides early reading) that have been found deficient in Polish children who later developed dyslexia (Experiment 2 and 3). However, this approach may not be optimal for blind children, since LS integration (Experiment 4) and phonological awareness (Dzięgiel-Fivet et al., submitted) bear relatively little importance for Braille reading.

LS integration in the brain of typical Polish readers

Basic sensory aspects of letter and speech integration has been mainly researched by comparing mean letter and speech sound activation to congruent LS pairs. This approach shows that left and right superior temporal cortex and planum temporale have stronger response to multisensory condition than the mean of unisensory conditions and these results

did not depend on language transparency (Calvert et al., 2000; van Atteveldt et al., 2004, 2007).

In Experiment 3, we established that in typical readers super-additivity effect was present at both time points, at the beginning of the reading instruction, in bilateral STG/planum temporale and the left fusiform whereas two years later, in bilateral frontal and right ventral occipito-temporal regions in addition to the regions involved in TP1.

In Experiment 4, for the sighted group that included older children and adults, we observed a super-additive effect in bilateral STG/planum temporale and bilateral occipital cortex, including fusiform gyrus. Involvement of visual cortex and specifically the left fusiform gyrus in audiovisual integration was previously found during audio-visual exposure to letters and ambiguous speech sounds (Romanovska et al., 2021). In this study, fusiform gyrus activation was positively associated with reading fluency and phoneme deletion and was lower in readers with dyslexia than in controls, which indicated that better reading and phonological skills were linked to increased left fusiform audiovisual activation. Although, we have not compared directly the super-additivity effect between typical and dyslexic readers because of largely unequal group sizes, in Polish readers with dyslexia we also observed super-additivity effect in the fusiform gyrus bilaterally.

If we combine the findings coming from different samples tested in Experiments 3 and 4, the pattern of activation for super-additive effect is largely similar in sighted Polish readers. The only difference might be the activation of bilateral frontal regions in typical readers at TP3 (i.e. in the second/third grade), which is absent at TP1 in Experiment 3 and not visible in Experiment 4, performed on more experienced readers than Experiment 3. Perhaps super-additive effect in the frontal cortex could be described by an inverted U-shaped developmental trajectory, with growing specialization at the shift from the pre-reading to the reading stage which levels off with higher expertise (for review see Chyl et al., 2021).

For higher level integration of letter and speech sound association, two different patterns of activation were previously described with either higher activation to congruent condition (congruency effect) or to incongruent condition (incongruency effect) most probably related to language transparency, the task used in fMRI scanner or participants' age/reading experience. Based on the results from Experiments 2, 3, and 4 we can rule out that in Polish typical readers the direction of the congruency effect depends on participants' age/reading experience. Specifically, in Experiment 3 we did not observe any differences between time points in the congruency effect in typical readers. Incongruency effect was found in the sighted Polish readers in Experiment 2 and 4 in the left superior temporal cortex among other regions and in the frontal areas in Experiment 4. The left inferior frontal gyrus and superior frontal gyrus were known to be crucial regions in maintaining focus on phonemes (Gelfand & Bookheimer, 2003; Proverbio et al., 2018). Differences in activation to congruent vs.

incongruent LS pairs in left Heschl's sulcus and Planum temporale were putatively attributed to feedback from superior temporal sulcus and gyrus (van Atteveldt et al., 2004). Importantly, the incongruity effect was present also in longitudinal studies (Wang et al., 2020, Karipidis et al., 2021) on German-speaking children, so maybe orthographic transparency is not as important as we previously thought. Nevertheless, age and reading experience are, to some extent, related to higher level multisensory integration, as we found a correlation between reading fluency and incongruity effect in Experiment 3. These positive correlations were in different brain areas depending on time point - at TP1 in the left superior temporal and fusiform gyri and at TP3 in the left superior parietal lobule and cuneus. These findings could imply that in beginning readers, with time and reading experience the dorsal attention network becomes more involved in matching audiovisual information because the modulation of visual attention is a function of the parietal cortex (Vidyasagar 1999; Saalman et al., 2007). This kind of control might be crucial during the stages of reading when children practice fluent reading and learn to focus their attention to distinguish mirror-letters (Vidyasagar 1999; Pammer et al., 2006; Grainger & Ziegler 2011; Dehaene et al., 2010a). Contrary to our expectations, the incongruity effect did not reverse into the congruity effect in more experienced typical readers. Temporal and frontal areas seem to be the regions of letters and speech sound integration in Polish. However, longer longitudinal studies need to be conducted to fully understand the trajectory of letter and speech sound integration in the brain

LS integration in atypical readers

In this thesis, I was also interested in learning how the process of letter and speech sound association looks like in atypical reading development. I was mainly interested in whether a family risk of dyslexia (Experiment 2), dyslexia (Experiment 3), and visual deprivation (Experiment 4) affect the brain activation pattern during letter and speech sound processing.

In those experiments, we established that generally, disruption in letters and speech sound association could be related to reading difficulties, i.e., the familial risk of dyslexia or dyslexia per se (Experiment 2, Experiment 3). In line with the findings that FHD+ children may present atypical patterns of print and speech processing (Centanni et al., 2019), we showed that children with familial risk of dyslexia differ from those without such risk even during the first year of reading instruction. Brain activity in the left planum temporale/Heschl's sulcus for the incongruent condition was significantly decreased in the FHD+ than in the FHD- group. At the same time, there were no group differences for the congruent condition. In addition, children who developed dyslexia had significantly higher responses than the typical reading group in the left superior temporal cortex (left planum temporary/superior temporal gyrus and

left planum temporale/Heschls' sulcus regions of interest) for congruent LS pairs.

From Experiment 3, we know that children with dyslexia presented increased activation to congruent LS pairs compared to typical readers in the left planum temporale/Heschls' sulcus at both time points. We think that in Polish readers, effective feedback from STS to the auditory cortex results in an incongruency effect in the superior temporal cortex. Less efficient reading skills therefore are related to lower feedback, and, in consequence, higher congruency effect is observed in readers with dyslexia. Similar pattern was found for blind Braille readers. Results from Experiment 4 showed that during multimodal LS processing, the blind differ from the sighted in the most cited and explored area of multisensory integration - the superior temporal cortex (Beauchamp et al., 2004; Macaluso et al., 2004).

The blind group, in comparison to the sighted, showed a congruency effect in the right superior temporal gyrus, while an incongruency effect was present in the sighted group. The way of decoding or the amount of exposure to reading can play an important role in letter and speech sound integration, but in these two groups of atypical readers it differs in its origin. For the blind group, the way of decoding and the tactile modality of reading might affect the congruency effect. For dyslexic or even for children with a risk of dyslexia (here: familial risk) early difficulties with letter knowledge and phonological awareness might influence the development of congruency effect. It seems that the superior temporal cortex plays a crucial role in letter and speech sound integration also in atypical readers, though its pattern of activation differs.

Chapter II.7. Conclusions

This thesis showed that letter and speech sound association is strongly connected to phonological abilities in the Polish language. Additionally, children learn letter and speech sound association during the first year of reading instruction, but to be mastered, this process needs more time, until 3rd grade. In typical reading development, while brain activity decreases in response to unimodal presented letters and speech sounds, it increases as children process multimodal visual-auditory pairs of letters and sounds, especially in bilateral temporal areas. In atypical reading development, we can observe differences connected to the familial risk of dyslexia and dyslexia itself by significantly affecting the brain's letter and speech sound integration. Children diagnosed with dyslexia show the opposite activation pattern to typical reading children. Moreover, we can also observe the integration of letters and speech sounds in the brain of blind people. However, the process differs from sighted people and is more similar to people with dyslexia than typically reading children, which can be related to lower exposure to printing or a lower reading speed.

Chapter II.8. Limitations

The most significant limitation for Experiments 1 and 4 has been the Coronavirus pandemic. Research sessions conducted in schools started before the pandemic and were planned to be followed later, but then the pandemic occurred. Conducting research in schools was limited as they were closed for a long time, and whole classes were sent home for quarantine. Small but significant changes in the testing procedure were needed. For Experiment 4, the most difficulties were connected with the need to wear masks during the fMRI scans and the behavioral sessions. In addition, closing of schools for the blind significantly limited the recruitment of teenagers and their ability to visit the Nencki Institute.

For Experiments 2 and 3, another concern was that the children who participated in the study were either kindergarteners or first graders, which may have affected their reading training. Currently, children in Poland begin learning to read in the first grade. However, at the time of this longitudinal study an educational reform had been conducted, and it was parents who decided whether or not their 6-year-old child was sent to school. Even though reading training is not part of the kindergarten curriculum, parents often teach their children letter names and basic reading skills. We overlooked checking the "actual" length of the reading education each child had received. Behavioral sessions with a reading level assessment were conducted before the fMRI session, not on the day of the scan. Unfortunately, there were instances when the gap between the behavioral and fMRI sessions was longer than a month. Given that reading ability changes quickly during the first school year, children could have made significant progress during that time.

Chapter II.9. Future directions and usefulness in practice

Using a longitudinal design and a significant sample size is the current study's greatest attribute; 67 children in a three-step longitudinal study and a group of 42 blind participants give us more powerful results. The most useful longitudinal neuroimaging studies of reading follow kids from the pre-reader to the reader stage, with full automatization of this process. However, conducting such studies is exceedingly challenging. The starting population must be augmented to include children with familial risk of dyslexia diagnosis because only 10% of children will ultimately be diagnosed with the condition, severely restricting recruitment. However, this only raises the likelihood of choosing a child who will later receive a dyslexia diagnosis to roughly 40%.

Even though, as discussed in Experiment 1, intervention studies aimed at helping children learn and master LS association during the first years of reading instructions were not always the most effective, future longitudinal research on behavioral and neuroimaging aspects of letter and speech sound integration should be conducted, with additional training for letter knowledge and phonological skills. However, the study's timeframe should be longer and should contain more time points, especially during the fastest development of this skill. This type of study will be challenging to proceed with, but the outcome and usefulness of the results may be beneficial for children, their parents, and educators.

As it has been commonly discussed across countries with different languages and educational systems, in order to remediate dyslexia one needs to focus more on the first months of reading instruction. Waiting until the 3rd grade to start intervention can be too late and children may be too discouraged and frustrated to learn to read. Moreover, this can lead to significant consequences for life quality in terms of psychological and educational attainment.

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Publications overlapping with the work described in the thesis:

Plewko, J., Chyl, K., Bola, Ł., Łuniewska, M., Dębska, A., Banaszkiewicz, A., Wypych, M., Marchewka, A., van Atteveldt, N., and Jednoróg, K. (2018). Letter and Speech Sound Association in Emerging Readers With Familial Risk of Dyslexia. *Front. Hum. Neurosci.* 12:393. doi: 10.3389/fnhum.2018.00393