Colored Reading: an Appeal for Using Synesthetic Association Training to Improve Reading Fluency in Children with Dyslexia

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0 ABSTRACT

Dyslexia is defined as a variable and often familial learning disability involving difficulties in acquiring and processing language that is typically manifested by a lack of proficiency in reading, spelling, and writing. Dyslexia is characterized by the inability to integrate information across multiple areas of the brain. The consequent failure to develop representations of the knowledge on a topic based on its associated attributes results in difficulty in reading. In contrast, synesthesia may be seen as a hyperassociative condition, possibly due to a failure to properly segregate areas into distinct networks. Synesthesia could therefore be regarded as a disorder opposite of dyslexia on a spectrum of a developmental disorder of association. It has been shown that, in some individuals and to a certain extent, synesthesia can be trained. This training could be beneficial for dyslectics. In this study I provide an overview on the neurodevelopmental aspects of dyslexia, synesthesia and the overlap between these conditions. I review the evidence on synesthetic training in non-dyslexics and hypothesize on the potential benefits of this training in dyslexics. Furthermore, the methods of a study to explore these benefits are proposed.

0	ABST	RACT	p. 1		
1	INTRO	ODUCTIO	DN	p. 4	
2	DYSLEXIA				
	2.1	Introd	Introduction		
		2.1.1	Definition	p. 7	
		2.1.2	Prevalence	p. 7	
	2.2	Readir	Reading in normal population		
		2.2.1	Reading from a neurobiological perspective	p. 8	
		2.2.2	Reading from a cognitive viewpoint	p. 9	
	2.3	Cause	p. 10		
		2.3.1	Cognitive deficits	p. 11	
		2.3.2	Neurobiological theories of developmental dyslexia	p. 16	
		2.3.3	Genetics	p. 21	
	2.4	Key fir	ndings dyslexia	p. 22	
3	SYNE	p. 24			
	3.1	Introd	Introduction		
		3.1.1	Definition	p. 24	
		3.1.2	Prevalence	p. 25	
	3.2	Inducer		p. 25	
		3.2.1	Cultural tools	p. 26	
		3.2.2	Higher-lower distinction	p. 26	
	3.3	Concu	Concurrent		
		3.3.1	The special role of color	p. 26	
		3.2.2	Projector-associator distinction	p. 27	
	3.4	Causes		p. 28	
		3.4.1	Disinhibited feedback theory	p. 29	
		3.4.2	Cross-activation theory	p. 29	
		3.4.3	Hybrids	p. 30	
	3.5	The ne	p. 31		
	3.6	Function of synesthesia			
		3.6.1	Benefit of synesthesia in adulthood	p. 35	
		3.6.2	Benefit of synesthesia during development	p. 36	
	3.7	Develo	Development of synesthetic pairings		

	3.8	Key fin	idings synesthesia	p. 39			
4	THE RELATION BETWEEN GC-SYNESTHESIA AND DYSLEXIA						
	4.1	Overlap between synesthesia and dyslexia					
	4.2	Prevalence of dyslexia among synesthetes					
		4.2.1	Prevalence of dyslexia in the Synesthesia Battery	n. 43			
		4.3.2	Prevalence of dyslexia among Carmichael's data	p. 13			
		433	Prevalence of dyslexia in the GNO study	p: 54			
		434	Overall discussion prevalence dyslexia among synesthetes	p. 5 i			
		4.3.4		p. 50			
5	TRAINING SYNESTHESIA AND THE REMEDIATION OF DYSLEXIA						
	5.1	Acquired synesthesia					
		5.1.1	After brain damage and sensory substitution devices	p. 58			
		5.1.2	Chemically induced synesthesias	p. 59			
		5.1.3	Posthypnotic suggestion	p. 59			
		5.1.4	Training synesthesia	p. 60			
	5.2	Remediation of dyslexia		p. 63			
	5.3	Has sy	nesthetic training ever been proposed for dyslexics?	p. 64			
c							
6	PROPO	OSED STUDY METHODS					
	6.1	Participants					
	6.2	Age of children					
	6.3	Control group					
	6.4	Tests					
	6.5	Duration					
	6.6	Trainin	ng materials	p. 71			
7	SUMM	ARY		p. 75			
8	ACKNOWLEDGMENTS			p. 76			
9	REFERENCES			p. 77			

1 INTRODUCTION

For most people, comprehension of a text follows automatically and effortlessly following the fluent movement of the eyes from left to right over a text. Unfortunately this automaticity of reading is not a quality enjoyed by people with dyslexia. For dyslexics, reading is piecemeal and laborious. In perhaps much the same way dyslexics fail to automatically recognize words, according to people with grapheme-color synesthesia, most people miss out on the colors of words and letters. Experiencing colors while reading letters and words is an interesting and uncommon phenomenon, and part of a phenomenon called synesthesia. Whereas fully normal in other respects, people with synesthesia experience additional sensations normally not attributed to stimuli. Many forms of synesthesia have been reported. For instance, for a lexical-taste synesthete the word 'glass' may evoke the taste of lemon-pie, a C-sharp on a piano can be perceived as an indigo blue scribbly line by a music-shape synesthete whereas the letter 'A' can be experienced as a bright red sensation by a grapheme-color synesthete.

It is a fascinating idea that a significant minority of people's subjective experiences differ radically from those of the rest of us. Understanding the processes resulting in the experience of these extra perceptions in synesthetes may provide valuable insights into the mechanisms involved in the processing and perception of external stimuli in non-synesthetes, making synesthesia a scientifically interesting field in addition to being an interesting or quirky condition. The relevance of synesthesia was illustrated by Ramachandran and Hubberd (2001b) in which a link was made between synesthesia and metaphor (e.g. bitter cold), creativity (synesthetes scored higher on tests of creativity) and it was even suggested that synesthesia may have been pivotal in the evolution of language. Moreover, synesthesia may provide a valuable insights as to the binding problem; how our different senses are combined into one unified percept (Sagiv & Ward, 2006).

Whereas synesthesia isn't considered a harmful condition for which treatment is required, intervention for dyslexics is in high demand. As perhaps the most common neurobehavioral disorder, dyslexia affects about 5 to 20 percent of children (Interagency Committee on Learning Disabilities, 1987: Shaywitz et al., 2008). Reading has become indispensable in our society and dyslexia has been associated with reduced educational attainment, lower academic self-esteem and less reading after school hours (Norton et al., 2014). Dyslexic scholars in the Netherlands are compensated with additional time during exams and with extra financial support from the government. Often intervention methods aimed at enhancing reading skills are also provided during primary and secondary school period (www.dyslexieweb.nl; www.dyslexiewegwijzer.nl). Millions of Euro's are spent on intervention of

dyslexia annually. Although some dyslexics may eventually be able to read accurately (Finn et al., 2014), fast and fluent reading is rarely achieved (Blomert, 2011).

Even though dyslexia and (grapheme-color) synesthesia may appear to be very different conditions, they actually could be quite similar in several aspects. As reviewed in greater detail below, both can be described as developmental disorders of cortical connectivity. In a nutshell, synesthesia can be characterized as an excess of connectivity between otherwise distinct sensory modalities, whereas a lack of connectivity between different parts of the reading network results in dyslexia. In other words, both can be seen as opposite ends of a spectrum of aberrant cortical connectivity (Mitchell, 2012).

Recent research on synesthesia has shown that a range of behavioral, physiological and phenomenological markers of synesthesia can be trained in people without synesthesia (Rothen & Meier, 2014; Bor et al., 2014). As these training paradigms are expected to promote cortical connectivity between the associated neural modalities (Colizoli et al., 2015), it might be worth considering whether these particular training methods could promote an alternative and beneficial functional connectivity in dyslexics. According to Wilson (2013) our minds are active and strategic associators which re-use one domain of thought (e.g. phonemes) in representing another (e.g. letters). In doing so, the brain 'exploits' isomorphisms for representational purposes. From the kiki-bouba effect (Fig. 1) to metaphorical thinking, we all use isomorphisms for cross-modal representations regularly.



Fig. 1. Already in 1929 Köhler showed that the human brain somehow attaches abstract meanings to the shapes and sounds in a consistent way. Known these days as the kiki-bouba effect, the vast majority of people select the curvy shape as "bouba" and the jagged one as "kiki" when asked to assign these names to the two shapes.

Moreover, Watson et al. (2014) further argue that the *conscious* synesthetic experiences are the result of remnants from early learning challenges in which the domain of the synesthetic experience (e.g. color) was used to map newly learned categories (e.g. letters). This natural but implicit cross-modal learning strategy could potentially be employed as a remedial method for dyslexics. According to Shaywitz and Shaywitz (2005), learning to read first implies the insight that spoken words can be broken up into elemental particles, so called phonemes. After that, extraction of grapheme (the smallest semantically distinguishable unit in a written language) to phoneme rules can be made in which the shape of the grapheme is mapped on the corresponding phoneme. At first, this will be effortful and rule-like. In normal readers this gradually becomes more automated as cross-modal representations begin to form in which letters automatically elicit pathways of letter-sound and visaversa. In the course of decoding graphemes to phonemes, something goes haywire in dyslexics, whether it is already in the acquisition of grapheme-phoneme rules (e.g. Shaywitz & Shaywitz, 2005), in the speed of accessing the (sub)lexical phonology (e.g. Wimmer and Schurz, 2010) or in the neural integration of letters and speech sounds (e.g. Blau et al., 2009; 2010; Froyen et al., 2011; Hahn et al., 2014, Harrar et al., 2014).

I propose that the use of synesthetic associations may be a way around the grapheme to phoneme impairment in dyslexics by providing another dimension of representational mapping. The aim of this thesis is to explore the connections between both conditions and to lay the theoretical groundwork for a study in which a synesthetic training method is proposed as a possible remedial tool for improving reading speeds in dyslexic children.

First a comprehensive review of dyslexia is given. Then the strange and fascinating world of the synesthete is explored. Known relations between synesthesia and dyslexia are examined. Moreover, an attempt to estimate the prevalence of dyslexia among synesthetes will be made. Next some of the current remedial methods of dyslexia and the possibility of acquiring synesthesia with training are reviewed. Together these topics form the theoretical basis for the hypothesis that training synesthetic associations may be a successful alternative intervention method for a subset of dyslexic children. I will then continue to propose specific training material, selection and screening of subjects and the method by which the validity of this new intervention method can be tested. Although the primary focus of this study is the amelioration of reading fluency in dyslexic children, the methods employed might have the additional benefit of acquiring new insights in developmental aspects of synesthesia.

2 DYSLEXIA

2.1 Introduction

2.1.1 Definition

While dyslexia is sometimes referred to as word blindness, it is important to note that dyslexia is not strictly a present or absent condition like, for example, actual blindness. Currently, The Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-5; American Psychiatric Association, 2013) uses the term 'dyslexia' for a subset of specific learning disorders characterized by substantial and quantifiable problems with accurate or fluent word recognition, poor decoding, and poor spelling abilities compared with age-matched peers. These problems have their onset during school-age years and persist into adulthood and may not be caused by other factors such as lower intellect, visual or auditory impairments, other mental or neurological disorders, psychosocial adversary, insufficient knowledge of the language of instruction, or inadequate educational instruction (American Psychiatric Association, 2013). As of yet, no blood tests or imaging techniques are available to unequivocally determine whether someone is dyslexic. Instead of a dichotomous condition, dyslexia is increasingly regarded as one end of a spectrum of reading proficiency (e.g. Danache et al., 2014; Shaywitz et al., 1992). According to the DSM-5, dyslexia is "... a neurodevelopmental disorder with a biological origin that is the basis for abnormalities at a cognitive level that are associated with the behavioral signs of the disorder. The biological origin includes an interaction of genetic, epigenetic, and environmental factors, which affect the brain's ability to perceive or process verbal or nonverbal information efficiently and accurately." (American Psychiatric Association, 2013).

2.1.2 Prevalence

The absence of a clear definition makes determining the exact prevalence of dyslexia difficult since this is directly dependent on the used cutoff values. Although it might be somewhat arbitrary who from the spectrum of reading proficiency falls within the dyslexia box, this doesn't mean that dyslexia isn't a reality and a real global burden. With an estimated prevalence of dyslexia ranging between 5 to 20 percent (Interagency Committee on Learning Disabilities, 1987; Shaywitz et al., 2008) independent of the population, over millions of children worldwide are at risk for illiteracy and social exclusion (Shaywitz & Shaywitz, 2005). While there is no biological validity in the cutoff points used for determining who is dyslexic, they are essential in determining who is eligible for remediation resources and compensation rules in schools, as well as for researchers in comparing a dyslexic population with typical readers.

2.2 Reading in normal population

Before we further explore the details of what seems to go haywire in dyslexics, it might be useful to explain some of the basics of reading. That is, the processes involved in reading and how learning to read is achieved to begin with. The processes involved in reading and learning to read can be approached from two interrelated viewpoints, a neurobiological and a cognitive frame of reference. Respectively, they put their emphasis on *where* and *which* processes are active.

2.2.1 Reading from a neurobiological perspective

Reading is a skill developed only about 5500 years ago. This is considered a too short of a time span for humans to have evolved specialized brain areas specifically for the development of such a recent and culturally variable activity as reading on a genetic level (Gazzaniga et al., 2009, p. 404). Therefore, learning to read entails that the brain has to reorganize and recruit other pre-literacy skills in a process of neuronal recycling such that pre-existing cortical systems are harnessed for the novel task of recognizing written words (Dehaene & Cohen, 2011). The Visual Word Form Area (VWFA) for example, is a little region located somewhat behind the left ear in what is called the fusiform gyrus. In proficient readers, the VWFA responds strongly upon seeing letter strings while in illiterate people this area just fires upon seeing certain objects (Dehaene & Cohen, 2011). While the VWFA still fires upon seeing certain objects such as faces, it has been adapted through the development of literacy to process written words. In order to read, a myriad of cortical systems have to adapt and correctly interact with each other. Together these cortical systems makeup the reading network.



Fig. 2. Lateral view of the brain showing three cortical systems of the reading network: **(A)** the Visual Word Form Area, **(B)** the dorsal temporoparietal cortex, and **(C)** the lower frontal lobe area and Broca's area. (Modified picture, original from L. Flowers, Retrieved July 12, 2017 from https://reading-interventionsinfo. wikispaces.com/ Neurological+Research) As excellently reviewed by Benitez-Burraco (2010), the reading network seems to be mainly comprised of three processing systems in the left cerebral hemisphere shown in Fig. 2. One of these systems is the aforementioned VWFA, located in the ventral part of the occipitotemporal region and is integrated by several areas of the middle temporal and middle occipital gyrus (Fig. 2A). The VWFA is associated with the recognition of a range of objects such as faces. During the process of learning to read VWFA function is partly re-assigned or further specialized to also receive information from areas from both hemispheres that deal with processing visual stimuli of a written form (Dehaene & Cohen, 2011). The VWFA specifically makes sure the visual nature of written words and their sequences are perceived and recognized quickly during reading.

The second processing system of the reading network is located in the dorsal temporoparietal cortex and makes up part of the angular and supramarginal gyrus and includes parts of the posterior regions of the upper temporal lobe (Fig. 2B). Responsible for analyzing words, this system functions as an integrating region where associations between written symbols (graphemes) and their respected auditory form (phonemes) are produced and consolidated during reading (Benitez-Burraco, 2010).

The third processing system of the reading network is located in the lower frontal lobe area and Broca's area in particular (Fig. 2C). This area is considered to be involved in the syntactic organization and speech motor execution, as well as being a component in verbal working memory. It is in control of assigning phonological values to phonetic traits during word perception and production. Together, the latter two processing systems of the reading network form what is known as the phonological system (Benitez-Burraco, 2010).

2.2.2 Reading from a cognitive viewpoint

From a cognitive perspective, reading requires a smooth interaction between three 'lexicons'. The semantic lexicon stores the meaning of words, the phonological lexicon stores the auditory form of words and the orthographic lexicon stores the visual form of words. The semantic and phonological lexicons develop naturally by exposure to the natively spoken language. However, the orthographic lexicon needs to be explicitly acquired. The dual-route theory of reading (Coltheart et al., 2001) is one of the most widely accepted theories of how we (learn to) read and sheds light on how we build our orthographic lexicon.

The dual-route theory of reading postulates there are two mechanisms by which we read; a slow indirect (phonological) sub-lexical route and a fast direct (orthographic) lexical route. When a child starts to read, the dual route theory postulates the indirect phonological route is used. This infers that firstly, one must become aware that spoken words can be broken up into constituent sound parts (i.e. phonemes). This is called phonetic awareness. Phonemes can then be represented by corresponding visual symbols (i.e. graphemes). During the first two years of learning to read, letter recognition and letter knowledge gradually build up (Blomert, 2011). By applying phoneme-grapheme correspondence rules every spoken word can be now represented by a string of symbols and visa-verse. At first, this rule-like method is laborious and effortful.

During the course of years, however, these letter-speech associations gradually become faster and automatic. In effect, they form into crossmodal representations in which both modalities are intrinsically linked to each other (Blomert, 2011). During the sub-lexical route, the mental representation of a string of graphemes (i.e. written words) has to be connected to the semantic lexicon via phonological code (Vandermosten et al., 2012). This phonological route of reading is slow because every letter has to be serially sounded out. It is intuitively easy to comprehend that unfamiliar words are processed this way. Only at the end of the word, its phonological representation can be linked to semantics (when learned what the word means). Perhaps this could be compared with counting five cats in a picture. A toddler has to count each cat individually, while adults directly see there are five cats without counting. Likewise, after enough exposure, an orthographic lexicon is gradually build up. Groups of letters become recognizable chunks and the written form of familiar words is increasingly recognized as a whole.

The orthographic or lexical route is thought to be a connection from recognizing the whole word much like seeing a picture and automatically knowing what it means (Daheane & Cohen, 2011). The orthographic route is believed to be a more or less direct link between the visual form of the whole word (orthographic lexicon) and its meaning (semantic lexicon) ^{1*}. The above-mentioned Visual Word Form Area (VWFA) is thought to be the neural locus of the orthographic lexicon (Daheane & Cohen, 2011). Skilled readers are believed to mostly employ this form of reading. This is the fastest route and is used for frequently used words that we are familiar with. Also, exception words, which are words that are pronounced differently than serial decoding would dictate, have to be read via this route. English language, for instance, has a deep orthography with a lot of exception words. This makes it harder to predict the pronunciation based solely on the written word. Whereas Dutch, with its shallow or transparent orthography, has a much clearer one-to-one grapheme-phoneme correspondence. Differences in orthography thereby pose different constraints on learning to read as well as in the development of dyslexia (Sprenger-Charolles et al., 2011).

2.3 Causes

In the search for causes of dyslexia, it is important to recognize that dyslexia is a behavioral outcome of reduced reading proficiency. Simply said: dyslexics are just poor readers. However, not every dyslexic is the same. Neither in the overall degree of reading proficiency, nor in the degree of deficits in specific skills subserving overall reading competence. Furthermore, differences between dyslexic readers (DR) and normal readers (NR) are group differences and are not diagnostic at an individual level. Identifying the underlying

¹*Interestingly reading involves a progression from reading aloud to sub-vocalization while speed-readers make an effort to skip subvocalization entirely. It is fascinating and almost incomprehensible for us these days, but historically silent reading was considered unusual (Jajdelska, 2007, p. 5). I would like to hypothesize that in those times reading was more an embodied cognition with letters being mapped to actual vocalization and/or lip movements. Now it seems we map reading to sub-vocalization, while counting interestingly is still often accompanied with lip movements, nodding one's head or using fingers.

cause(s) of this heterogeneous condition has turned out to be difficult and can be approached on various levels of abstraction. Firstly, the behavioral outcome of dyslexia (poor reading skills) is thought to originate from specific cognitive deficits. Cognitive deficits are problems in specific skills that are thought to facilitate the reading process. By comparing test scores on these specific skills between dyslexic and normal readers, researchers have tried to identify specific skills that are affected in dyslexics and determine how this results in poor reading and spelling performance. Moving up to a higher level of causation, cognitive deficits are thought to originate from functional and anatomical brain differences. In dyslexics, certain brain areas respond differently to certain inputs compared to normal readers, certain brain areas may be larger or smaller and communication between brain areas may be atypical. Lastly, dyslexia is highly heritable (Benítez-Burraco, 2010). Therefore the observed functional and anatomical differences using fMRI studies may, in turn, originate from the interaction of a genetic profile and environmental factors.

To complicate matters even further, these levels mutually influence each other. For instance, a lifetime of poor reading skill is likely to reduce exposure to text, which in turn influences the functional response of certain brain areas to text, which in turn affects the anatomical development of brain areas and the communication between them. Although purely speculative, it's not inconceivable that environmental factors and a lifetime of struggling with dyslexia may even cause epigenetic changes affecting future offspring with a certain predisposition. Altogether this makes it challenging, if not impossible, to uniformly identify the underlying cause of the heterogeneous condition collectively described as dyslexia.

Furthermore, it often remains unclear whether the identified cognitive deficits or structural and functional brain abnormalities are a primary cause of dyslexia or if they are the result of a lifetime of dyslexia. In an attempt to address this potential obstacle, studies on dyslexia often include reading-matched controls, which are younger individuals with the same reading proficiency in addition to age-matched controls (e.g. Hoeft et al., 2007).

An understanding of the proposed underlying causes is essential when attempting to develop potential therapeutic interventions which could serve as an alternative for, or supplement to, existing remedial methods. Although the purpose of this study is not to elucidate the underlying cause of dyslexia, some of the findings on all the aforementioned levels of causation will be reviewed.

2.3.1 Cognitive deficits

In order to better understand the poor reading skills in dyslexics, cognitive researchers have mainly studied the presence of specific deficits. This is often done by comparing the performance of dyslexics and controls on highly specific skills that are thought to subserve the reading process. Some deficits are purely perceptual (stimulus-induced), while others are of a more complex reading related nature (task-induced). Prediction studies then look at which deficits best predict future reading abilities. While there are strong correlations between the presence of certain deficits and dyslexics on a group level, they are not diagnostic on the individual level (although see Geiger & Lettvin, 1997). In other words, the presence of a certain deficit doesn't predict if a person has or will develop dyslexia. On the other hand, the absence of a specific deficit in a dyslexic proves more than its presence, for it shows that this specific deficit then cannot be the sole cause of dyslexia (van Bergen et al., 2014b; Valdois et al., 2004). Although many contributing or core deficit theories have been postulated, none of them provide an all-encompassing explanation for the wide range of behavioral symptoms and the many manifestations of dyslexia (Vellutino et al., 2004). Furthermore, as van Bergen et al. (2014b) have mentioned, single deficit models cannot readily explain the high comorbidity rates of dyslexia with many other developmental disorders such as Attention-Deficit/Hyperactivity Disorder (ADHD), dyscalculia, Specific Language Impairment (SLI) and speech-sound disorder. Instead of just one underlying core deficit, dyslexia is increasingly regarded as an endophenotype caused by an interplay of deficits, each variably and independently contributing to the severity and type of reading problems (e.g. McGrath et al., 2011; van Bergen et al., 2014b).

In my own opinion, a pitfall in using deficit theories is that they find differences that are dependent on the initial criteria of dyslexia. In other words, they find reading related problems that are part of the reading competence defining dyslexia. However, early detection of deficits in these more basic skills of reading has been shown to have a predictive value on later reading competence and dyslexia in particular (e.g. Dandache et al., 2014). Moreover, deficit theories are useful in sorting out more specific and underlying problems often encountered in dyslexics. Furthermore, deficit theories offer insights to which skills can be strengthened to take some of the barriers of reading away. Since many of the existing remedial methods aim to tackle these deficits, it is worth to review some of the major deficits found in the dyslexic population. Broadly speaking, most deficits can be found in and are grouped together in terms of three compartments of the reading network which relates graphemic representations in the occipitotemporal cortex to phonemic representations in the frontal cortex via grapheme-phoneme bindings at the temporoparietal cortex (Serniclaes et al., 2015). Thus, these three sites and sources of dyslexia respectively are audio-phonemic deficits, graphemic deficits and grapho-phonemic deficits (Serniclaes et al., 2015).

2.3.1.1 Audio-phonemic deficits

Currently, the predominant view entails that dyslexia is mainly caused by a phonological deficit (Shaywitz & Shaywitz, 2005; 2008). This means that there is a problem with accessing, processing and/or manipulating the sound structure of speech. The central thought behind this is that development of phonological skills is required for grapheme-phoneme decoding, the first step in the process of learning to read (Dandache et al., 2014). Phonological deficits are observed in three interrelated broad areas: phonological awareness, rapid automatized naming, and verbal short-term memory.

2.3.1.1.1 Phonological awareness

Phonological awareness (PA) refers to the conceptual understanding and explicit awareness that spoken words consist of individual speech sounds (phonemes) and combinations of speech sounds such as syllables (Dandache et al., 2014). Dyslexics often perform poorly in tasks involving the manipulation of phoneme segments within words or pseudowords. PA has often been shown to be the second best predictor of future reading competence, whereas family risk was shown to be the best predictor (Dandache et al., 2014). However, the transparency of the conventional spelling system of a language (orthography) is a strong moderator of PA's predictive power. For instance, in a meta-analysis, Landerl and colleagues (2013) found the more opaque the orthography, the stronger PA's predictive power.

A dominant view in English literature on dyslexia is that phonemic awareness precedes the linking of letters to sounds, and has therefore long been regarded as a precursor of and predictor for future reading skills (Shaywitz & Shaywitz, 2005). However, Blomert and Williams (2010) argue that phonemic awareness is mainly a consequence of learning to read and not a necessary precursor. For instance, illiterates also show difficulties in tasks requiring them to segment individual phonemes. After a basic literacy training, however, they start to show phonemic awareness insights. McNorgan et al. (2013) also refer to this reciprocity between orthographic knowledge and phonemic awareness.

Dyslexics also have more trouble processing speech sounds and therefore their speech perception is poorer and less precise (e.g. Griffiths & Snowling, 2002). Speech perception experiments suggest that dyslexics find it difficult to extract discrete phonological representations from the speech signal (Vandermosten et al., 2012). According to the "allophonic" theory of dyslexia by Serniclaes et al. (2004), a PA deficit is possibly the consequence of a more drastic difference in the mode of speech perception. Dyslexic children show weaker categorical perception, which is the degree to which acoustic differences between variants of the same phoneme are less perceptible than differences of the same acoustic magnitude between two different phonemes. In other words, while the objective difference between two spoken /d/'s may be the same as between /d/ and /b/, most of us are tuned to perceive only the latter as really different. While born with an ability to discriminate all potential phoneme categories, sensitivity for acoustic differences that are not relevant for phoneme perception in the native language is deactivated during early childhood. However, dyslexic children maintain a higher sensitivity to phonemic distinctions irrelevant in their linguistic environment (Serniclaes et al., 2004). While dyslexics appear to discriminate between subphonemic (allophonic) variants of the same phoneme, controls do not. When speech sounds are perceived in allophones instead of phonemes, linking these to phoneme-sized graphemes may be problematic (Serniclaes et al., 2015).

Supposedly, poor phonological representations impede the acquisition of consolidated letter-speech associations in dyslexics. Poor performance in various phonological domains is thought to arise from less mature or underspecified phonological representations, in particular at the sub-lexical input level

13

(Vandermosten et al., 2012). However, Norton and colleagues (2014) suggest evidence indicates dyslexia is more likely to be caused by a weakness in *accessing* otherwise intact phonological representations. For instance, according to Boets et al. (2013) the observed weakened structural and functional connectivity in inferior frontal and temporal regions in DR suggests an inefficient access to phonological representations, rather than weakened representations, as the source of the PA deficit in dyslexics. Furthermore, Blomert and Williams (2010) found that a phonological awareness deficit and a letter-speech sound association deficit only rarely co-occurred in the children with a familial risk for dyslexia. This finding also challenges the widely accepted assumption that PA deficits 'cause' reading deficits via 'unstable' or otherwise corrupted letterspeech sound associations.

2.3.1.1.2 Naming speed

The second deficit in phonological skills often observed in dyslexics is naming speed. Naming speed is the efficiency of phonological code retrieval from long-term memory (Vandermosten et al., 2012). Naming speed ability is typically assessed through the Rapid Automatized Naming (RAN) procedure which measures how quickly subjects can name objects, pictures, colors or symbols aloud. Dyslexics were shown to perform significantly slower at this test (e.g. Araujo et al., 2011; Vellutino et al., 2004). Especially in transparent orthographies such as German and Finnish, naming speed was shown to be a strong predictor of future reading skill (Danache et al., 2014). It was shown that children with both PA and RAN deficits develop most severe reading problems (Danache et al., 2014), further indicating dyslexia to be caused by an interplay of deficits. It is thought that naming speed deficits arise due to a pervasive problem in accessing or retrieval of phonological word forms or less stable phonological representations in general (Danache et al., 2014; Araujo et al., 2011). This explains why naming speed is often considered a deficit within the phonological system. However, according to Araujo and colleagues (2011), the nature of the object naming deficit may also be related to a problem in early visual processing. They found that manipulating the objects' dimensionality (2D vs. 3D) and color (greyscale vs. color) affect object naming latencies in dyslexics differently compared to controls.

2.3.1.1.3 Verbal short-term memory

The third component of the phonological system is verbal short-term memory (VSTM). This is the system responsible for the storage, retrieval, and processing of stable associations between spoken and written material (Danache et al., 2014). Several studies have demonstrated impaired VSTM performance in dyslexics, most notable in beginning readers. It is believed that when semantic knowledge has grown, context is able to compensate for memory deficits (Dandache et al., 2014).

2.3.1.2 Graphemic deficits

Uni-modal processing deficits specific to the visual sensory system have also been reported. Deficits in the visual processing system include selective visual attention (e.g. Valdois et al., 2004) and differences in the distribution of central versus peripheral visual recognition (e.g. Schneps et al., 2007). Dyslexics display an asymmetric and wider, more peripheral, distribution of visual perception (or attention) in the direction of reading (Geiger et al., 1994; 1997; Lorusso et al., 2004a; Schneps et al., 2007). Furthermore, on a lower visual processing level a magnocellular deficit has been postulated (Stein, 2001; Nandakumar & Leat, 2008). Responsible for contrast detection, the magnocellular pathway is essential for functions such as motion detection (Stein, 2001), detection of edges and during visual search tasks (Cheng et al., 2004). In adult dyslexics, reduced activation was also found in the cortical area associated with motion perception (i.e. area MT)(e.g. Cornelissen et al., 1998a; 1998b). However, this seems more likely a consequence of rather than the cause of a reading disability (Englund & Palomares, 2012; Olulade et al., 2013).

2.3.1.3 Grapho-phonemic deficits

While the research mentioned above was mainly directed at cognitive processing deficits that contribute to reading problems, a growing body of evidence is now indicating a more specific problem in the formation of audio-visual representations. Hahn and colleagues (2014) argue that efficient reading ultimately relies on the formation of cross-sensory associations between speech sounds and letter combinations that in time become automatic multisensory representations. It is important to clarify that automating letter-speech sound processing is different from just letter knowledge (Froyen et al., 2011). Indeed, the most commonly accepted phonological deficit account of dyslexia is increasingly linked to impairments in grapho-phonological conversion (Kronschnabel et. al., 2014). An experimental design that tests deficits in the formation of automatic multisensory representations might logically be hard to disentangle from independent contributions of unisensory deficits. McNorgan et al. (2013, p. 2) also emphasize that; "failure to properly integrate phonological and orthographic representations could be attributable to a failure of the phonological, orthographic or integration processes in isolation or in combination."

Hahn et al. (2014) mention a clever experiment by Birch and Belmont (1964) in which subjects were asked to match intervals between sequences of tones with the spacing between dot patterns. Reading impaired children were found to be significantly less accurate in matching the dot with tone patterns. A study by Blomert and Vaessen (2009) which measured speed and accuracy of letter-speech sound identification and discrimination, showed that accuracy between normal and impaired readers did not differ anymore after second grade. However, response latencies continued to decline till the fifth grade in normal readers (i.e. they got faster), whereas response latencies in impaired readers did not decrease after the third grade (in: Froyen et al., 2011, p. 635). According to Schneider and Chain (2003), this suggests weak or no automatization of the

learned letter-speech associations (i.e. hampered formation of automatic cross-modal representations). Further evidence that dyslexia may be caused by a multisensory integration deficit that hampers the formation of orthographic-speech sound representations is mostly limited to imaging studies and will be addressed in section 2.3.2.

2.3.1.4 Other deficits

Another category of potential causal explanations for dyslexia relates to more basic processes that may underlie the more proximal phonological weaknesses (Norton et al., 2014). Specific learning deficits such as in associative learning and rule learning have been found (Hahn et al., 2014). Also, as mentioned before, high comorbidity rates of dyslexia and ADHD suggests the involvement of the attention system in dyslexia. Attention deficits such as in selective attention, attention shifting and visual spatial attention have been associated with dyslexia (Hahn et al., 2014; Norton et al., 2014).

2.3.2 Neurobiological theories of developmental dyslexia

A more direct way of determining the causes of dyslexia is by looking at the brain by means of various imaging and brain recording techniques. Broad patterns of areas deviating in functional activation have been found in DR as well as structural abnormalities (Norton et al., 2014). In addition, a different connectivity profile appears to characterize the dyslexic brain (Finn et al., 2014, Vandermosten et al., 2012). It is important to note that functional differences in relative neural activity between DR and NR are often investigated by means of the same tasks or conditions used in the cognitive deficit experiments and only reflect a differential sensitivity to reading demands rather than a broader dysfunction of those regions (Norton et al., 2014). In other words, it doesn't mean that an area of the brain doesn't function, it just responds differently to a certain task or stimulus. In addition to task-induced group differences, more basic perceptual processes or stimulusinduced differences in neural activity are also observed (e.g. Blau et al., 2010). On the other hand, structural differences such as gray matter volume and neural architecture are often observed via a more passive approach while investigating anatomical abnormalities.

A relatively new and promising method of inquiry is connectivity research. Differences between DR and NR are found in functional connectivity (e.g. Horwitz et al., 1998; Finn et al., 2014) and structural connectivity between different areas (e.g. Richlan et al., 2013; Vandermosten et al., 2012). Functional connectivity research not only measures the magnitude of activation of certain brain areas but also how they interact and timely synchronize their activations. Structural connectivity research is directed at the size and microstructural organization of white matter tracts responsible for connecting various brain areas. Unsurprisingly, structural and functional deviations are often shown to be interrelated. Functional differences are found in

brain areas in which structural differences in gray matter are also observed (Norton et al., 2014). Unfortunately, the relationship between white matter (WM), gray matter (GM), functional activations and how abnormalities in these domains exert influence over each other during development remains unclear (Richlan et al., 2013).

2.3.2.1 Functional differences

As mentioned previously, the reading network is mainly comprised of a left-hemispheric network of frontal, temporoparietal and occipitotemporal cortical regions including the VWFA. Compared to non-impaired readers, functional magnetic resonance imaging (fMRI) studies have shown altered activity in all these areas in dyslexic children as well as in dyslexic adults (Finn et al., 2014, Richlan et al., 2013). The most commonly observed functional brain differences in dyslexics of all ages are hypoactivation of temporal, parietal and fusiform regions of the left hemisphere during reading tasks (Norton et al., 2014). Increased activation has also been reported in left inferior frontal and sometimes in homolog right-hemisphere regions (Norton et al., 2014). Hyperactivation of homolog right-hemisphere regions are thought of as compensatory mechanisms for reduced activations of the normal reading network. Hoeft et al. (2007) conclude that areas of hypoactivation in dyslexia (i.e. left parietal and bilateral fusiform cortices) illustrate functional abnormalities pertained to dyslexia, whereas certain areas of hypoactivation (i.e. left inferior and middle frontal gyri, caudate, and thalamus) related to their current level of reading ability independent of dyslexia.

Studies in pre-reading children identified as at-risk for dyslexia (due to a familial history of dyslexia or low performance on predictive tests) have already shown the presence of functional and structural abnormalities in left temporal and occipitotemporal brain areas characterizing dyslexia (Richlan et al., 2013). More precisely, a whole-brain analysis of unisensory visual and auditory group differences in children around the age of nine by Blau and colleagues (2010) revealed reduced unisensory responses to letters in the fusiform gyrus. Moreover, a reduced activity for processing speech sounds was observed in the anterior superior temporal gyrus, planum temporale/Heschl sulcus, and superior temporal sulcus. Together, the neural integration of letters and speech sounds in the planum temporale/Heschl sulcus and the neural response to letters in the fusiform gyrus explained almost 40% of the variance in individual reading performance. According to Blau and colleagues (2010), this indicates that an interrelated network of visual, auditory and heteromodal brain areas contributes to the skilled use of letter-speech sound associations necessary for learning to read. Furthermore, previous work by Blau and colleagues (2009) also showed underactivation of the superior temporal cortex during the integration of letters and speech sounds in adult dyslexic readers. According to the authors, this reduced audiovisual integration is directly associated with a more fundamental deficit in the auditory processing of speech sounds, which in turn predicts performance on phonological tasks. Their data provide a neurofunctional account of developmental dyslexia, in which phonological processing deficits are linked to reading failure through a deficit in neural integration of letters and speech sounds (Blau et al., 2009).

These differences are observed in early childhood. In an event-related potential (ERP) study, Van Zuijen et al. (2013) not only found different responses to a deviant auditory stimulus between at-risk 2-month-old infants compared to controls but also differences within the at-risk group between infants who later developed reading difficulties and the ones who did not.

Brain imaging studies show that "... sensory specific letter and speech-sound input in low level sensory areas not only converge but integrate in the superior temporal sulcus (STS), immediately followed by feedback to 'sensory specific' auditory areas in the superior temporal gyrus (STG) signaling the adequacy of this letter-speech sound integration ... Letters thus systematically modulated the response to speech sounds in auditory cortex." (in: Froyen et al., 2011, p. 636). In other words, the visual sight of letters influences what the brain 'hears'. Perhaps in analogy with the McGurk effect in which the visual sight of articulating lips influences the perception of sounds (McGurk & MacDonald, 1976). In dyslexics, however, not only the response to speech sounds in isolation was shown to be reduced, but also letter speech-sound integration. Moreover, when presented with incongruent letter-speech pair (e.g. the letter A with the sound /o/) normal readers immediately suppressed letter speech-sound integration. In contrast, adult and beginner (8-9 years) dyslexic readers don't display this suppression effects, similarly activating letter-speech sound integration for existing and non-existing letter-speech sound integration, these findings suggest that dyslexics do automate the integration of letter-speech sound but have no discrimination between valid and invalid ones. Therefore dyslexics seem to store both useful and useless multisensory representations.

2.3.2.2 Structural differences

As for structural differences in dyslexics, in a meta-analysis Richlan and colleagues (2013) found reduced gray matter volume (GMV) in the right superior temporal gyrus and left superior temporal sulcus. Moreover, these structural differences are in line with previous observations on functional brain abnormalities in dyslexic readers (Richlan et al., 2013). Krafnick et al. (2014) also found dyslexic children to show less GMV in multiple regions compared to age-matched controls. However, when contrasted with GMV of ability-matched children, only the right central gyrus GMV was found to differ. Likewise, differences in white matter volumes were not significant. According to Krafnick and colleagues (2014), this indicates that GMV differences in dyslexics in both their own study and those by others are largely explained by differences in reading experience. This also means that these anatomical differences may not be inevitable and could potentially be avoided with proper remedial methods. On the other hand, Richlan et al. (2013) point out that recent studies indicate the presence of both functional and structural abnormalities in left temporal and occipitotemporal brain regions before reading onset. Therefore it appears there may be some initial functional and anatomical differences between 'normal' children and those who later develop dyslexia, and these differences get bootstrapped because of deviating experience.

2.3.2.3 Connectivity

Finding structural abnormalities and deviating functional activity of certain brain areas has undeniably taught us much about the nature of dyslexia. However, the connectivity and timed interaction between these areas may prove to be as important as the relative activation or size of these areas. Finn and colleagues (2014) argue that activation-based analyses of fMRI data don't tell much about how different brain regions interact and therefore might sketch an incomplete picture of the neural mechanisms of dyslexia. Functional connectivity analyses, on the other hand, can detect how activity between areas may be differently synchronized in dyslexics. They argue that "this synchrony between anatomically distinct regions might be equally or more important for cognitive performance than the magnitude of activation in any single region" (Finn et al., 2014, p. 397). Differences in connectivity can be structural (i.e. white matter tracts) or functional (i.e. timely interaction of activity between multiple brain areas).

2.3.2.3.1 Structural connectivity

First, it may be important to explain what structural connectivity analysis looks at and how it is measured. Communication between (distant) brain regions is facilitated by white matter tracts. The integrity and structural coherence of a white matter tract give an indication of the workings of that tract. The integrity of white matter fiber tracts can be examined with Diffusion Tensor Imaging (DTI), which measures the degree and directionality of the diffusion of water within a small region. In white matter, there is a high degree of diffusivity parallel to the direction of the tracts. The degree of directional diffusivity is reflected by Fractional Anisotropy (FA) values which are measured with DTI. Higher FA values indicate greater connectivity between the connected brain regions and more efficient information processing along the tract (Gullick & Booth, 2014).

While there are several major white matter tracts in the brain, the arcuate fasciculus (AF) in particular seems to fulfill an important role in the integrative processing necessary for reading. The AF arcs from the temporal lobe (e.g. superior temporal gyrus (STG)) to the inferior frontal gyrus (IFG) and tends to be left lateralized. Thus, the AF connects regions important for auditory processing and usage of crossmodal information, with the region particularly involved in the formation of integrated representations for new or unfamiliar items (Gullick & Booth, 2014). If the AF supports the integration between phonology and orthography, connectivity along this tract may directly impact reading ability. Indeed, reading skill is shown to be predictive for white matter connectivity along the AF. Gullick and Booth (2014) showed that crossmodal brain activity is specifically related to connectivity in the AF, supporting its role in phoneme-grapheme integration ability. Moreover, both in adults and children with dyslexia the left AF showed decreased FA values, indicating a decreased connectivity along that tract (Vandermosten et al., 2012). In particular, Boets et al. (2013) found the integrity of the segment of the AF that directly connects posterior temporal and frontal areas to be

significantly reduced in dyslexics. Boets et al. (2013) suggest this result provides neuroanatomical evidence that corroborates the deficiency in functional connectivity between left IFG and left STG.

2.3.2.3.2 Functional connectivity

Using PET, Horwitz et al. (1998) compared correlations of regional cerebral blood flow of the left angular gyrus with other language regions in DR and NR during a single word reading task. The left angular gyrus was found to be functionally disconnected from other parts of the reading network in men with developmental dyslexia (Horwitz et al., 1998). The angular gyrus is located in the parietal lobe. Its strategic location between areas processing touch, vision, and hearing has led to speculations that this area could be of importance in metaphors and cross-modal associations in general (Ramachandran & Hubbard, 2003). Among other functions, the (left) angular gyrus is associated with complex language functions and is thought to be involved in mapping visually presented inputs onto linguistic representations (Horwitz et al., 1998). While Horwitz et al. (1998) found a strong functional connectivity of the left angular gyrus with extrastriate occipital and temporal lobe regions in NR, in DR the left angular gyrus was found to be functionally disconnected from visual areas, from Wernicke's area, and from the inferior frontal cortex.

In a whole-brain functional connectivity analysis, Finn et al. (2014) compared the connectivity profiles of DR to NR. They observed a decreased connectivity along the visual pathway as well as between visual and prefrontal regions. The former implies a disrupted information transfer along the visual pathway. The latter further suggests that dyslexics are less able to focus attention on texts and thereby are less able to control activity in the visual pathway. This finding supports evidence that dyslexia is at least in part a disorder of attention and may shed light on the high comorbidity with ADHD. While the magnitude of functional activity of visual areas may not differ between DR and NR, the strength of the connections between them and other reading related areas do seem to differ. These results, therefore, underscore the importance of functional connectivity research. In addition, a decreased lateralization of language to the left hemisphere was found. While dyslexics do eventually specialize language to the left hemisphere, they do so at a slower rate and to a lesser extent than non-impaired readers. Dyslexics continue to rely more on bilateral systems with right-hemisphere homologs not only being more active but also more strongly connected to the rest of the brain.

Finn et al. (2014) also observed that dyslexics showed an altered connectivity of the posterior Cingulate Cortex (pCC). The pCC is thought to function as a cortical hub, integrating information from distinct brain regions and networks. The pCC is part of the Default-Mode Network (DMN), a network of regions which are active when subjects are devoid of any particular tasks. The DMN (including the pCC) is particularly active during internally directed attention while relatively inactive during externally directed attention (Leech & Sharp, 2013). In DR, Finn and colleagues (2014) found the activity of the pCC to be better synchronized with other areas of the DMN (dorsal and ventral cingulate cortices) and medial prefrontal cortex. In contrast, pCC

activity is better synchronized with visual association regions such as the dorsal visual pathway and left fusiform gyrus in normal readers. The authors suggest that a stronger connectivity between the pCC and the visual areas in normal readers could reflect better integration and cognitive control of visual information. Interestingly, in people with ADHD, functional connectivity within the DMN is reduced and pCC function is abnormal, further suggesting a link between ADHD and dyslexia (Leech & Sharp, 2014).

Finn and colleagues (2014) also found a reduced and altered connectivity to the VWFA in adult DR. While this difference in connectivity of the VWFA hasn't yet manifested in young readers, the gap widens with age as good readers further develop the use of this network. Connections of this node in adult NR may reflect successful information transfer between the VWFA and bilateral extrastriate cortices (visual association areas), left IFG (mapping of word form to language), and left medial PFC (attentional modulation). On the other hand, DR showed increased connectivity of the VWFA to other bilateral visual association areas and to the right primary auditory cortex which indicates compensatory circuits and a slow 'sounding out' strategy of reading. Lastly, Finn et al. (2014) found an increased connectivity to the left IFG in the reading network of DR, which involved medial PFC, anterior cingulate, and left caudate. Although multifunctional, this region is particularly associated with phonology. This finding, therefore, further supports the notion that DR continue to depend on arduous mental articulation, while NR gradually shift to faster visual-based systems during the long course of proficient reading acquisition.

According to Finn et al. (2014) together these findings suggest that by integrating visual information and adjusting their attention to visual stimuli, NR are able to recognize words on the basis of their visual properties. DR on the other hand, employ different reading circuits and rely on laborious phonology-based 'sounding out' strategies into adulthood (Finn et al., 2014).

2.3.3 Genetics

Let us briefly end with what might be considered the most fundamental and tenacious cause of dyslexia: genetics. While environmental factors play a significant role in the eventual presence and severity of the condition, longitudinal- and twin studies have shown that dyslexia is highly heritable. Between 30 and 50 percent of children of parents with dyslexia ultimately develop reading difficulties (Dandache et al., 2014). Genes associated with dyslexia have shown to be involved in neuronal migration and axon guidance during the formation of the cortex in animals (Benitez-Burraco, 2010) and are associated with variation in lefthemisphere white matter and reading skill in humans (Norton et al., 2014). More specifically, it has been shown that various cognitive abilities such as phonological processing, orthographic processing, and spelling also have a strong genetic origin (Benitez-Burraco, 2010). Moreover, not every type of dyslexia is affected equally by genetic factors. Phonological dyslexia, for instance, is found to be more heritable than orthographic dyslexia (Siegel, 2006). Phonological dyslexics have more trouble reading pseudowords while orthographic

dyslexics have more trouble reading exception words. So, unfortunately, there appears to be a 'hardwired' susceptibility for a range of behavioral characteristics found in dyslexics. However, genetics only partly explains the phenotype in multifactorial conditions such as dyslexia while the remainder is determined by environmental factors. As van Otterloo and colleagues (2009a) noted, familial risk of dyslexia may be used to detect developmental dyslexia at an earlier preliterate age and offers opportunities to investigate whether early intervention may reduce the risk and severity of dyslexia later in life.

2.4 Key findings dyslexia

Although the problem of dyslexia has been studied for a long time, the precise nature of the problem remains rather elusive. A lot of details about dyslexia have been given in this chapter, some of which may contradict each other. In order to leave the reader with some sense of what is important to remember about dyslexia, some of the key findings are listed below.

- Dyslexia is increasingly regarded as one end of a spectrum of reading proficiency.
- Prevalence of dyslexia ranges between 5 to 20 percent.
- In order to read, the brain has to reorganize and recruit cortical systems for the novel task of recognizing script.
- The underlying causes dyslexia can be approached on various levels of abstraction, which again may all mutually influence each other and with environmental factors such as education and exposure to text.
 - Dyslexia is thought to originate from specific cognitive deficits.
 - Cognitive deficits arise from functional, connectivity and anatomical brain differences.
 - Structural/anatomical brain differences originate partly from a genetic profile.
- Instead of one core deficit, dyslexia is increasingly regarded as an endophenotype caused by an interplay of deficits, each variably and independently contributing to the severity and type of reading problems.
- Deficits are found in three domains; audio-phonemic deficits, graphemic deficits and graphophonemic deficits.
- A phonological deficit is a problem with accessing, processing and/or manipulating the sound structure of speech. These problems are apparent in phonological awareness, rapid automatized naming, and verbal short-term memory.
- Phonological processing deficits are linked to reading failure through a deficit in neural integration of letters and speech sounds.

- A growing body of evidence is now indicating a more specific problem in the formation of crosssensory associations between speech sounds and letter combinations that in time become automatic multisensory representations.
- Dyslexics do seem to automate the integration of letter-speech sound but have no discrimination between valid and invalid ones.
- Broad patterns of areas deviating in functional activation have been found in DR as well as structural abnormalities. In addition, a different connectivity profile appears to characterize the dyslexic brain.
- DR display reduced activation of temporal, parietal and fusiform regions of the left hemisphere during reading tasks.
- Increased activation has been reported in left inferior frontal and sometimes in homolog righthemisphere regions and may reflect compensatory mechanisms.
- Dyslexics display a decreased connectivity along the AF tract, especially in the segment that directly connects posterior temporal and frontal areas.
- Dyslexics specialize language to the left hemisphere at a slower rate and to a lesser extent than NR.
 In other words, dyslexics continue to rely more on bilateral systems with right-hemisphere homologs not only being more active but also more strongly connected to the rest of the brain.
- Adult DR display a reduced and altered connectivity to the VWFA. While this difference hasn't yet
 manifested in young readers, the gap widens with age as good readers further develop the use of this
 network.
- DR continue to depend on arduous mental articulation, while NR gradually shift to faster visual-based systems.
- Between 30 and 50 percent of children of parents with dyslexia ultimately develop reading difficulties.

3 SYNESTHESIA

3.1 Introduction

While in the previous chapter the underlying mechanisms of dyslexia were reviewed, this chapter addresses the complex nature of synesthesia. Unlike dyslexia, however, synesthesia generally isn't considered a disability for which treatment is required. Instead of a complex problem, synesthesia can better be viewed as a complex answer to many of the remaining enigmas in neuroscience (Harvey, 2013). In the neurosciences, understanding how something goes 'wrong' can tell a lot about how the brain normally functions. Therefore, understanding the basis of synesthesia, where one type of stimulus evokes the sensation of another, is likely to provide valuable insights into the underlying neural pathways of subjective experience, as well as cognitive theories in numerical cognition, automaticity, cross-modal interaction and awareness (Cohen-Kadosh & Henik, 2007a). As discussed in the previous chapter, a growing number of scientist believe dyslexia results from a failure in the neural integration of letters and speech sounds, which in turn hampers the efficient formation of automatic multisensory representations needed to read fluently. On the other hand, graphemecolor synesthesia is characterized as an abnormal integration of letters with colors which during the course of reading development gradually create automatic multisensory representations. In other words, synesthetes develop something which dyslexics appear to be missing, albeit with another modality. Therefore, knowledge of how and why this happens in synesthetes may be well informative for the understanding and remediation of dyslexia.

3.1.1 Definition

The word synesthesia originates from the Greek word *syn* and *aisthesis*, meaning "together" and "perception" respectively (Ramachandran & Hubbard, 2005). Synesthesia is often somewhat incorrectly described as a mixing of the senses. People with synesthesia report that an attribute of a sensory stimulus (e.g. its shape, meaning or sound) leads to the experience of an additional perception (Ward, 2012). The most common forms of synesthesia are triggered by letters, words, days of the week and months and usually bring about an experience of color or spatialization. However, numerous forms have been documented, some leading to some strange experiences. For instance, experiencing different colors sensations for particular swimming styles (Nikolíc et al., 2011) or the taste of cold, leftover potato scraps with congealing pot-roast gravy upon hearing the word *clue* (Simner & Haywood, 2009). Currently, up to 150 disparate forms of synesthesia is called the 'inducer', and modality of the experience itself the 'concurrent' (Grossenbacher & Lovelace, 2001). In this way, any form of synesthesia can minimally be described as an inducer-concurrent pair, such as music-color synesthesia when music elicits sensations of color. However, synesthesia is a highly heterogeneous phenomenon, extending beyond a simple description of an inducer-concurrent pair.

24

While the defining characteristics of synesthesia are still much disputed (e.g. Simner, 2012a, 2012b; Cohen Kadosh & Terhune, 2012; Eagleman, 2012), there are three aspects most researchers agree upon. First of all, the associations which synesthetes experience show a remarkable internal consistency. The synesthetic associations are idiosyncratic, often highly specific and found to be consistent over long periods of time. Testing the consistency of associations, such as used in the Synaesthesia Battery (Eagleman et al., 2007; Carmichael et al., 2015), has been the gold standard to identify synesthetes. However, Eagleman (2012) also points out that synesthetic consistency scores don't show a clear bimodal distribution that divides synesthetes from controls. Therefore, including only people with high-consistency scores may guarantee these people are truly synesthetic, but may also place inappropriately tight restrictions. The second aspect is the automaticity of concurrents. Although attention to the inducer is required, synesthetes have no voluntary control over their concurrents (Mattingley, 2009; Rich & Mattingley, 2010). While non-synesthetes can imagine a blue '9' and change it to a red '9', no such control exists for the synesthetic experience. If their '9' is blue, this color will automatically rise to their consciousness. The third aspect is the conscious perceptual reality of the concurrent. Synesthetes are not 'merely' imagining it. Although synesthetic colors aren't confused with real colors, for synesthetes there is a certain perceptual reality to the experience.

3.1.2 Prevalence

Anecdotally, many people with synesthesia don't realize their experiences differ from the rest of the population. Again, they don't suffer from it and don't seek help for the condition. Estimates of the prevalence of synesthesia have varied as widely as from 1 in 4 (Calkins, 1895) to 1 in 25.000-100.000 (Cytowic, 1993; 1997), partly due to differences in definitional criteria as well as differences in a focus on different subtypes (in: Simner et al., 2006). Moreover, most of these estimates relied on self-referral. When large samples of the population were screened for most types of synesthesia, and the outcomes combined with an objective measure such as internal consistency, a prevalence rate of at least 4% was found, without any male-female bias (Simner et al., 2006). Most recently a Dutch survey of a semi-representative population (age 20-26) in which many forms of synesthesia were assessed found a surprisingly high prevalence rate of 24.18% (Rouw & Scholte, 2016). In another recent (and largest to date) prevalence study by Simner and Carmichael (2015), the prevalence of grapheme-color synesthesia was found to be 1.39% of the population.

3.2 Inducer

While the focus of this study is on grapheme-color synesthesia, for a better understanding of synesthesia it's important to have a closer look at the characteristics of the various inducers that trigger the synesthetic percept.

3.2.1 Cultural tools

While many studies have focused on the sensory-perceptive nature of synesthesia, most inducers are in fact acquired cultural tools and most commonly are of a linguistic nature, such as letters, numbers, and words (Hochel & Milán, 2008; Ward, 2012; Watson et al., 2014). In fact, Simner (2007) suggested language plays a central role as inducers of synesthesia as linguistic stimuli are inducers in 88% of the total reported cases of synesthesia (Simner et al., 2006; Mankin et al., 2016). Especially words that are learned in an ordinal fashion, such as days and months of the year are common inducers (Eagleman, 2009; Simner et al., 2006). The fact that letters of the alphabet are also learned in an ordinal style has led to the hypothesis that these subtypes may also be grouped together as colored sequence synesthesias (Novich et al., 2011).

3.2.2 Higher-lower distinction

Ramachandran and Hubbard (2001a) further hypothesized that a distinction between '*lower*' and '*higher*' synesthetes exists. For lower synesthetes, the inducer needs to be physically perceived (e.g. the printed number 3), whereas in higher synesthetes merely the concept of a specific inducer causes the synesthetic experience (e.g. number 3 in roman numerals or just thinking about the number). However, it is important to note again that synesthesia differs from normal imagery in its involuntary nature, its internal consistency, and automaticity of the concurrent (Eagleman et al., 2009).

3.3 Concurrent

The synesthetic percepts of synesthetes are highly idiosyncratic. Again, to paint a full picture of this condition it is important to highlight some of the characteristics of the concurrents as they may vary in domain, form or location from one synesthete to the next.

3.3.1 The special role of color

First of all, it is important to emphasize the important role color plays in synesthesia. Between 80.6% to 95% of reported concurrents, involve color (Eagleman & Goodale, 2009). Rich and Mattingley (2002, p9) proposed that this might be due to the uniqueness of color as a visual experience:

"Whereas most objects can be represented across multiple perceptual domains (for example, a tennis ball can be perceived by sight, by the sound it makes when hit with a racquet, or by its weight and texture when held), surface colours have no perceptual correlate in any other modality. Moreover, color names must be learned, as must the visual symbols that constitute written and spoken language. To what extent might these facts provide a clue to the prevalence of colour-graphemic synaesthesia? Perhaps synaesthetes inherit a predisposition for co-activation of categorical information within the language and colour domains."

Considering colors are often one of the first categorical concepts learned and might therefore form the scaffolding on which to map other newly learned categories.

3.2.2 Projector-associator distinction

Subjective differences also exist between synesthetes as to *where or how* the concurrents are perceived. GCsynesthetes may be phenomenologically divided into *projectors* and *associators* (Dixon et al., 2004). Projectors report to perceive synesthetic colors outside their own body space, either superimposed on the fonts themselves (*surface-projectors*) or on some externalized near-space like an imaginative screen (*spaceprojectors*). Associators, on the other hand, report that their synesthetic colors exist in an internal mental space. Associators can be further divided into *see-associators* and *know-associators*. The former 'sees' synesthetic colors in 'the mind's eye' while the latter just knows the color of the grapheme at some propositional level without having the association of seeing it (Ward et al., 2007). Some researchers may exclude know-associators from real synesthetes, whereas for others it may illustrate the wide and spectral range of the condition.

Behavioral tests, such as the synesthetic congruency tasks, in which either the physical color or synesthetic color of a letter must be named, provide support for the distinction between projectors and associators (Ward et al., 2007). On a given trial, the display color and synesthetic color can either match (congruent) or mismatch (incongruent). Dixon et al. (2004) found projectors showed a greater congruency effect (incongruent minus congruent reaction time) when naming the displayed color compared to naming the synesthetic color, whereas associators showed the opposite pattern (in; Chiou & Rich, 2014). It's hypothesized that synesthetic colors of projectors emerge earlier in the visual system and are therefore expected to act more like real colors than in associators (Chiou & Rich, 2014). Real colors are known to affect visual search tasks. For instance, if someone is asked to find the letter 'C' among a group of 'G's it helps tremendously if the letter 'C' has a different color than the 'G's. However, this clear 'popping out' effect of color hasn't been found in projector synesthetes (Ward et al., 2010; Sagiv et al., 2006). Instead, synesthetic colors seem to affect search times more like canonical color memory does in a normal population (e.g. when searching for a banana among other fruits is easier to find when it is yellow instead of purple) (Chiou & Rich, 2014).

Some neuroimaging studies have also provided support for a neurological distinction between associators and projectors. Rouw and Scholte (2010) compared volume and density of neuronal gray matter (GM) between associators and projectors, as well as their functional response to graphemes. They found projectors to have more GM in cortical areas involved in perception and action, whereas associators had an increase of GM in cortical areas involved in memory encoding and retrieval. Moreover, in a previous study, Rouw and Scholte (2007) also found projectors to display greater connectivity (more coherent white matter) in the inferior temporal cortex compared to associators. Van Leeuwen and colleagues (2011) observed that cross-activation of hV4 (the area associated with color perception) was induced via a bottom-up pathway within the fusiform gyrus in projectors. In contrast, associators showed hV4 activation via a top-down pathway involving the parietal lobe, indicating differences in effective connectivity within the same network of active brain regions between projectors and associators (van Leeuwen et al., 2011).

However, according to Simner (2013), the phenomenological differences between projectors and associators may also emerge from individual differences in the ability to form visual mental images and may therefore be an independent quality instead of a real difference in their synesthesia. Barnett and Newell (2008) found synesthetes in general reported experiencing more vivid mental images compared to controls. Results from a principal component analysis of questionnaires measuring individual differences in synesthetic phenomenology suggest that projectors and associators are not opposites along a single dimension, but both exist as separate dimensions of experience (Anderson & Ward, 2015). That is, some synesthetes may even claim to be both and others claim to be neither. Some authors have further objected to the dichotomy of the projector-associator distinction because a synesthete's description may be biased by the phrasing of the questions (e.g. Simner, 2012; Eagleman, 2012). Eagleman (2012) points out that although there are differences in spatialization among individuals, there is no sound evidence that it is binary. Eagleman (2012) therefore refers to data from Rouw and Scholte (2007), in which he claims people scored smoothly along a projector-associator spectrum rather than a bimodal distribution. The nature of many disorders (e.g. Autism Spectrum Disorder and Attention Deficit Hyperactivity Disorder) are increasingly understood as spectral instead of binary. Perhaps synesthesia and some of its aspects may also be better understood as a spectral condition.

3.4 Causes

While there is a general consensus that synesthesia is somehow caused by an aberrant cross-activation of one cortical area by another, the underlying neural mechanisms that mediate the unusual crosstalk seen in synesthesia are not well understood (Bargary & Mitchell, 2008a, 2008b; Barnett et al., 2008b). Most models regarding the neurophysiological basis of synesthesia mainly differ on two still unresolved issues. The first is whether cross-activation between concurrent and inducer is direct or mediated via some other cortical area(s). The other issue is whether synesthesia is caused by extra connections not present in non-synesthetes (i.e. structural difference) or by a disinhibition of normal connections (i.e. functional difference) (Bargary & Mitchell, 2008a). The two most influential models are the disinhibited feedback theory (Grossenbacher and Lovelace, 2001) and the cross-activation theory (Ramachandran and Hubbard, 2001a). In the following chapter, these two main theories, as well as their derivatives, are shortly reviewed.

3.4.1 Disinhibited feedback theory

According to the disinhibited feedback theory, synesthesia is the consequence of defects in inhibitory cortical areas which normally suppress crosstalk between brain areas. Synesthesia could result from either disinhibition in the feedback from multimodal regions such as the superior temporal sulcus (Grossenbacher & Lovelace, 2001) or from areas involved in executive control such as the prefrontal cortex (Cohen Kadosh et al., 2009) to unimodal sensory areas (in: Chiou & Rich, 2014). Compared to non-GC-synesthetes, Rouw and Scholte (2007) also found increased structural connectivity in multimodal regions such as the superior parietal and frontal cortex in GC-synesthetes. Indirect evidence for the disinhibited feedback theory comes from the synesthesia-like experiences elicited by hallucinogens (Grossenbacher & Lovelace, 2001) as well as after hypnosis (Cohen Kadosh et al., 2009). Both are thought to affect inhibitory mechanisms. Moreover, some authors have pointed to a common involvement of an aberrant serotonergic system in genuine, acquired and drug-induced synesthesias (e.g. Brogaard, 2013; Luke & Terhune, 2013). However, although drug- and hypnotic induced synesthesia appears superficially similar to genuine synesthesia, other authors have argued that both are actually not quite that comparable (e.g. Anderson et al., 2014; Sinke et al., 2012a). The most notable evidence for the disinhibited feedback theory comes from studies indicating the required involvement of higher-level cortical areas in consciously identifying the concept of the inducer before the concurrent can be perceived. For most synesthetes, it is the concept of a letter that determines the synesthetic color and not its low-level visual characteristics. For instance, the semantic context of an identical grapheme (such as the **O** in "G**O**" or "**O** 1 2") determines the perceived synesthetic color, a phenomenon not adequately addressed by direct cross-activation theories. So while the disinhibited feedback theory is a plausible mechanism for synesthesia, so far it is mainly supported by indirect behavioral evidence and still lacks strong direct evidence of malfunctioning neuronal inhibition (Chiou & Rich, 2014).

3.4.2 Cross-activation theory

The other main theory, the (direct) cross-activation theory, suggests excessive neural connections directly between the cortical areas serving the modalities of the inducer and concurrent. According to this view, Ramachandran and Hubbard (2001b) suggested GC-synesthesia would be the cause of direct, excessive connectivity between the area processing graphemes (fusiform gyrus) and the adjoining area processing color (hV4). A diffusion tensor imaging study of GC-synesthetes by Rouw and Scholte (2007) indeed found greater structural connectivity in the inferior temporal cortex, a region considered housing these two modalities. Increased structural connectivity in this area was not only related to the presence of GC-synesthesia, but also to the subjective nature of the experience (projector-associator distinction).

3.4.3 Hybrids

Other, more recent models can be regarded as hybrids of both main theories. As Carmichael and Simner (2013) suggest, the cross-activation and disinhibited feedback models are not mutually exclusive. Any feedback that simultaneously activates neurons will strengthen interconnectivity between those neurons according to the Hebbian principle (i.e. neurons that fire together, wire together). Cross-activation models suggest altered neural connectivity to be the prime cause of synesthesia, whereas feedback models view altered connectivity to be an indirect consequence of disinhibited feedback (Carmichael & Simner, 2013). In other words, cross-activation models stress the role of structural brain differences whereas feedback models focus on the role of functional brain differences (Rouw et al., 2011).

3.4.3.1 The two-staged cascade cross-tuning model

Since the parietal cortex is thought to facilitate feature binding in normal perception, many authors have pointed to the necessary involvement of the parietal cortex in the anomalous binding in synesthetes (Rouw & Scholte, 2007). The two-staged cascade cross-tuning model (Hubbard, 2007) further elaborates on the cross-activation theory by incorporating the role of attentional mechanisms of the parietal lobe necessary to bind the two features in one unified percept at a later stage. Rouw and Scholte (2007) indeed observed a greater structural connectivity (i.e. more coherent white matter tracts) of the left superior parietal cortex in GC-synesthetes compared to controls. Moreover, in another study in GC-synesthetes, Rouw and Scholte (2010) also found an increase in gray matter exactly superior in location to the earlier found increase in white matter (i.e. Rouw & Scholte, 2007) characterizing GC-synesthesia.

3.4.3.2 Conceptual-mediation neurocognitive framework

To explain the behavioral evidence for the role of conceptual knowledge and the attributes of synesthetic colors, Chiou and Rich (2014) suggested the need for a framework that emphasizes the role of high-level processing in synesthesia. The re-entrant model by Smilek et al. (2001) incorporates a role for high-level processing. Besides direct cross-talk between involved modalities, this model also includes feedback from higher-level areas that represent the concept or meaning of the inducer, such as the anterior inferior temporal lobe (in: Chiou & Rich, 2014). Chiou and Rich's (2014) conceptual-mediation neurocognitive framework of synesthesia posits that synesthetic mappings between inducers and concurrents are similar to typical conceptual mappings between objects and their perceptual attributes (e.g. the concept of a banana with its canonical shape, taste, and color). According to their hub-and-spoke model, the inducer and concurrent are linked within a conceptual-level representation or supramodal "hub". While the subjective (bodily) experience of its resultant concurrent (e.g. a color) may then require activation of "spokes" in the perception-

related cortices. In other words, for synesthetes and non-synesthetes alike the inducer is first identified at a conceptual level. The activation of this core concept propagates through a semantic network to associated nodes of its conceptual attributes, like the concept of bananas will activate the association of yellow and curved. In this view, the semantic network in synesthetes activates a conceptual attribute (e.g. color) that is absent or weak in non-synesthetes. Moreover, the strength of this activation may reflect the nature of the experience; stronger activation may lead 'seeing' the color (i.e. projector) whereas a weak activation may result in 'knowing' the color (i.e. associator). The model doesn't necessarily rely on either disinhibited feedback or cross-activation, but suggests synesthesia, like memories, may emerge from more global changes in a distributed cortical network.

Now, for our ability to understand the exact mechanisms of synesthesia it may be preferential to describe one clear route by which input is processed and from which the synesthetic percept follows. It could result from disinhibited feedback or from direct extra connections between the modalities. However, there is evidence for both mechanisms (or neither of them; see Hupé & Dojat, 2015) and as mentioned before, there is really no reason there should be only one way. Chiou and Rich (2014) hub-and-spokes model seems a very plausible scenario of how conceptual knowledge may influences synesthesia, but it doesn't necessarily exclude the influence of direct connections between the involved modalities either. The wetware of the brain may likely be far more complicated than the intuitive and workable, but perhaps simplistic, descriptions that characterize the above-mentioned models pertain.

3.5 The neural correlates of synesthetic experience

Since synesthesia is often described as a neurological condition, many researchers have searched for the neural correlates of the subjective experience of synesthetes. Most neural mechanisms of synesthesia are believed to reflect functional or structural differences in connectivity at the cortical level relative to the neurotypical brain (Ward, 2012). Many functional and structural (group) differences between synesthetes and non-synesthetes have been reported, as well as differences within groups of synesthetes of the same type (e.g. associator-projector distinction). Indeed, most published works claim to have found neural correlates of synesthesia (Hupé & Dojat, 2015). Based on the reviews by Rouw et al. (2011) and Hupé and Dojat (2015) an overview of brain areas believed to be involved in synesthesia is given. For the purpose of this work and its audience in mind, certain details and nuances are omitted. Interested readers are therefore referred to the original reviews. Furthermore, it is important to note that Rouw et al. (2011) uphold a qualitative outlook upon which areas are likely candidates considering convergent results of some studies, despite weak statistical evidence or inconsistent results with other studies. Their work can, therefore, be considered exploratory and gives concrete directions for future studies. On the other hand, Hupé and Dojat (2015) seem to hold a very critical disposition, in that, as long as there are inconsistent results and no strong statistical evidence they believe there really isn't yet much to say about the workings of synesthesia.

31

Moreover, this has led them to infer that with our current tools it might not even be possible to find the subtle neural correlates of synesthesia.

Most of the neurological models presume that color centers should be activated when GC-synesthetes read, hear or imagine letters and words. In other words, the experience of the concurrent should reflect some activity of that associated modality in the brain. Therefore, many studies have either tried to find some differences in functional activity between GC-synesthetes and controls when confronted with graphemes, or between synesthesia-inducing and non-inducing graphemes within synesthetes. More specifically, whether a functional difference can be found within the region strongly associated with color perception (hV4) is of particular interest. Despite inconsistent results due to differences in experimental setup, Rouw et al. (2011) advocate that it is reasonable to conclude that activity in color areas can be obtained in response to synesthetic color experiences. However, hV4 is not the only area associated with color perception, nor is color perception its only function. Rouw et al. (2011) therefore also claim that activation of color regions due to synesthesia is not limited to hV4.

By way of nine whole-brain studies, Rouw et al. (2011) identified six brain locations that seem related to synesthesia. These locations emerge when, despite their differences, minimally three out of nine studies converge in reported locations. The first region related to synesthesia is a bilateral activation in the occipitotemporal cortex, which also includes hV4. Rouw et al. (2011) suggest this nonspecificity (i.e. why not only hV4) might be due to differences in measurement methods. However, they say it also seems to support the notion that synesthetic color perception involves a more widespread network of ventral occipitotemporal areas. Overall, Rouw et al. (2011) show that some of the brain areas in occipitotemporal cortex, which are activated by real colors, are activated by synesthetic colors as well. The second and third region of interest Rouw et al. (2011) identified come from clusters of activation almost exclusively located in posterior parietal cortex. These clusters were found in the left or right superior parietal lobule and in the (left) inferior parietal lobule, with the latter specifically as either near the intraparietal sulcus or in the angular gyrus. These regions are believed to function in the binding of the sensations. The fourth region is the bilateral insula and operculum, which could be related to the conversion process of external stimuli to different internal stimuli, as well as assigning an accompanying emotional value to the synesthetic experiences. Studies have also found increased activation in either the left or right precentral gyrus, which is associated with (preparatory) motor responses. According to Rouw et al. (2011), this suggests a larger network of brain areas is involved in synesthesia or reflects additional aspects of the synesthetic experience. Finally, the involvement of the frontal cortex may reflect the need for increased cognitive control to resolve the conflict between internally and externally generated sensations during a synesthetic experience. More specifically, some studies found increased activations adjacent to the right dorsolateral prefrontal cortex.

Rouw et al. (2011) further conclude synesthetes also have a structurally different brain compared to controls. These anatomical differences were found in terms of gray matter, as well as in white matter tract coherency as measured with fractional anisotropy (FA). According to Rouw et al. (2011), findings of increased gray matter in hV4 combined with findings of increased connectivity (increased FA) near the fusiform gyrus in the neighborhood of hV4, support the theory of cross-activation of inducer to concurrent by means of structural differences. Also, the superior parietal lobe appears to be larger in linguistic-color synesthetes than controls. Moreover, gray matter density of sensory areas appears to be increased in synesthetes, even in areas which aren't necessarily related to the synesthetic modality. Rouw et al. (2011) conclude that having the general 'trait' as well as a particular 'type' of synesthesia is not only related to regions which process the involved modalities, but also with large-scale anatomical differences throughout the brain.

While Rouw et al. (2011) took a qualitative view upon the limited data available, Hupé and Dojat (2015) are more skeptical. They critically reexamined all the studies that have searched for the neural correlates of synesthetic experiences, as well as the structural differences related to synesthesia. Firstly, Hupé and Dojat (2015) asked whether any functional correlate of the synesthetic experience has been identified yet and whether these are the same as those involved in a comparable non-synesthetic experience (e.g. color centers activated in GC-synesthetes). When looking for a functional neural correlate of a synesthetic experience one asks: 'what brain areas are uniquely activated during a synesthetic experience'. However, this is not as straightforward as it may seem. For instance, when a particular brain area is found to activate differently in synesthetes and non-synesthetes, it isn't necessarily directly related to the synesthetic experience. These differences could also arise from secondary characteristics that may need to be included to fully describe the synesthetic experience but are not specific to the experience of synesthesia, such as differences in attention, emotion, or imagery (Hupé & Dojat, 2015). Among 25 studies, Hupé and Dojat (2015) didn't find any clear functional correlate of synesthetic colors. A few significant differences (in six studies) between synesthetes and controls were reported in the frontal and parietal cortex (whole brain analysis). When restricting the analysis to the visual cortex only a few results (in five studies) were compatible with the involvement of color regions in synesthesia.

Hupé and Dojat (2015) also investigated whether the synesthetic experience comes from structural brain alterations. They reviewed studies that explored structural alterations using MR imaging by means of structural morphometry (changes in GMV, WMV or modifications in FA) or changes in connectivity. Hupé and Dojat found no conclusive evidence so far of any morphological difference between synesthetes and controls, in particular not in regions supposed to code the synesthetic experience (e.g. color). As to differences in connectivity, most studies were interested in discovering whether synesthesia was either due to connectivity changes between the regions (of the fusiform gyrus for grapheme-color synesthesia) coding the inducer and the concurrent (cross-activation theory), or due to a difference of neuronal transmission (disinhibited feedback theory), possibly more widespread. However, Hupé and Dojat concluded that, overall, no consistent difference in functional connectivity was observed between synesthetes and controls. They concluded that all structural studies that looked for differences between synesthetes and controls were severely

underpowered. Therefore any observed structural differences between two small groups of synesthetes and controls may be related to random differences that exist between any two groups of people, rather than synesthesia, given the very large number of potential individual differences that may have a morphometric counterpart. The risk of finding such false positives when dealing with multiple comparisons was powerfully demonstrated by Bennett et al. (2009) who were able to find 'evidence' of a dead salmon engaged in a perspective-taking task in fMRI data. In conclusion, Hupé and Dojat did not find any clear-cut empirical evidence about the neural correlates of the subjective experience of synesthesia, nor did they find any structural or functional anomaly in the brain of synesthetes that could explain synesthesia. According to the authors almost all published synesthesia papers described in their review were unsupported due to statistical errors, questionable methodological choices, or low statistical power. Instead, their review shows that the brains of synesthetes are functionally and structurally similar to the brains of non-synesthetes.

However, the absence of significant difference is of course not the proof of the absence of difference. Synesthetes have a different subjective experience which must be reflected in the brain. Hupé and Dojat are, however, skeptical that our current tools are able to correctly study the subtle brain mechanisms of synesthesia in group analyses of a small number of individual brains. Like Chiou and Rich (2014), Hupé and Dojat (2015) suggest that synesthetic associations may be a special kind of childhood memory which is deprived of its autobiographical content. If so, finding the neural correlates of synesthesia may still be out of reach for as long as we can't detect the signature of memory content in the brain (Hupé & Dojat, 2015).

3.6 Function of synesthesia

For the last two to three decades synesthesia research has been primarily focused on demonstrating the genuineness of synaesthetes' reports and the 'psychological reality' of their sensory experiences (Simner, 2007). Moreover, because synesthesia has mainly been regarded as a perceptual phenomenon, much research has focused on its sensory characteristics (Simner, 2007). However, as of yet, the function of synesthesia has not received a lot of attention and remains rather elusive. It is conceivable that synesthesia may just be a neural glitch or abnormality without any beneficial function, or an exaggerated version of some other beneficial trait (e.g. cross-modal perception) common to us all (Simner et al., 2006). However, its relatively high prevalence rate and the fact that synesthesia has a genetic component, suggest an advantage and selective pressure on putatively associated genes. Therefore, contemplating the possible biological and cognitive functions of synesthesia may be a fruitful inquiry as to how and why it arises in some but not in others. On the other hand, the genetic component of synesthesia may be inherited, whereas the explicit associations and individual differences between synesthetes are influenced by other factors. Furthermore, in a twin study of color-sequence synesthesia (an umbrella-term for synesthesias induced by sequential stimuli such as letters, numbers, months and days of the week), monozygotic and dizygotic twins only showed a

pairwise concordance of 73.9% and 36.4%, respectively (Bosley & Eagleman, 2015). These findings strongly suggest a major role for learning in both shaping and engendering synesthesia (Bor et al., 2014).

3.6.1 Benefit of synesthesia in adulthood

Before getting into hypotheses as to why synesthesia might develop, let's look at some secondary characteristics of synesthetes. Besides serving as an interesting dinner conversation, are there any benefits to having synesthesia in general and GC-synesthesia in particular? Synesthesia is associated with certain perceptual and cognitive strengths and weaknesses (Rich et al., 2005). Interestingly, synesthesia as a general trait has been linked to a particular personality profile of increased openness and fantasizing (Banissy et al., 2013; Rouw & Scholte, 2016), as well as increased neuroticism and emotionality and decreased conscientiousness (Rouw & Scholte, 2016). This may explain why synesthetes have certain dispositions towards creative hobbies and occupations (Rich et al., 2005; Ward et al., 2008) as well as the higher prevalence of synesthetes among art students (Rothen & Meier, 2010).

Certain perceptual and cognitive benefits and disadvantages have also been reported in GC-synesthetes in particular. For instance, synesthetes with color as their concurrent are better at color discrimination than non-synesthetes but seem to have an impaired motion perception (McCarthy & Caplovitz, 2014). Some studies (e.g. Ramachandran & Hubbard, 2001a; Palmeri et al., 2002; Hubbard et al., 2005) found GC-synesthetes to perform better at certain visual search tasks, which would also suggest synesthesia is a perceptual phenomenon, arising early enough in visual processing to influence attention mechanisms. However, results of other more robust group studies (e.g. Edquist et al., 2006; Gheri et al., 2008; Rothen & Meier, 2009) showed no significant differences in performance between synesthetes and controls in visual search tasks. According to Chiou and Rich (2014), search times more closely resembled those of canonical object knowledge instead.

Compared to controls, GC-synesthetes were also found to be significantly better at guessing the meaning of words in unfamiliar languages (i.e. sound-symbolism), which suggests synesthesia coincides with more general heightened multi-modal skills unrelated to their synesthesia (Bankieris & Simner, 2015). Interestingly, dyslexics display just the reverse pattern. Compared to controls, Drijvers et al. (2015) found dyslexics to be impaired in their ability to make sound-symbolic associations.

Synesthetes often claim to use their synesthetic percept as a mnemonic tool (Rich et al., 2005) and many single case studies of synesthetes with exceptional memory have been documented (in: Rothen & Meier, 2009). Indeed, Rothen et al. (2012) found that synesthetes tend to have a better visual memory than verbal memory. Further evidence of enhanced memory performance in GC-synesthetes has been found for tasks using stimuli that induce a synesthetic percept as well as stimuli that do not (Pritchard et al., 2013). GC-synesthetes also displayed superior color working memory compared to controls, but interestingly did not differ in grapheme working memory (Terhune et al., 2013).

Another cognitive ability which may be affected in GC-synesthetes is mathematical proficiency. In a largescale survey by Rich and colleagues (2005) synesthetes reported mathematics both as an area of weakness as well as of strength significantly more often compared to controls, with the former being more prominent. Also, it has been shown that children with GC-synesthesia between 7 and 15 years old experience difficulties in numerical tasks when digits are shown in their incongruent colors (Green & Goswami, 2008).

In summary, both benefits and weaknesses have been shown to be correlated with having synesthesia later in life. It is, however, unclear whether these traits are imposed by synesthesias or if the brain profile predisposing to synesthesia also predisposes to these benefits and weaknesses. Regardless if such characteristics are facilitated by synesthesia, these secondary benefits seem very unlikely the primary function of synesthesia nor the advantages which evolutionary pressure selected for.

3.6.2 Benefit of synesthesia during development

Since (GC-)synesthesia progressively develops in early childhood during written language acquisition (Simner & Bain, 2013), it also seems logical to find its possible function during this period. Indeed, there are some authors who have speculated on the function of synesthesia during this period. For instance, Watson et al. (2012) showed that synesthetes can learn rule-based categories using internally-generated synesthetic colors, suggesting synesthesia can be exploited when learning the kind of material taught in many classroom settings. It is, therefore, worthwhile to explore this crucial period and the development of synesthesia during this phase of life.

First, one needs knowledge of culturally acquired symbols for the development of GC-synesthesia. This means that GC-synesthesia, such as in its adult form, cannot yet exist in infancy (Simner & Bain, 2013). Likewise, to my knowledge, there are no illiterate adult GC-synesthetes. It is only when letters and numbers are learned, that the type of representations required to drive GC-synesthesia can be established (Simner & Bain, 2013). A predisposition for synesthesia may already be present before the learning of letters, as well as certain enhanced cross-modal representations (e.g. shape-color) that drive or bootstrap future GC-associations. However, in behavioral terms, GC-synesthesia develops alongside a growing familiarity with letters and numbers (Simner et al., 2009, Simner & Bain, 2013). Evidence that (GC-)synesthesia is intricately entwined with learning comes from developmental studies following the progression of GC-synesthesia during childhood. Simner and Bain (2013) followed the development of GC-synesthesia in children of age 6/7 years old till 10/11 years old over three testing sessions. First of all, they observed that synesthesia develops from relatively fluid pairings of graphemes with colors to more fixed associations later on. Secondly, the number of graphemes with a fixed color pairing also increases during childhood. Moreover, there was a significant individual variation in progression, both in consistency and number of synesthetic associations. In some cases synesthesia even disappeared completely over time. In like manner, Meier et al. (2014) even showed
synesthesia attrition occurs across the adult lifespan with a decline in the number of consistent graphemecolor associations and shifts in the concurrent color spectrum. In short, Simner et al. (2009) and Simner and Bain (2013) observed that besides a hereditary component, synesthesia is an acquired trait with a protracted development. It would be interesting to find out what factors may have differed between those who have consolidated their synesthesia and those who have 'forgotten' it. The fact that the development of graphemecolor associations coincides with the learning and particularly the *mastering* of written symbols strongly suggest these associations have a possible function during this process.

It is important to note that knowledge of letters and numbers is already present before their concepts are being 'enriched'. While eight-year-old synesthetes know the full alphabet, they don't have a full complement of synesthetic colors (Simner et al., 2009). This means there is a temporal gap between complete knowledge of the alphabet and a consistent neurological mapping of inducers to their concurrents. If synesthesia serves a function in reading and writing, this temporal gap suggests that synesthesia aids in the quick and adequate appliance of alphabet knowledge rather than formation of alphabet knowledge itself.

In a comparative study between drug-induced and genuine synesthesia, Sinke and colleagues (2012a) concluded that while drug induced synesthesias are best understood as enhanced bottom-up processes, genuine synesthesia is more about top-down concept formation than sensory processing. The authors suggest synesthesia to "... be a kind of (unconscious) compensatory strategy to concretize abstract entities in order to better cope with them" (Sinke et al., 2012a, p.1431). In other words, assigning readily available labels (e.g. color) to abstract concepts (e.g. letters) helps the brain to deal with such concepts. These labels transform an ill-defined abstract concept into a more concrete entity by linking it to a system of pre-existing knowledge. While most people link graphemes to phonemes, as mentioned in the previous chapter, synesthetes seem to add a system of representation (e.g. color).

Wilson (2013) regards synesthesia as an extreme end of a continuum of a general human tendency to create mappings across domains. According to Wilson (2013), humans are active, strategic associators, which use one domain of thought to aid in representing another. For instance, when using metaphors, we refer to corresponding or similar relationships to represent and clarify something else. Wilson points to the resemblance of synesthesia with embodied cognition, where we use the representation of our body as a map for other concepts to be understood. For instance, in the way we use our hands and gestures to represent spatial relationships and shapes, our fingers to externalize the cognitive load of counting and the way social relations are articulated in terms of bodily experiences of temperature and proximity. In this respect synesthesia is another way the human brain exploits isomorphisms for representational purposes. One might object by pointing out that synesthetic associations are idiosyncratic and seem rather arbitrary. Therefore, they don't appear to be grounded in a commonly understood isomorphism such as counting and the number of fingers. However, I would claim such direct relation doesn't have to be necessary for it to be useful. The

brain may just as well devise its own arbitrary system for representational purposes to ease cognitive load. Like a mnemonic aid, it doesn't necessarily need a valid reference to reality for it to work.

It is, however, unclear in what degree we all use such strategies of other types of representation. While some studies have observed different patterns of activation in synesthetes (e.g. Sinke et al., 2012b), synesthetes may only differ from non-synesthetes in the degree their brain applies such strategies or in the degree these strategies permeates their consciousness.

3.7 Development of synesthetic pairings

We have already seen that the consistency and number of GC-associations increase over time during the period of mastering the written script. Adult GC-synesthetes can even acquire new synesthetic graphemecolor percepts for newly encountered foreign graphemes (Blair & Berryhill, 2013). However, what factors determine the color letters get assigned? There are reasons to believe the associations don't necessarily have to be firmly grounded in reality for them to be useful. However, the development of a truly arbitrary system would be hard to imagine too. Some sort of mechanism should drive the associations, for it is unlikely the brain employs some sort of 'random color' generator. Indeed, synesthetic associations may not be so random as they might appear and a number of regularities have been reported that shouldn't be there if the associations are truly arbitrary. For example, Rich et al. (2005) found that the letter 'D' elicited brown in 47% of their Australian synesthetic subjects, 'A' elicited red in 36%, and 'O' for white in 56%. So which factors drive these consistencies? Several causal factors for the association of specific colors with graphemes during grapheme learning have been proposed in various studies. For instance, Rich et al. (2005) suggested that colors are first assigned to items forming conventional sequences (e.g. numbers, days of the week). Then later, these associations are generalized to graphemes and even to words. However, this only shifts the initial color association from graphemes to sequences and doesn't elaborate how parts of the sequence are getting their colors. Others have found that the factors that affect synesthetic grapheme-color correspondence are systematically associated with several grapheme properties. These factors are the graphemes visual shape, sound, meaning or concepts, frequency, ordinality, and memory related to the graphemes (Rich et al., 2005; Asano & Yokosawa, 2013). To complicate matters even more, the magnitude of impact of each factor also appears to differ across writing systems (Asano & Yokosawa, 2013). For native English GC-synesthetes for instance, sound is expected to have a weak impact on synesthetic colors because graphemes are in most cases arbitrarily associated with several phoneme representations (Asano & Yokosawa, 2013).

Recent work has identified shape-color associations as the primary association from which graphemes derive their colors (Brang et al., 2011; 2013). Interesting as it may be, this finding, unfortunately, doesn't elaborate how and why a certain shape gets its associated color. However, similar trends for certain grapheme-color associations are also observed in the non-synesthetic population when faced with a forced-choice test (Simner et al., 2005). Rouw et al. (2014) also found regularities in letter-color and day-color preferences both in synesthetes and non-synesthetes, and across different languages (Dutch, English, and Hindi). These findings suggest that abstract concepts (i.e. the inducers) are closely connected to perceptual representational systems in all of us. Synesthetic associations may therefore be grounded in cross-modal mechanisms common to us all. Certain cross-modal associations are deeply rooted in our natural environment. For example, the way concepts like *up/above/high* are associated with *bright/light/lite* is easily traced back to natural associations such as the sun's dominance in our upper field of vision and the buoyancy of lighter objects. Other intuitive example is how *small* is associated with a *high* pitch whereas *big* with a *low/loud* sounds, which might find its origin in animal sounds and colliding objects in general. *Red* may obviously thank its associations become ingrained with our language and culture, and subsequently reinforced and bootstrapped by their endurance in our culture (e.g. we speak of high tones and indicate the hot water tap with a red color). These naturally occurring and culturally extended cross-modal associations may serve as a basis upon which a future synesthete can build a more elaborate idiosyncratic system.

3.8 Key findings synesthesia

A lot of information about synesthesia has been given in this chapter. Before I revisit some of the connections between synesthesia and dyslexia in the next chapter, and most importantly why training synesthesia may benefit dyslexics. It may be useful to have a short summary of the most relevant aspects of synesthesia that have passed this review.

- Synesthesia is a highly heterogeneous condition with even considerable differences among synesthetes with the same form of synesthesia.
- Synesthesia may be more common than formerly believed.
- Synesthesia is associated with a particular personality profile as well as certain cognitive strengths and weaknesses.
- Inducers are mostly of a linguistic nature and concurrents usually involve color.
- Synesthesia depends on the (conscious) identification of the concept of the inducer.
- Although there is a hereditary predisposition for the development of synesthesia, it is also an acquired trait with a protracted development.
- The associations between graphemes and colors both grow in number and consistency during the period of written language acquisition.

- Synesthesia is believed to aid during the imposed challenges of learning cultural artifacts such as graphemes.
- In synesthetes, evidence indicates both the presence of extra connections as well as a disinhibition of normal circuitry.
- Some evidence suggests direct cross-activation between the involved modalities, however, it also points to the necessary involvement of higher level conceptual cortices.
- To some degree, non-synesthetes may share some of the cross-modal mechanisms at work in synesthetes
- The scheme of particular, idiosyncratic grapheme-color pairings is believed to originate from other cross-modal associations, in particular shape-color associations, and get bootstrapped during the period of learning and efficiently applying graphemes. These other cross-modal associations may be more or less prominent in us all, and in turn, originate from naturally occurring associations bootstrapped by culture.

4 THE RELATION BETWEEN GC-SYNESTHESIA AND DYSLEXIA

This chapter will first shortly revisit some of the overlap and differences between the two conditions. However, not much is known about the prevalence of dyslexia among synesthetes. Therefore, in order to find out whether dyslexia is rarer among synesthetes, this work will make an own attempt to find out the level of comorbidity of the two conditions.

4.1 Overlap between synesthesia and dyslexia

Although both conditions lay at the heart of the specific identification of written script, synesthesia and dyslexia have been scarcely linked to each other in existing literature. Some of the more explicit connections between the two conditions have already been mentioned. For instance, Mitchell claims both conditions are disorders of cortical specialization. Mitchell (2012, p. 1) characterized dyslexia as "... the inability to integrate information across multiple areas and the consequent failure to develop representations of the knowledge of some category based on its associated attributes". According to Mitchel (2012), synesthesia portrayed as a hyper-associative condition, can be regarded as the opposite of dyslexia. Synesthesia can also be described in similar terms of the above characterization of dyslexia. In synesthetes there is an excessive ability to integrate information across multiple areas, which leads to the development of representations of the knowledge of some category (e.g. letters) based on its additional attributes (e.g. color). Also, the way Froyen et al. (2011) and Hahn et al. (2014) respectively characterize dyslexia as a specific cross-modal association deficit and impairment of multisensory integration seems like the opposite of synesthesia. Clues of an inverse relation between synesthesia and dyslexia can also be found in sound-symbolism studies. Bankieris and Simner (2015) found GC-synesthetes outperformed controls on understanding unfamiliar (sound symbolic) foreign words. Contrary to synesthetes, Drijvers et al. (2015) found dyslexics are impaired in their ability to make sound-symbolic associations relative to controls. These results suggest that both synesthesia as dyslexia co-occurs with the abnormal functioning of multi-modal skills. In other words, the type of cross-modal integration necessary for sound symbolism appears to be heightened in synesthetes while diminished in dyslexics. Moreover, both conditions involve some of the same (abnormal functioning) brain areas or connections between them. This may not come as a surprise, considering many of these areas' involvement in the processing of written script. The most that cautiously can be said is that some of the abnormalities found in both conditions appear to be opposites of each other. In other words, while synesthesia may be characterized with hyperactivity in a certain region, dyslexia may typically be characterized with less activity of that region. Listing the abnormalities and functions of these areas/connections with respect to the condition, and especially the differences in these areas/connections between the two conditions goes beyond the scope of this thesis. Many of these findings are either not fully resolved or highly disputed within their respected fields. Of course, it is preferable to describe the exact neurological mechanism of how training synesthesia may relieve some of the problems dyslexics face. However, since the exact neurological mechanisms of both conditions are not yet fully understood, such task would be too speculative and far beyond my understanding of the material. Instead what follows here is an attempt to find whether the two condition are of such different and opposing nature as to exclude each other. Considering the above, I predict the prevalence of dyslexia to be significantly less among GC-synesthetes compared to controls.

4.2 Prevalence of dyslexia among synesthetes

Again, both synesthesia and dyslexia are regarded as disorders of cortical specialization, with contrasting positions in a spectrum of functional and structural connectivity in the brain in general, or between relevant modalities in particular. If indeed the two conditions situate themselves on opposite ends of more general spectral disorder, the two conditions are not expected to be comorbid. That is, the prevalence of dyslexia among (GC-)synesthetes should be significantly less than those who are not. Vice versa, the prevalence of (GC-)synesthesia should also be significantly less among dyslexics compared to those who are not.

On the other hand, the two conditions may also not be opposite ends of a more general spectral disorder. The development of synesthesia is increasingly regarded as a learning mechanism because concurrents are useful for gaining mastery over the inducer domain (Watson et al., 2017). According to Watson et al. (2017), synesthesia should, therefore, be more common among those who faced greater childhood learning challenges, such as caused by language differences. Indeed, Watson and colleagues (2017) showed that differences in early language challenges, such as orthographic transparency and native versus non-native multilingualism, effects the prevalence of synesthesia. That is, the prevalence of synesthesia is higher among those with a more difficult language environment. This 'learning hypothesis' of synesthesia could lead to two outcomes with respect to the comorbidity of dyslexia and synesthesia. On the one hand, dyslexics experience greater learning challenges in becoming literate than non-dyslexics. According to the learning hypothesis, they are therefore more likely to develop GC-synesthesia than non-dyslexics. One can, therefore, expect to find more synesthetes among dyslexics and vice versa. On the other hand, synesthesia may actually help those with a predisposition of dyslexia to overcome (some of) their handicap. Dyslexia is a spectral condition, thus any possible advantage synesthesia may provide may help and shift those border case dyslexics just enough to be excluded from the dyslexia category. In that case, one can expect to find less reported dyslexia among synesthetes compared to the normal population. In conclusion, the learning hypothesis of synesthesia may both suggest a higher and lower prevalence of dyslexics among synesthetes, depending on how much influence synesthesia may have on literacy acquisition in children with a predisposition to develop dyslexia.

Unfortunately, there hasn't been any documented attempt to find prevalence rates of synesthesias among dyslexics. This is perhaps due to the unobtrusive nature of synesthesia and its fringe status in science. There

is also no official reported prevalence rate of dyslexia among synesthetes. However, there are three datasets from studies which besides tests for synesthesias also inquire whether the participant suffers from dyslexia. The first is the Synesthesia Battery (www.synesthete.org), an online test for multiple forms of synesthesia (Eagleman et al., 2007). The second dataset (Carmichael, personal communications, Oct. 24th 2016) is an extension of previous studies by Carmichael et al. (2015) and Simner and Carmichael (2015). The former aimed to validate the online Synesthesia Battery with a randomly recruited sample from the general population, the latter was a prevalence study with a special interest in potential skewed male/female ratio's among synesthetes. The third study (van Leeuwen, personal communication, Apr. 25th 2016) is the Great National Research on language and perception (translated from Dutch: 'Groot Nationaal Onderzoek naar taal en waarneming'), from here on referred to as GNO. The GNO is an online test for multiple synesthesias and sound-symbolism (gno.mpi.nl). Here, a first attempt will be made to find out how common dyslexia is among synesthetes. While an own analysis was made from the Synesthesia Battery data, the prevalence rates of dyslexia among synesthetes from the latter two datasets were obtained via personal communications with the authors.

4.2.1 Prevalence of dyslexia in the Synesthesia Battery

The online 'Synesthesia Battery' (www.synesthete.org) was developed by Eagleman and colleagues (2007) to provide researchers with a standardized test battery for a range of different types of synesthesias. The Synesthesia Battery begins by asking participants which type(s) of synesthesia they believe to have, with twenty possible choices and a text-box for any other variant not listed. Based on their answers participants are further directed to questions intended to quantify traits across many groups of synesthetes and to steer them to the appropriate tests for their form(s) of synesthesia, such as a grapheme-color test. Moreover, several questions in the survey are meant to gather contextual (e.g. handedness, the presence of synesthesia among family members) and neuropsychological data (e.g. autism, dyslexia, head trauma and tumors).

4.2.1.1 Results Synesthesia Battery

Raw data from the Synesthesia Battery was obtained via contact with Josh Jackson, Sean Judge and Scott Novich from Eagleman's lab. This included all test results up till the first of October 2014. Unfortunately, the data contained many missing values. None of the different synesthesia tests, nor the questions in this survey were mandatory. This means not all participants completed both the test for grapheme-color synesthesia and all the questions of the personal survey. Some tests were not administered or completed, nor were all the personal questions answered. Also, there were 74319 battery id's of which 72469 unique user id's. This means some people took the tests more than one time. In this analysis, only unique user id's were included with their latest battery id. Of all the entries (N=74319), only 14 participants answered the question about dyslexia with a clear 'no', while 3374 times it was answered with 'yes'. All the other entries on the dyslexia question were left blank. Therefore, it is reasonable to assume that most of these absences were likely to be meant as a 'no'. However, the absence of an answer could also imply a refusal to answer the question or just an uncompleted survey. By lack of a better strategy, an assumption was made that the number of participants who would refuse to answer, while in fact being dyslexic, wouldn't be significant. On the other hand, after a closer inspection of the personal survey data, it became obvious that not all surveys were completed. Therefore not all absences of an answer to the dyslexia question could be taken as a 'no' to that question. In an effort to rid the data of incomplete entries on the personal survey, further analysis excluded participants who didn't fill in whether any family members have synesthesia. The presence of an answer on this particular question seemed the most viable criterion for which survey was actually completed. That is, participants who answered this question tended to answer subsequent questions, while participants who didn't answer this question also left subsequent questions blank.

Battery ID (N=74319)				
Unique users (N=72469)				
Answered family question (N=67663)				
Took GC-consistency test (N=25452)				
Passed criteria #1 (N=15809)				
Passed criteria #2 (N=6676)				
192	563	1110	3289	
192	371	547	2179	

Fig. 3. Schematic depiction of the analysis of groups and subgroups of participants of the synesthesia battery. Numbers under the dotted line represent the number of self-reported dyslexics in that group including those in subsequent subgroups. The additional bar displayed directly under are the number of dyslexics in that group excluding those of further subgroups.

After excluding those who left the 'synesthesia in the family' question blank, a total of 67663 unique participants remained. Although the choice of using this criterion to exclude any uncompleted forms is debatable, it certainly excluded a great portion of unfinished surveys. Then, further analysis only included participants who took the grapheme-color test. This left us with 25452 participants who provided a 'valid' survey, as well as a completed grapheme-color test. Fig. 3 provides an overview of the data into these relevant subgroups. The grapheme-color test consists of two consecutive parts: a grapheme-color consistency test and a speeded congruency test.

4.2.1.1.1 Results after GC-consistency test

The first and foremost criteria to pass in order qualify as GC-synesthete is a grapheme-color consistency test (criteria 1). Here, participants were presented with a single grapheme which they had to match with a color by navigating their mouse over a color palette. After a color was selected, the next grapheme was presented. All the 36 letters and numbers were presented three times in randomized order. Participants are considered GC-synesthetes when three times the same (or similar) colors are chosen for a number of graphemes. After the test, a consistency score was given for each participant (for further elaboration how consistency scores are calculated, see Eagleman et al. (2007)). It is important to note that the height of the consistency score is negatively correlated with the consistency of colors given to the graphemes. In other words, the lower the consistency score, the more consistent answers were given. Only consistency scores below 1.0 were ranked as synesthetic (i.e. criteria 1). Of the 25452 included participants (i.e. unique users who answered the 'synesthesia in family' question and took the GC-consistency test), 15809 were considered GC-synesthetes according to criteria 1 only (see Table 1). Among these GC-synesthetes, 3.56% claimed to have dyslexia (N=563). Thus, dyslexia is still self-reported among GC-synesthetes. However, its prevalence rate is lower than the 5.67% (N=547) found among the participants who failed the consistency test (N=9643). A chi-square test, X^{2} (df 1, N=25452) = 64.01, P < .001), confirms a significantly lower proportion of dyslexics among synesthetes according to criteria 1.

Table 1: Number and percentages of dyslexics and non-dyslexics among GC-synesthetes and those who are not GC
synesthetes among participants of the synesthesia battery after consistency test (<1) criteria only.

(N=25452)	GC-synesthetes	Non-GC-synesthetes
Dyslexics	563 (3.56%)	547 (5.67%)
Non-dyslexics	15246	9096

Also, a dyslexia prevalence rate of 5.16% (N=2179) was found among participants who didn't take a grapheme-color test (N=42211). Although these participants were not tested, it is unlikely there are many (or any) GC-synesthetes in this group. A self-report of GC-synesthesia would have directed them to the GC-test. It is, therefore, safe to assume these aren't GC-synesthetes. When the group of consistency tested non-GC-synesthetes (N=9643) is combined with the group of untested participants (N=42211), a prevalence rate of 5.26% (N=2726) was found among these non-GC-synesthetes (N=51854) (see Table 2). Again, a chi-squared test, X^2 (*df* 1, N=67663) = 75.34, P < .001), indicates a strong significant dependency between self-reported dyslexia and the presence of GC-synesthesia according to criteria 1.

Table 2: Number and percentages of dyslexics and non-dyslexics among GC-synesthetes and those who are not GC-synesthetes among participants of the synesthesia battery after consistency test (<1) criteria only, considering untested participants as non-GC-synesthetes.

(N=67663)	GC-synesthetes	Non-GC-synesthetes	
Dyslexics	563 (3.56%)	2726 (5.26%)	
Non-dyslexics	15246	49128	

4.2.1.1.2 Results after speeded congruency test

In an effort to exclude the possibility of any cheating on the consistency test, for instance with a 'cheat-sheet' that translates graphemes into colors, Eagleman et al. (2007) also administered a speeded congruency test immediately after the consistency test. During this test, participants were sequentially presented with a colored grapheme for one second. For half of the trials, the color of the grapheme was identical to the previously reported synesthetic color from the consistency test. In the other 50% of trials, the grapheme was presented in one of the colors the participant reported for another grapheme. It was made sure that this incongruent color was sufficiently different from the previously reported synesthetic color of that grapheme. Each trial, participants were asked to judge as quickly as they could whether the color of the grapheme was congruent or incongruent with their synesthetic color. Eagleman and colleagues (2007) found that this test was able to discriminate synesthetes from non-synesthetes based on accuracy (94% versus 67% correct responses, respectively), as well as average reaction time (0.64±0.78 sec. versus 0.91±0.87 sec., respectively). Unfortunately, average reaction times are too variable to be diagnostic on an individual level and reflect only group differences. However, Eagleman et al. (2007) claim synesthetes have no trouble performing above 90% correct rates, while non-synesthetes perform well below that rate. Therefore, further analysis only considered participants with an accuracy of >90% on the speeded congruency test to be labeled synesthetes. Moreover, to further prevent any possible cheating with cheat sheets, a decision was made to disqualify participants

with an average reaction time of above 2 seconds. This time limit was chosen to still be well above the average reaction time plus standard deviation of synesthetes.

Together, these more conservative criteria (<1 on consistency test, >90% accuracy & <2 sec. mean reaction time on speeded congruency test) will be referred to as 'criteria 2'. After criteria 2, 6676 participants were identified as GC-synesthetes, of which 2.88% self-reported dyslexia (N=192) (see Table 3). Again, this is significantly lower, X^2 (*df* 1, N=25452) = 47.86, P < .001), than the 4.89% (N=918) among the GC-tested participants (N=18776) who failed to meet criteria 2 (i.e. the consistency test, the speeded congruency test, or both).

Table 3: Number and percentages of dyslexics and non-dyslexics among GC-synesthetes and those who are not GC-synesthetes among participants of the synesthesia battery after both consistency test (<1) criteria and speeded congruency test (accuracy >90% and <2 sec. mean reaction time).

(N=25452)	GC-synesthetes	Non-GC-synesthetes	
Dyslexics	192 (2.88%)	918 (4.89%)	
Non-dyslexics	6484	17858	

Additionally, when the non-tested participants (N=42211) are also considered as non-GC-synesthetes, there are 60987 non-GC-synesthetic participants of which 3097 claim to have dyslexia (see Table 4). This gives a prevalence rate of 5.08% among non-GC-synesthetes participants, almost double compared to the 2.88% among verified GC-synesthetes (N=192). A chi-squared test confirms a strong significant correlation, X^2 (*df* 1, N=67663) = 63.01, P < .001).

Table 4: Number and percentages of dyslexics and non-dyslexics among GC-synesthetes and those who are not GC-synesthetes among participants of the synesthesia battery after both consistency test (<1) criteria and speeded congruency test (accuracy >90% and <2 sec. mean reaction time), considering untested participants as non-GC-synesthetes.

N=67663	GC-synesthetes	Non-GC-synesthetes
Dyslexics	192 (2.88%)	3097 (5.08%)
Non-dyslexics	6484	57890

4.2.1.2 Discussion Synesthesia Battery

To my knowledge, this is the first reported attempt to find the prevalence rate of dyslexia among GCsynesthetes. On the whole, these findings strongly suggest the prevalence rate of dyslexia among GCsynesthetes to be notably less than those among who are not GC-synesthetes. However, these results should be taken with caution for a number of reasons.

First of all, participants of the Synesthesia Battery cannot be considered as a representative sample of a normal population for a number of reasons. Participants have prior knowledge and expectations of the test and they aren't randomly selected from the population as a whole. Also, the group of non-GC-synesthetes may actually exhibit other forms of synesthesia. The prevalence of dyslexia among other forms of synesthesia wasn't further investigated. If dyslexia is indeed less common among all or certain forms of synesthesia, the obvious purpose of this test battery would have resulted in a general lower involvement of dyslexics. Moreover, because participants were not randomly selected, again overall prevalence rates of dyslexia among the participants may be skewed. It is conceivable that dyslexics may be more reluctant to participate in an online test involving letters.

Secondly, no objective measurements were applied to test whether participants were indeed dyslexic. Instead, dyslexics were identified by self-referral, which may not be very reliable.

Thirdly, the data contained many missing variables. In an effort to rid the data of meaningless blank entries on the questionnaire, perhaps an arbitrary selection method was applied. The sincerity on the dyslexia answer (i.e. blank entry implying a 'no') was based on whether participants answered the question if synesthesia runs in the family. This criterion could also have discarded valid entries or included invalid ones. Also, exclusively discarding entries on the basis of the absence of an answer to this question, actually discarded 85 'yes' entries on the dyslexia question. This should not have happened. The only purpose was to differentiate between an absence of answers meaning 'no' or 'just not answered'. This error was found while writing this discussion and couldn't be easily corrected. Future analysis should only exclude participants who didn't answer both questions. Other screening methods to assess the intention of blank entries may be more appropriate and could yield other results.

Moreover, the criteria for GC-synesthesia may have been too strict. For instance, the benchmark of <1 on the consistency test might have falsely excluded genuine GC-synesthetes. In their 2007 paper, Eagleman et al. also warn that this data-driven threshold is merely an optimal division between two populations whose scores vary along a distribution and therefore should not be considered fool-proof cut-off for discriminating synesthetes from non-synesthetes. Rothen et al. (2013) reexamined the sensitivity of this threshold and found that a cut-off value of 1.43 more closely separated synesthetes from non-synesthetes. Although the <1 benchmark could have also falsely included non-synesthetes, the subsequent speeded congruency test should have acted as some safeguard against these wrongly identified participants.

48

Also, a lot of participants who were initially identified as GC-synesthetes by the standards of the consistency test were later disqualified as such after the speeded congruency test. The speeded congruency test may be a valid method to discriminate the two groups and a useful approach to prevent cheating. However, these additional criteria (>90% accuracy and <2 sec. mean reaction time) disqualified 57.8% of the formerly identified GC-synesthetes. It is hard to imagine this many people would have either been cheating on the consistency test or being falsely identified by it. Instead, it is perhaps more likely these numbers reflect some other exclusion criteria. For instance, it is not yet clear what happens if participants did not finish the speeded congruency test. Would this result into a low accuracy and/or a breach of the average reaction time threshold?

In an effort to examine which criterion contributed to the exclusion of so many participants, the required accuracy and maximum mean reaction time were manipulated to be less conservative. Increasing the maximum mean reaction time didn't yield much more GC-synesthetes. However, lowering the required accuracy on the speeded congruency test did. This less conservative criteria 3 (i.e. <1.0 on GC-consistency test, >85% accuracy and <2 mean reaction time on congruency test) did drastically raise the number of GC-synesthetes from 6676 to 9628 (see Table 5).

Table 5: Number and percentages of dyslexics and non-dyslexics among GC-synesthetes and those who are not GC-
synesthetes among participants of the synesthesia battery after both consistency test (<1) criteria and speeded
congruency test (accuracy >85% and <2 sec. mean reaction time).

(N=25452)	GC-synesthetes	Non-GC-synesthetes
Dyslexics	283 (2.94%)	827 (5.23%)
Non-dyslexics	9345	14997

Nonetheless, lowering the required accuracy to 85% didn't much change the difference in dyslexia's prevalence rates between groups. Even with the less conservative criteria 3, dyslexia among GC-synesthetes (N=9628) still only accounted for 2.94% (N=283), compared to 5.23% (N=827) among confirmed non-GC-synesthetes (N=15824), X^2 (*df* 1, N=25452) = 75.06, P < .001). When confirmed and unconfirmed non-GC-synesthetes (N=58035) are combined, a dyslexia prevalence rate of 5.18% (N=3006) was found (see Table 6). This difference in prevalence rate was again found to be significant, X^2 (*df* 1, N=67663) = 89.62, P < .001).

Table 6: Number and percentages of dyslexics and non-dyslexics among GC-synesthetes and those who are not GC-synesthetes among participants of the synesthesia battery after both consistency test (<1) criteria and speeded congruency test (accuracy >85% and <2 sec. mean reaction time), considering untested participants as non-GC-synesthetes.

N=67663	GC-synesthetes	Non-GC-synesthetes
Dyslexics	283 (2.94%)	3006 (5.18%)
Non-dyslexics	9345	55029

Lastly, it is unclear whether the speeded congruency test fully prevented cheating. A few possible ways to cheat still come to mind. Firstly, some scored really high on the consistency test, which may also be achieved by choosing complete black or white for all the graphemes. Similarly, it is not clear whether the consistency test required a minimum number of graphemes with a synesthetic color. For instance, it would be easy to pass both tests when only one or two graphemes are reported as having synesthetic colors. Besides the fact this would make it easy to be able to cheat, even if this would be a genuine synesthetic experience, most researchers agree that genuine GC-synesthetes should have synesthetic experiences for the majority of graphemes. In an effort to put up some guidelines when to consider (trained) synesthesia genuine, Colizoli et al. (2014) placed the minimum inducer-bandwidth at >5 inducers as well as the concurrent-bandwidth at >5 concurrents for 36 letters and numbers. That is, someone should at least have a synesthetic experience for more than five different graphemes, as well as have at least more than five different color experiences for the set of 36 graphemes (i.e. different graphemes can sometimes have the same color). It is unclear whether the Synesthesia Battery has put any safeguards into place to prevent such tactics. Furthermore, even with the added average time limit of 2 seconds on the speeded congruency test, there would arguably still be enough time to look up the appropriate response for a given grapheme.

In fact, there are signs that suggest cheating may still have taken place. In an effort to see whether there was a correlation between reported dyslexia and the height of the consistency score, participants were grouped by consistency scores with increments of 0.2 (see Table 7).

GC-consistency score	Self-reported dyslexia	Number of participants	Percentage of reported dyslexia in specific consistency group
< 0.2	No	257	5.17 %
	Yes	14	
0.2 - < 0.4	No	888	2.52 %
	Yes	23	
0.4 - < 0.6	No	2470	3.02 %
	Yes	77	
0.6 - < 0.8	No	2001	2.63 %
	Yes	54	
0.8 - < 1.0	No	868	2.69 %
	Yes	24	

Table 7: Number and percentages of dyslexics among participants of the synesthesia battery after criteria 2 (N=6676) grouped by consistency score of increments of 0.2.

Interestingly, and contrary to expectations, a marked increase in reported dyslexia was found in the group with the highest consistency scores (0 to 0.2). At the same time, reported dyslexia among the other groups (i.e. consistency scores between 0.2 to 0.4, 0.4 to 0.6, etc.) remained fairly constant. Moreover, this sharp increase of reported dyslexia among the highest consistency scoring participants was found both among those who passed the subsequent speeded congruency test (N=271) with 5.17% dyslexics (N=14) as well as those who failed it (N=504) with 6.55% dyslexics (N=33). If these high consistency scores are correct and genuine, the diverging prevalence rates of dyslexia within this highly consistent group cannot easily be accounted for. However, if any of the above-discussed cheating practices took place, they can be expected to result in high consistency scores such as these. Indeed, the prevalence rate of dyslexia among these very high consistency scoring participants closely resembles those found among the (tested and non-tested) participants without GC-synesthesia. While these results obviously do not prove any cheating, a closer inspection of the individual test results from these participants may be in order. While admittedly this is speculation, but should closer inspection indeed find prove of misconduct and (fully) disqualify this group as GC-synesthetes, a dyslexia prevalence rate of only 2.78% (N=178) is found among the remaining verified GCsynesthetes (N=6405), that is those who scored between 0.2 and 1.0 and weren't disqualified by the speeded congruency test. When all the other participants (N=61258) are grouped (i.e. those who answered the

synesthesia in the family question, but either didn't pass consistency test or the speeded congruency test, or scored suspiciously high on the speeded congruency test) a prevalence rate of 5.08% (N=3111) was found.

Despite the reservations mentioned above, the results from the Synesthesia Battery indicate a substantially lower prevalence rate of dyslexia among GC-synesthetes compared to those who are not. Moreover, the dyslexia prevalence rate found among those who were not classified as GC-synesthetes resembles the lower tail end of estimations found in the normal population (e.g. 5-10%, Maughan, 1995; 5-17.5%, Shaywitz & Shaywitz, 2005). Also, criteria to qualify as GC-synesthete were deliberately taken very strict to minimize false positives and exclude possible cheaters. Therefore, it is reasonable to assume those who passed are genuine GC-synesthetes (although with the possible exception of those scoring extremely high on consistency). Most importantly, the Synesthesia Battery provides the largest sample of tested GC-synesthetes asked about dyslexia to date.

4.2.2 Prevalence of dyslexia among Carmichael's data

The second dataset from which the prevalence rate of dyslexia among GC-synesthetes can be obtained comes from a recent study by Carmichael et al. (2015). Armed with a randomly recruited sample from the general population (N=2847), the aim of this study was to validate the 'snapshot' GC-synesthesia tests from Eagleman's Synesthesia Battery against conventional long-term retesting. Moreover, the fact that participants were not self-referred provided a reliable prevalence rate of synesthesia in the general population. Using the same cut-off point as Eagleman et al. (2007) of <1 on consistency scores, Carmichael et al. (2015) found the prevalence of GC-synesthesia (either letters, digits or both) in their sample to be 1.2%. Their results were in line with a prevalence rate of 1.4% (colored letters and digits) or 2% (either letters, digits or both) found in the widely cited prevalence study by Simner et al. (2006). The authors concluded that the Synesthesia Battery is indeed a valid methodology for assessing synesthesia. Unfortunately, the article doesn't mention a prevalence rate of dyslexia among their 2847 participants. However, it was reasonable to suspect that this study also included the survey with the dyslexia question. Therefore, a request to share these results was sent to D. Carmichael (Oct. 23th, 2016). Indeed, their study also included self-report measures regarding the diagnosis of 24 conditions, including dyslexia. Moreover, since their 2015 article, another round of testing was conducted. These new participants were added to the previous 2847 subjects from the Carmichael et al. (2015) article, accumulating to 3893 participants in the study by Simner and Carmichael (2015). Meanwhile, a study by Rothen et al. (2013) concluded that a cut-off score of 1.43 on the Synesthesia Battery was the point at which maximum sensitivity in distinguishing between synesthetes and non-synesthetes was achieved. Indeed, when this more lenient cut-off point was applied in Carmichael et al. (2015) prevalence rates were found to be even more similar to those found with conventional long-term tests and retests by Simner et al. (2006). Therefore, Simner and Carmichael (2015) used both Eagleman's original <1 as well as Rothen's <1.43 cut-off point. The latest data which I received (D. Carmichael, personal communication, 24-10-2016) also uses

52

Rothen et al. (2013) more lenient cut-off point of <1.43. The same cohort was used as in Simner and Carmichael (2015) with the exception of participants who indicated having synesthesia but scoring over 1.43. These were removed from the sample, leaving a total of 3742 participants.

4.2.2.1 Results Carmichael's data

Using the cut-off criteria of <1.43 on Eagleman's Synesthesia Battery, Carmichael found 95 GC-synesthetes and 3647 confirmed non-synesthetes. Interestingly, these new results suggest the prevalence of GCsynesthesia in the general population at 2.5%, more than double compared to the prevalence rate of 1.2% previously found in the Carmichael et al. (2015) study. However, most relevant are the number of participants who self-reported dyslexia in the synesthetic and non-synesthetic population. Contrary to the findings from the Synesthesia Battery, Carmichael and colleagues (D. Carmichael, personal communications, Oct. 24th 2016) actually found the prevalence of dyslexia to be higher among synesthetes compared to non-synesthetes, although the difference was non-significant. In their (extended) study, they found 8.42% (N=8) of the GCsynesthetes (N=95) reported to suffer from dyslexia, compared to 5.68% (N=207) of the non-synesthetes (N=3647) (see Table 8). A Fisher's exact test finds the association between dyslexia and GC-synesthesia not to be significant (p = 0.26).

	<i>,</i> ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	
(N=3742)	GC-synesthetes	Non-synesthetes
	8	207

(8.42%)

87

Table 8: Number and percentages of dyslexics and non-dyslexics among GC-synesthetes and non-synesthetes found in

 Carmichael et al. (unpublished) population.

(5.68%)

3440

4.2.2.2 Discussion Carmichael's data

Unfortunately, the relatively small number of GC-synesthetes in this study restricts making any firm conclusions about the reported prevalence of dyslexia in this group. Among non-synesthetes however, a similar dyslexia prevalence rate was found to those among non-GC-synesthetes in the online Synesthesia Battery (5.08% off all the participants who didn't do the tests or didn't pass Eagleman's criteria). Moreover, among all the participants (N=3742) in Carmichael's study, dyslexia was reported 5.75%. Among all participants of the Synesthesia Battery, the dyslexia prevalence rate was found to be about 5% (numbers varied a little depending on whether any exclusion criteria was used). This finding may suggest that the

Dyslexics

Non-dyslexics

prevalence rates of dyslexia found among the participants of the online Synesthesia Battery are representative for a general population. In other words, the Synesthesia Battery doesn't seem to be particularly biased for or against the participation of dyslexics. It is important to note that Carmichael used a different, more lenient, cut-off criteria than I did on the Synesthesia Battery. It is conceivable that this difference may be responsible for the discrepancy in prevalence rates of dyslexia among synesthetes between the two data sets. In other words, perhaps there may be disproportionately more dyslexics among those who scored between 1 and 1.43 on the consistency test compared to those who scored <1. Also, Carmichael didn't use the speeded congruency test as an additional criterion to distinguish between synesthetes and non-synesthetes as I did on the Synesthesia Battery data. In conclusion, Carmichael (personal communication, 2016) didn't find a significant difference in the prevalence of dyslexia among synesthetes compared to non-synesthetes. However, the discrepancy between these results and those found in the Synesthesia Battery may be driven by the difference in definitional criteria for synesthesia used.

4.2.3 Prevalence of dyslexia in the GNO study

Lastly, recently there was a large Dutch study (GNO) concerning language and perception, specifically how different senses cooperate to make sense of the world and each other. Participation in this study was largely promoted on a popular Dutch science television program (NTR; de Kennis van Nu, 2016) as well as in a popular science magazine (Quest). The study was not specifically introduced as concerning the topics of synesthesia or dyslexia. However, both dyslexics and synesthetes could possibly have recognized it as such. Like the Synesthesia Battery, participants were offered a range of online tests designed to assess the level of cooperation between different senses. Included were tests whether the participant associated colors with either graphemes (i.e. consistency test), days of the week, months of the year, or music and tones, but also whether sounds were associated with meaning or shape. Moreover, participants were also asked about some basic personal details such as age, gender, self-rated level of creativity, native language, level of education and most relevant here, whether he or she suffers from dyslexia. Unfortunately, the results of this study are not published yet. Therefore I contacted Tessa van Leeuwen (Feb. 10th, 2016), one of the instigators of the GNO study, to share some of the preliminary results.

4.2.3.1 Results GNO

So far, the results from 14.979 participants were analyzed (see Table 9). In total, 1128 synesthetes were identified, of which 44 reported to suffer from dyslexia (3.90%). These synesthetes can be further divided into 534 GC-synesthetes (i.e. who scored in the synesthesia range on one or more of the short and/or long tests on letter-color, number-color, or Cyrillic letter-color synesthesia) and 594 synesthetes of other types (i.e. who exhibited other forms of synesthesia but no GC-synesthesia). Among the 534 GC-synesthetes, 18 claimed to

suffer from dyslexia (3.37%). Among the other 594 synesthetes, 27 reported being dyslexics (4.55%). However, the difference in prevalence rates of dyslexia between the two groups of synesthetes (i.e. GC-synesthetes vs. other synesthetes) is not significant (t-test; p = 0.31). Surprisingly, among the remaining non-synesthetic participants (N=13.851), only 419 reported dyslexia (3.03%). When synesthetes of other types are combined with non-synesthetes to form a group of non-GC-synesthetes (N=14445), a chi-squared test with Yates' continuity correction, X² (*df* 1, N = 14979) = 0.059, p = 0.81, also doesn't find a significant difference in the prevalence of dyslexia between GC-synesthetes and non-GC-synesthetes,.

Table 9: Number and percentages of dyslexics and non-dyslexics among synesthetes of all included types, GC-synesthetes, other types of synesthetes, non-synesthetes and non-GC-synesthetes in GNO study.

(N=14979)	synesthetes	GC- synesthetes	Other synesthetes	Non- synesthetes	Non-GC- Synesthetes
Dyslexic	44 (3.90%)	18 (3.37%)	27 (4.55%)	419 (3.03%)	446 (3.09%)
Non-dyslexic	1084	516	567	13432	13999

4.2.3.2 Discussion GNO

Like the results from Carmichael's unpublished study, the preliminary results from the GNO study do not indicate dyslexia to be less prevalent among synesthetes, or GC-synesthetes in particular, compared to non-synesthetes in this cohort. Interestingly, the prevalence of dyslexia among GC-synesthetes in this study (3.37%) is comparable with the one found for GC-synesthetes in the Synesthesia Battery after the consistency test only (3.56%). Like Carmichael et al. (unpublished) the GNO study also didn't further tested participants with a speeded congruency test.

Interestingly, the overall prevalence of self-reported dyslexia in the GNO study was remarkably low compared to the ones found in the Synesthesia Battery and Carmichael et al. (unpublished) study. This may have also caused a minimal difference between the prevalence rate of dyslexia among GC-synesthetes and non-synesthetes. A few potential explanations for this seeming underrepresentation of dyslexics come to mind. Firstly, the study relied on self-referral and not on a random selection of the general population. Although the objectives of the study were not explicitly stated, the way it was promoted didn't make it inconceivable to have a bias for synesthetes and people with strong cross-modal inclinations to respond. This may have resulted in fewer dyslexics if, in fact, it is true that generally, these people are less prone to dyslexia. Also, the study was promoted via popular science media, resulting in an unrepresentative demographic of relatively old and highly educated participants. Both age and educational level could have negatively impacted the

prevalence of dyslexia in the sample. Diagnoses of dyslexia has increased tremendously over the last decades, and is usually diagnosed during struggles in some educational situation. Therefore it is reasonable to assume that older people are less likely to self-report dyslexia in general (i.e. they are less likely to be diagnosed with dyslexia). Dyslexics may also be underrepresented among the highly educated, because their handicap may often hamper attaining a higher education. Thirdly, dyslexia, or the level of inconvenience it causes, may be less prevalent in the Netherlands because of its orthography. We have already seen that the orthography of the language places different challenges on the reading network, which leads to other distributions of different forms of dyslexia from one orthography to the next. Moreover, *self-report* of dyslexia might also be different across countries. In the Dutch school system, there are strict compensation measures for dyslexics. In order to apply for such measures, dyslexia has to be officially diagnosed. Having a thorough system of diagnosing dyslexia might provide a Dutch participant a clearer distinction between regarding herself a poor reader and actually having dyslexia compared to participants from countries in which such systems are not equally well in place.

Finally, there is a discrepancy that needs to be addressed. While van Leeuwen reported 44 dyslexics among all synesthetes, these were later subdivided into 18 dyslexics among GC-synesthetes and 27 among synesthetes of other types. However, 18 plus 27 dyslexics give a total of 45 dyslexics. Although it won't dramatically change the overall results, this means that somewhere down the line one dyslexic synesthete was mistakenly included in both groups.

4.2.4 Overall discussion prevalence dyslexia among synesthetes

In conclusion, the prevalence rates of dyslexia among GC-synesthetes found in the data from the Synesthesia Battery are inconsistent with the preliminary results from studies by Carmichael et al., and the GNO. It is therefore still unclear whether a difference exists in the prevalence rate of dyslexia among GC-synesthetes compared to non-synesthetes. Nevertheless, the fact that dyslexia is still reported among GC-synesthetes suggests it is unlikely the two conditions are at opposite ends of a more general spectral condition. The presence of both conditions in one person raises some intriguing questions worthy of further inquiry. For instance, when such a dyslexic GC-synesthete misidentifies a word while reading, does she also experience the wrong color? Also, are there any differences between 'normal' dyslexics and synesthetic dyslexics in terms of deficits or reading proficiencies? The fact that dyslexic GC-synesthetes do exist either means GC-synesthetes can still develop dyslexia or vice versa, dyslexics are still able to 'get' synesthesias. While there is a multitude of early (pre-reading) markers known for dyslexia, GC-synesthesia is believed to develop only in late childhood (e.g. Simner et al., 2009; Simner & Bain, 2013). It is, therefore, reasonable to believe that the problems of dyslexia are manifested before a notable onset of GC-synesthesia. Hence, while dyslexics may have difficulties making automatic cross-modal connections between grapheme and phoneme domains, some are evidently able to create connections between other domains (e.g. grapheme to color). This means

(at least some) dyslexics are able to acquire the automatic cross-modal connections our remedial method proposes. With that in mind, let us have a look at some instances and studies in which synesthesia was acquired later in life and which methods are currently employed to remediate dyslexia.

5 TRAINING SYNESTHESIA AND THE REMEDIATION OF DYSLEXIA

In this chapter, recent findings on the ability for non-synesthetes to acquire or train synesthetic associations will be discussed. Also, some of the currently most common and effective methods for remediation of dyslexics will be briefly reviewed. The strengths and weaknesses of these methods, as well as their differences compared to a synesthetic training paradigm, will be discussed. Lastly, the differences between this study and a somewhat comparable proposal by Altschuler et al. (2004) will be explored.

5.1 Acquired synesthesia

The third chapter only discussed developmental synesthesia in which synesthetes typically report having the condition for as long as they can remember. However, synesthesia or certain phenomenological and behavioral markers of synesthesia can also be acquired later in adult life. Lasting acquired synesthesias have been documented after sudden brain damage and the use of sensory substitution devices. Also, certain psychedelic drugs have been reported to temporarily induce experiences similar to synesthesias. Moreover, and most concerning for this thesis, there have also been explicit attempts to acquire synesthesias in healthy non-synesthetes by means of hypnosis and training. These different forms of acquired synesthesia will shortly be reviewed.

5.1.1 Synesthesia after brain damage and sensory substitution devices

Sometimes synesthesia is spontaneously acquired after the loss of sensory input due to sensory deprivation or brain damage, or via the use of sensory substitution devices (Ward, 2012). In all these cases, the impaired modality comes to act as the synesthetic concurrent. For instance, visual experiences after the loss of sight can be induced by sound (i.e. auditory-visual synesthesia) or by touch (i.e. touch-vision synesthesia). Reversely, the sensation of touch or pain after the loss of somatosensory input (e.g. due to amputation or paralysis) may be induced by visual observation of touch in the location of the phantom limb (i.e. visual-touch synesthesia). Damage to the peripheral auditory system can lead to tinnitus (phantom sounds), which is believed to be induced by somatosensory inputs (i.e. somatosensory-auditory synesthesia) (Ward, 2012).

Sensory substitution devices have also been reported to induce various synesthetic percepts. For example, tactile sensations to sounds have been reported in deaf people after receiving cochlear implants. Visual sensations have also been reported by blind(folded) people after using a substitutional device which converts the image of a camera to a pixelated array of electrodes worn on the tongue (Bach-y-Rita & Kercel, 2003).

5.1.2 Chemically induced synesthesias

Researches on psychoactive substances has often reported the transient induction of synesthesia. Luke and Terhune (2013) reviewed 35 studies of drug-induced synesthesias, most of which relate to lysergic acid diethylamide (LSD), mescaline, and psilocybin. However, other drugs such as ketamine, ayahuasca, MDMA, but also common drugs such as alcohol, caffeine, tobacco and cannabis have also been implicated in granting synesthetic percepts to the user (Luke & Terhune, 2013). While under the influence of certain drugs, similar forms of synesthesia are reported as in 'genuine' developmental synesthesia, most commonly auditory-visual synesthesia. However, other inducer-concurrent associations which are not known to occur in synesthetes have also been documented. There is strong evidence suggesting serotonin agonists in particular are responsible for the elicitation of synesthesias. Drugs which are serotonin agonists have a higher prevalence rate of reported synesthesias compared to drugs which are not. Moreover, serotonin agonists are also known to enhance existing synesthesias. While genuine and drug induced synesthesias are in a lot of respects very different (see for a comparison; Sinke et al., 2012a), both may involve serotonergic hyperactivity as a potential factor (Brogaard, 2013). Brang and Ramachandran (2008) also implicated serotonin S2a receptors in synesthesias. If so, this also means that there might be pharmacological ways to assist the acquisition of synesthesia, for instance by microdosing LSD during training sessions. Of course, there are major legal and ethical objections to this, especially when dealing with children. Nevertheless, it is an interesting scientific hypothesis which may provide valuable insights as to the neurochemical development of synesthesia.

5.1.3 Posthypnotic suggestion

Using posthypnotic suggestions, Cohen Kadosh and colleges (2009) managed to induce abnormal cross-modal experiences in non-synesthetes similar to those reported in GC-synesthetes. It is suggested that hypnosis can affect levels of inhibition. For instance, it has been shown that hypnosis can alter color perception and brain activation via modulation of hV4 (Kosslyn et al., 2000). In their study, Cohen Kadosh et al. (2009) hypnotized a group of non-synesthetes to associate digits with colors. This association served as a posthypnotic suggestion during a subsequent digit detection task. During this task, participants were instructed to identify a black digit with either a congruent or incongruent colored background. Synesthetes are known to have a longer reaction time and make more errors when the background has the same color as the associated color for that digit or letter. Likewise, participants who received the post-hypnotic suggestion showed significantly more errors than controls when the digit was displayed on the congruent background. It is important to note that during this task the participants are fully awake (not hypnotized) and they are not aware of the previously learned associations during hypnosis. Also, phenomenological reports by participants who received the post-hypnotic suggestion, such as seeing license plates in the associated colors, matched those of genuine synesthetes. This study challenges the idea synesthesia is caused by extra structural connectivity, or at least

that it is a sine-qua-non condition. Moreover, these results further indicate synesthesia can be acquired later in life, at least for highly suggestible people.

5.1.4 Training synesthesia

Recently there has been an upsurge in research whether synesthesia can also be acquired through training in healthy non-synesthetes. To be able to answer this question it is important to firstly define a working definition of genuine synesthesia. For instance, while chemically induced synesthetic experiences can bear strong resemblances with those of genuine synesthetes, psychedelic drugs don't turn a non-synesthete into a genuine synesthete. In a comprehensive literature review on developmental aspects of synesthesia and specific training procedures in non-synesthetes, Rothen and Meier (2014) set a few criteria any trained synesthesia should adhere to in order to be considered genuine synesthesia. To consider the trained synesthesia to be genuine, trained inducers would have to (1) consistently and (2) automatically elicit (3) the associated concurrent experience with perceptual qualities on a subjective phenomenological basis (4) for the great majority of the inducers' occurrences (5) over an extended time period. This conservative approach would exclude chemically induced synesthesia as well as know-associator synesthetes, who do not report subjective phenomenological color experiences.

However, it is important to note that although genuine synesthesia may be an outcome of the here proposed synesthetic training for dyslexics, it is not the purpose of this training. As Rothen and Meier (2014, p. 3) also state; "As there is evidence that synaesthesia is associated with cognitive benefits, and cognitive training can lead to transfer effects, it is a promising avenue for future research to investigate transfer effects of synaesthesia training." It is certainly informative for the field of synesthesia research to examine if participants eventually develop (genuine) synesthesia or any behavioral or physiological markers of the condition such as a synesthetic Stroop effect. Also, scores on acquired synesthetic traits should be measured to see if they correlate with changes in reading skills. However, the main purpose is to make dyslexics read faster, not to make them synesthetes per sé. That said, let us have a closer look at what synesthetic training studies have found.

Altogether, Rothen and Meier (2014) reviewed seven synesthesia training studies (i.e. Kelly, 1934; Howells, 1944; Meier & Rothen, 2009; Rothen et al., 2011; Rothen et al., 2013; Colizoli 2012; Kusnir & Thut, 2012; Cohen Kadosh et al., 2005; Nunn et al., 2002; Brang et al., 2011; Niccolai et al., 2012, see Rothen & Meier, 2014), but did not yet included the study by Bor et al. (2014) which will be discussed separately. The included studies variously differed in the type of trained synesthesia, used training method, number of trials, ratio of congruent versus incongruent trials and which tests were administered. The most relevant studies will be discussed in a nutshell, but for a complete overview of the details and results, I'll refer to the original review.

During a grapheme-color training study by Meier and Rothen (2009), participants were firstly trained to learn four letter-color associations. Then, participants had to indicate whether a displayed letter was shown in its correct color, following feedback if correct or not. Using this training method, Meier and Rothen (2009) managed to create automatic letter-color associations, as measured by a synesthetic Stroop task. In contrast to what is found before in genuine synesthetes, however, they did not find a synesthetic conditioning effect, nor any subjective phenomenological reports of associated color experiences, thus the effects cannot be regarded as synesthesia. Most importantly, it showed that a synesthetic Stroop effect alone is not enough as a diagnostic tool for synesthesia.

In a follow-up study (Rothen et al., 2011), the same training (i.e. non-adaptive) by Meier and Rothen (2009) was compared with an adaptive training procedure in which (i) participants had to indicate which color was associated with a black digit by pressing one of four keys, and (ii) had to judge whether the brightness of the digit in its correct associated hue was lighter or darker than the originally learned color. Again, both tasks were directly followed by feedback on results. Before and after this training, two synesthetic priming tasks were administered. In the first task, participants were required to indicate a target color, while in the second task a digit. The target color/digit was preceded by either congruent or incongruent digits/colors with the target. Rothen et al. (2011) found on average a larger priming effect with the adaptive training group, which suggests adaptive training to be more effective in creating automatic digit-color associations than non-adaptive training. Unfortunately, like Meier and Rothen (2009), no synesthetic experiences were reported after training.

A study by Colizoli et al. (2012) took a very different and original approach in order to train letter-color associations. Here 15 participants were asked to read books in which four different letters (a, e, s, and t) were consistently colored (red, orange, green, and blue). Moreover, participants were encouraged to use a web applet which colored these letters on Internet pages inside their browser. An advantage of this method is that participants could 'learn' these associations at their own pace and time and were not confined to a lab or boring repetitive tasks. As a result, participants were able to read 105.660 words on average over a time span of 2-4 weeks. Moreover, participants were only exposed to 'correct' associations, whereas in other training procedures the ratio of correct versus incorrect associations was much lower. Why this might be an important factor is discussed later. Participants showed a significant Stroop effect after training. Also, the Stroop effect was stronger for lower case letters than for upper case letters which appeared less frequent. A near significant correlation was also found between the rating of the statement "I am experiencing color when thinking about certain letters" and the magnitude of the Stroop effect. Colizoli et al. (2012) did not find any difference in performance on a perceptual crowding test. To conclude, like the previous studies, this particular training was able to induce automatic letter-color associations but not any of the perceptual aspects of synesthesia.

Kusnir and Thut (2012) tried to recreate the natural conditions in which GC-synesthetes may learn their associations in real life by manipulating the probabilities of encountering certain letter-color pairings. Their

study used a learning paradigm in non-synesthetes designed to implicitly train letter-color associations via a visual search task that employed statistical probability of encountering specific letter-color pairs. In short, participants had to indicate whether one of three specific letters were present in a circular array of six differently colored letters. Two of the target letters were shown 5 out of 6 times in a specific color, while the other letter wasn't. In a second experiment, they manipulated the target letters to be either opponent colors for half of the participants or non-opponent colors for the other half. The strength of letter-color associations was deduced by tracking differences in search performance between letters displayed in congruent colors compared to incongruent colors (i.e. color of the other color associated target letter). They found participants showed significant learning of specific letter-color associations (i.e. letter-color binding) in both experiments, with congruent letter-color pairings facilitating target detection while incongruent letter-color pairings impaired target detection. Moreover, compared to the non-opponent color condition, Kusnir and Thut reported greater interference for incongruent targets when opponent colors were used. It has been suggested that this "opponent-color effect", also reported in genuine synesthetes, can be seen as evidence for early stages in the visual processing of synesthetic colors (Nikolíc et al., 2007, in: Rothen & Meier 2014). Kusnir and Thut (2012) also suggest that their findings indicate that the letter-color associations were formed on a perceptual rather than a conceptual level and did not result from cognitive strategies. However, their training failed to lead to any conscious synesthetic experiences.

So far the above training studies have both failed to elicit synesthetic conditioned responses as well as any subjective reports indicative of synesthetic phenomenology. Bor et al. (2014) suggested that this might be because they lacked certain key components by which natural synesthesia develops. For instance, most previous training studies had limited training durations, failed to adapt task difficulty to improving performance, used arbitrary associations and were likely unable to sustain motivation during repetitive training tasks. Bor et al. (2014) therefore extended training time significantly, employed a range of measures to increase motivation (e.g. use of adaptive tasks), and used the most common letter-color associations found in synesthetic and normal populations. After 9 weeks of training 13 specific letter-color associations, Bor et al. (2014) showed participants passed a range of tests designed to demonstrate genuine synesthesia, such as color consistency tests, synesthetic Stroop tasks, and classical conditioning tests. Most importantly, the majority of participants indicated very similar phenomenological experiences for achromatic letters as genuine GC-synesthetes do. Moreover, letter-color associations with a strong semantic component (e.g. R \rightarrow red) induced particularly strong synesthesia-like behaviors on tests and subjective reports. This suggests conceptual associations are a major driving factor in the development of GC-synesthesia. Bor et al. also entertained the idea that early learning pressures (e.g. letters and digits) may lead to the formation of various semantic hooks (e.g. color associations). These semantic hooks aid memory and may then fossilize into synesthetic traits (Bor et al., 2014).

The above examples and studies show that many of the behavioral and physiological markers of synesthesia can relatively easily be acquired later in life. However, no training study has yet managed to 'convert' someone into a genuine synesthete. Still, Bor et al. (2014) argued, and perhaps till a certain degree showed, that this may have been more due to the limited duration and design of these studies than some inert quality developmental synesthetes may possess. Indeed, when Bor et al. (2014) made efforts to incorporate factors which govern the natural development of synesthesia in their training regime, most of the participants started to experience synesthetic percepts.

5.2 Remediation of dyslexia

This thesis proposes an alternative remedial method for dyslexia based on synesthesia training. However, what kind of remedial methods are currently offered to children with dyslexia and what are their results? Most importantly, why would a synesthetic training be a more effective replacement or a viable addition to those traditional methods? There is a huge market for the remediation of dyslexia. Ranging from self-help books, electronic reading aids to tutor assisted remediation in schools. There are scores of different remedial methods and reviewing all of these in depth is beyond the scope of this thesis. It is important to note that it is very hard to compare the effectiveness of remediation methods because there are so many contributing variables. Factors that may influence effectiveness and/or make it hard to compare one study to the next are: different languages (e.g. shallow versus deep orthographies; alphabetic versus logographic), measures of different reading ability skills (e.g. word and non-word reading accuracy/fluency, comprehension etc.), age of participants (e.g. pre-reading children up to adults), for varying periods of time (e.g. training time/intensity; short-term or long-term improvements), and via different media (e.g. computer-based intervention or with a personal tutor). All these variables may impact the responsiveness to a given intervention.

Most remedial efforts revolve around the central idea that dyslexics experience profound difficulties in decoding graphemes to phonemes and ineffective phonological processing is a core deficit underlying dyslexia. In order to strengthen that deficit, many interventions employ phonics (training letter-sound rules) or phonologically based training (e.g. phonological awareness training).

A review of phonics training for English-speaking poor readers by McArthur et al. (2012) suggested phonics training may be effective for improving some reading skills but not others. In their meta-analysis of 11 studies, phonics training seemed to have a large effect on nonword reading accuracy, a moderate effect on word reading accuracy, and a small-to-moderate effect on letter-sound knowledge. Phonics training may also have a small or moderate effect on word reading fluency, spelling, phonological output, and reading comprehension, but the authors concluded these results may have been found due to chance (McArthur et al., 2012).

According to Eden et al. (2004) studies have demonstrated that teaching children the principles of phonological awareness can raise scores on multiple measures of reading ability and is the most effective treatment for dyslexia. Moreover, the reading improvement of children receiving phonologically based interventions was associated with the normalization of previously underactivated left hemisphere regions (Eden et al., 2004). Nevertheless, while studies have shown phonologically based training may significantly increase reading accuracy, word reading fluency and comprehension are relatively unaffected by this type of training (Snellings et al., 2009). Indeed, Scheltinga et al. (2010) also confirm that word reading fluency skills of poor readers are hard to remediate. It may be important to note again that the effectiveness of a given intervention method might vary for different native orthographies. English-speaking dyslexics may benefit more from phonologically based interventions than Dutch dyslexics may do.

The structured, multisensory phonological intervention Eden et al. (2004) employed may in some aspects come close to the intervention this thesis proposes. Besides training in sound awareness (i.e. phonological awareness) and the establishment of rules for letter-sound organization (i.e. phonics), this intervention technique also includes sensory stimulation, articulatory feedback and imagery strategies to visualize and manipulate letters and words. What these additional techniques seem to have in common with a synesthetic intervention is that they address other distal modalities in order to bypass the original deficits.

5.3 Has synesthetic training ever been proposed for dyslexics?

The use of synesthetic training to improve certain cognitive functions isn't completely new. For instance, Rothen and Meier (2014) mention synesthetic training courses are offered to improve creativity and memory, and it has even been suggested as a form of psychotherapy. In like manner, using colored letters as a remedial tool for dyslexics has already been proposed in a rather obscure paper by Altschuler et al. (2006). Here the authors suggest to color certain letter pairs which are commonly confusing for dyslexics (e.g. b/d, and p/q/g), with their Stroop concordant color. For instance, 'b' could be colored in blue, 'p' in purple, and 'g' in green. These letter/color combinations take advantage of the strong, natural, unconscious association with the visual sight of a color and its name, better known as the Stroop effect. The mere sight of the color would therefore automatically raise the first letter of that color name. While Altschuler et al. (2006) suggest any association might hypothetically work, using natural associations would be a more effective approach. Interestingly, no reference to synesthesia was made in this paper. The absence of this connection is even more remarkable considering one of the authors is V.S. Ramachandran, perhaps one of the scientists most responsible of re-popularizing the field of synesthesia five years earlier (i.e. Ramachandran & Hubbard, 2001a; 2001b).

While the essence of Altschuler et al. (2006) proposed method is similar as to the one this thesis proposes, there are also some notable differences. Firstly, their underlying presumption as to what some of the barriers

of dyslexia differ. Altschuler et al. (2006) seem to suggest that dyslexia is, at least partly, caused by a visual ambiguity of certain letters. Adding an additional visual attribute (i.e. color) to these letters supposedly resolves this confusion. While the authors are correct in that this particular problem does exist among dyslexics, the problems and causes of dyslexia are unfortunately much more numerous and complicated than just some visual confusion between a couple of letters.

Moreover, they suggest these letters have to be constantly colored to be effective, not just for a training period. The increasing digitalization of reading material does make this option more possible than ever before. In fact, a rather similar program called TiB ("Taal in Blokjes") reader is already available on the market (www.taalinblokjes.nl/taal-in-blokjes-reader/). TiB reader is a digital application which uses word recognition software to color code different classes of letter information, such as long and short vowels, into contrasting colored blocks. Although these tools may be helpful when applicable, the reading problem remains when confronted with (uncolored) letters ubiquitous in our society. Many texts, such as movie subtitles at the cinema, are for the enjoyment of a general audience and won't be converted by the hands of a color scheme, let alone a personal one. Besides this practical problem, Altschuler et al. (2006) proposal addresses only the external world and doesn't relieve dyslexics' internal confusion. Thus, while this method may be helpful, it likely isn't really solving any root problems within dyslexics.

Furthermore, while Altschuler et al. (2006) propose to use 'natural' associations, they don't further elaborate as to which associations may constitute as 'natural', besides Stroop concordant colors. In fact, there are arguably not enough workable Stroop concordant colors to cover the whole alphabet. For instance, according to an extensive list of English color names (en.wikipedia.org/wiki/List_of_colors:_N-Z, accessed May 19th 2017) the only single word color names starting with a 'q' or 'x' are 'quartz' and 'xanadu' respectively. It is unlikely that these names elicit a Stroop effect when colored into concordant versus discordant colors. It may indeed be preferable to use a scheme of 'natural' color associations for letters. However, what constitutes as natural might be very personal. For synesthetes, their grapheme-color associations undoubtedly feel natural. Therefore, it might be very useful to look at how synesthetes develop their color scheme. Overall, there are certain trends apparent which are almost certainly influenced by color names. For instance, three studies respectively found the 'R' elicited red in 30%, 36% and 38% of the synesthetes and the color yellow for 'Y' in 50%, 45% and 42% of the synesthetes (Barnett et al., 2008a; Rich et al., 2005; Simner et al., 2005). However, many variables and environmental factors exist besides color names which may influence someone's natural color associations. Like the development of grapheme-color associations in synesthetes, a natural and effective color scheme for dyslexics would similarly depend on initial personal preferences with the ability to make regular adjustments. By being able to regularly adjust the used color scheme to current personal preferences, the variability of associated colors should be expected to decline and eventually converge to fixed colors due to the bootstrapping mechanism of being exposed to these associations. Moreover, like the

number of grapheme-color pairings in synesthetes increases over time, so too should the color schemes for dyslexics start simple to be able to grow and evolve into a full personal idiosyncratic system.

6 PROPOSED STUDY METHODS

In this chapter a few recommendations will be made in order to test the proposed intervention. These include matters concerning which participants and controls to use, which tests and measures to assess, and important aspects regarding the training material.

6.1 Participants

While there are sound reasons to believe synesthetic training would be most beneficial and effective for dyslexic children, dyslexic adults may also profit from this remedial technique. To find and test dyslexic adults is far easier. Also, reading skills have mostly stabilized in dyslexic adults. A study in synesthetic training in adult dyslexics doesn't have to control for normal developmental progress or ongoing convention remediation such as provided by schools. Therefore, any progress can directly be attributed to the intervention. For instance, a synesthetic training study in adults dyslexics can get straight to testing the effect which reading with consistently colored letters has on general reading skills. This makes testing the proposed remediation in adult dyslexics considerably less complicated and any evidence of a potential effect more robust. Therefore, a small pilot study in dyslexic adults should be considered as a practical and exploratory start of inquiry into the potential benefits of synesthetic training. Positive results in dyslexic adults would certainly justify a more extended inquiry of this intervention in children. If it works in adults, it can also be expected to work in children. Unfortunately, the other scenario is less telling. That is, if synesthetic training in dyslexic adults turns out to be ineffective, there are still reasons to suspect children could respond differently to the intervention. Therefore, synesthetic training as an intervention for dyslexia should foremost be studied in children.

6.2 Age of children

The age of the child participants must also be further specified. Considering the plasticity of their brains, the urgency of their problem and the developmental timeline of synesthesia and dyslexia, synesthetic intervention can expect to be most effective in children just starting reading acquisition. Most preferably the intervention starts even before the problems of dyslexia are apparent. In the Dutch school system, reading acquisition starts in the third grade, typically at age 6-7 years old, although by then many children are already familiar with many of the letters of the alphabet. Unfortunately, at this age, it might be hard to identify those prone to develop dyslexia. One way to start intervention before the onset of reading problems becomes apparent is to target children with a familial risk for dyslexia. That is, children with at least one parent affected with dyslexia. The percentage which, despite the intervention, still develop dyslexia could then be compared to either those who didn't follow an intervention or those following an alternative intervention program.

However, this would require a substantially large group in order to reach statistical significance. Moreover, this would take some years before the effect of the intervention might become apparent.

On the other hand, treating older children (say age 9 or older) in which reading problems have become apparent, tenacious and severe might also be problematic. The developmental timeline of synesthesia (Simner et al., 2009; Simner & Bain, 2013) suggests there might be a narrow window of opportunity during which the brain starts to form cross-modal associations as an aid in reading. Once an initial association is made, it will bootstrap itself, making it harder and harder for other associations to get same immediate holding. In other words, there might be a critical period for these alternative routes of cognition to form in order to become part of the default years later (and perhaps to reach their perceptual quality). Future studies may want to investigate whether such crucial period is likely or not.

The most practical period in which synesthetic training should commence therefore lies after reading problems are beginning to become apparent, but before classic grapheme-phoneme associations have become ingrained as the default. A preferable age group for potential subjects would therefore be around the end of the third grade, or around 7 years old. At this age or stage, parents and teachers are likely to be able to detect with some confidence who has difficulties with reading, despite normal intelligence and proper training. Moreover, by then children will have some of the basic skills needed to test and compare the effectiveness of the remediation later on.

6.3 Control group

In order to find out whether synesthetic training is effective, it is necessary to compare the development of reading skills of the synesthetic training group to a control group of comparable size, skills, age, gender, and IQ. However, what remediation program will the control group follow? There are several options:

- 1) Controls do not follow any intervention program or additional help.
- 2) Controls, but not the synesthetic training group, follow 'normal' intervention (i.e. phonics) provided by their school.
- 3) While both groups follow 'normal' intervention provided by their school, only the training group additionally follows synesthesia training.
- 4) Besides following conventional remediation, both groups will be confronted with colored letters in reading material. However, the synesthetic training group is presented with (idiosyncratic) consistent associations, while the grapheme-color associations are kept random for the control group.

The first option wouldn't be right for two reasons. Firstly, similar to a placebo pill, just providing *an* intervention, no matter what kind, already has an effect which should be controlled for (i.e. the Hawthorne-effect). Secondly, it would not be ethically sound to withhold any help to the children in the control group,

knowing they experience difficulties which should and can to a great extent be addressed with conventional remediation. The second option would provide a clear comparison between two remedial methods. However, since the validity of synesthetic training isn't yet assessed, we might withhold children in the test cohort from valuable and irreplaceable conventional remediation without providing a proven alternative. Therefore, this option should only be considered when there is strong evidence synesthetic training is also effective. The third option wouldn't exclude any children from missing conventional remediation but doesn't control for getting additional training either. The fourth option controls for providing additional training but doesn't withhold valuable conventional training either. Moreover, this option also separates the effect of imposing consistent grapheme-color associations from any potential effect of just reading with colored letters. Therefore, the fourth option seems the most preferable. A matter of concern might be that conventional remediation might disrupt the effectiveness of synesthetic training. Conventional remediation might prioritize grapheme-phoneme over grapheme-color associations and make the latter less effective.

6.4 Tests

As mentioned above, all participants should be tested on a number of measures. Firstly, in order to control for third-factor explanations of group differences, the following independent factors should be assessed:

- Age
- Gender
- Handedness
- Native language
- General non-verbal intelligence (Raven's Standard Progressive Matrices; Raven et al., 1998)
- Receptive vocabulary (Revised Amsterdam Child Intelligence Test (RAKIT); Bleichrodt et al., 1988)
- Also, subjects diagnosed with other relevant physical, neurological, or behavioral conditions, such as poor eyesight, tumors and strokes, or ADHD, should be excluded.
- Presence of one or multiple forms of synesthesia should be assessed before and after the intervention. This can be done with Eagleman's online Synesthesia Battery (Eagleman, 2007). As a reference point, a grapheme-color consistency test should be administered before the start of the intervention.

Other optional tests should also be considered. For instance:

• A personality test (c.f. Rouw & Scholte, 2016) might reveal whether certain personalities are more or less responsive to the intervention, or whether certain personalities are more likely to experience synesthetic percepts due to the training.

• Similarly, scores on a VVIQ test (Vividness of Visual Imagery Questionaire; Marks, 1973) may show to be predictive of certain outcomes of the study (e.g. Barnett & Newell, 2008).

The dependent variables most concerning are reading speed and comprehension. The Three Minute Test (Verhoeven, 1995) is designed to assess the fluency of (correct) word reading. Other reading-related cognitive skills should also be assessed in order to get a better understanding of which specific skills may be affected by the intervention. The following relevant tests are listed in van Otterloo et al. (2009a) and further described in Blomert and Vaessen (2009).

- Reading fluency: the number of correct words and pseudowords read aloud in 90 seconds, expressed in average speed per correct item in milliseconds.
- Phonological Awareness 1 (PA-blend): blend an incomplete number of verbally presented phonemes or phoneme strings into a word.
- Phonological Awareness 2 (PA-phon.del.): delete a phoneme from an auditory presented pseudoword and pronounce the resulting pseudoword (e.g. 'dauk' minus/d/).
- Phonological Lexical Processing (PLP, access/retrieval): correctly pronounce a perceived auditory presented word in which parts were deleted.
- Phonological Working Memory (PWM): repeat a sequence of auditory presented items in the same order: words in kindergarten and speech sounds and syllables in first grade.
- Letter Knowledge (LK): correctly name or sound out visually presented letters.
- Letter-Speech Sound Identification (LSSI): correctly match an auditory speech sound to one out of four visually presented letters.
- Letter-Speech Sound Discrimination (LSSD): make a same/different decision for congruent and incongruent letter-speech sound pairs.

Additionally, a test in Rapid Automatized Naming (RAN) should also be considered. Dandache et al. (2014) assessed rapid serial naming for five familiar colors, objects, numbers and letters. Typically, the child is instructed to read the symbols as fast and accurately as possible.

Aside from reading-related tests, certain synesthesia related measures should also be assessed. The following relevant measures are described in further detail in Bor et al. (2014):

- A color-naming Stroop task
- Synesthetic Stroop task
- Color consistency test
- Synesthetic conditioning

Besides these cognitive skill measures, various brain imaging before and after remediation are highly desirable. Unfortunately, these are costly and cumbersome compared to the above cognitive tests. In the end, the goal is to help dyslexic children read better and faster. No brain imaging technique directly assesses this. Therefore, brain imaging is not imperative for the primary reason of the study. However, if synesthetic training turns out to be an effective remediation method, brain imaging may show which functional and/or anatomical changes in the brain are correlated with the intervention, reading skills and possibly the development of synesthesia.

6.5 Duration

Admittedly, the time or amount of training needed for any potential results to reveal themselves is unknown since nothing similar like this has been studied before. Previous synesthesia training studies in adults (e.g. Bor et al., 2014) may indicate when certain synesthesia-like behavioral effects are expected to occur, but there is no strong reason to expect this to relate to other cognitive skills such as reading. However, simple intermediate tests (e.g. three-minute test) may provide some guidance during the study whether to continue or not. The amount of training can be measured in either time (e.g. one school year) or in the number of grapheme-color associations presented (i.e. amount of letters or words read) like in the study of Colizoli et al. (2016). Both time and exposure may be independent contributing factors.

6.6 Training materials

Essentially, the training material consists of colored letters. This may include colored alphabets, colored books (e.g. Colizoli et al., 2012; 2016), and an application which appropriately colors letters in ebooks and web pages (e.g. Colizoli et al., 2012; 2016; also TiB reader). While this seems very straightforward, the question remains which specific grapheme-color pairings will be trained. In other words, who should determine which color a certain grapheme should have? Is it wise to force a pre-made grapheme-color scheme or should the participant device their own idiosyncratic scheme?

A few aspects should be considered when catering a prefabricated grapheme-color scheme. The graphemecolor associations of both synesthetes and non-synesthetes (forced-choice and free choice associations) are not random and to a certain extent overlap. For instance, both are influenced by linguistic priming (e.g. G=Green, B=Brown, R=Red), although this mechanism was more dominant in non-synesthetes (Simner et al., 2005). However, Simner et al. (2005) also showed that the underlying principles responsible for the eventual choice of associations seem to differ for both populations. For instance, synesthetes tend to pair highfrequency graphemes with high-frequency color names. Moreover, synesthetes are also sensitive to the order in which colors are introduced into the human language (i.e. The Berlin and Kay typology). Therefore, synesthetes tend to associate high-frequency graphemes with the more fundamental color distinctions. The pairings non-synesthetes tended to make were to a certain extent driven by the sequential ordering of materials (i.e. A, B, C, etc.) and the ease of generating colors on demand (i.e. Battig and Montague norms). Simner et al. (2005) also found synesthetes used a significantly broader and more detailed set of color terms. These results suggest that when our participants devise their own idiosyncratic scheme from the beginning, they might end up with a scheme based on factors other than those by synesthetes. Whether this matters in terms of the intervention and/or the development of synesthesia is unclear. Considering this thesis assumes synesthesia to be a cognitive tool to aid reading acquisition, the underlying rules which drive the development of synesthesia may be more vital to that cause than the eventual outcome (i.e. synesthesia). Therefore, it is desirable to emulate the principles governing the development of synesthesia as closely as possible. For that reason, an initial grapheme-color scheme should be based on regularities observed in synesthetes.

On the other hand, to start with a full, predetermined grapheme-color alphabet without the possibility of any personal changes does not reflect the natural development of synesthetic association either. The development of synesthesia is an idiosyncratic and protracted trajectory (Simner et al., 2009; Simner & Bain, 2013). That is, grapheme-color associations become more numerous and increasingly fixed over time. During this period a personal scheme forms. Therefore, the presented grapheme-colors pairings in the training material should also grow in number and change over time. Unfortunately, this poses a practical problem. To regularly adjust grapheme-color pairings to a personalized scheme isn't a problem for digital reading material in which only some coding needs to be updated. However, physical materials such as books and alphabets are less easily adjusted according to new preferences in grapheme-color pairings. Therefore, the initial training material may consist of physical reading material. However, as soon as a personal scheme develops training material may largely consist of digital content.

In order for synesthetic training to resemble the natural development of synesthesia, the following recommendations may be considered regarding the training material:

- Associations should follow some of the driving factors which determine the regularities seen in synesthetes. In order to 'jump start' this process, (some) grapheme-color associations should initially be provided and not yet determined by participant themselves.
- These initial pairings should be based on general trends seen in the synesthetic population. Colors can be attributed probabilistically according to the frequency distribution of colors for a certain grapheme. This means a certain grapheme may be presented in various colors before a personal preference is properly determined. For example, 70% of GC-synesthetes may associate the letter 'A' with a red color, followed by 10% yellow, 8% white, 5% green, etc. Then, 70% of all the A's in the initial training material should be colored red, 10% colored in yellow, etc. However, in order not to make it too incongruently, it should be considered to use only the two or three most picked colors with
corrected probability. In the example of the letter 'A' this would be 80% red, 11% yellow and 9% white.

- The number of grapheme-color associations should increase over time. Therefore, participants should start with a few colored graphemes and grow their scheme from there. Graphemes with the least distributed associated colors should be considered first. That is, starting with the graphemes which a significant amount of synesthetes experience the same color. For example, a significant number of synesthetes associates the letter 'A' with the color red, while there is no significant agreement for the letter 'K'.
- The colors of graphemes are influenced by the linguistic environment, such as grapheme frequency and color names (Simner et al., 2005). Therefore, the participant's native language should be considered when training material is based on the above-mentioned trends of synesthetes. Dutch and English are similar in many respects. Both share the same ordinal alphabet (although Dutch officially has the letter ' ij') and most color names start with the same letter (e.g. Red/Rood, Blue/Blauw, Green/Groen). However, there are also differences which may have an effect on grapheme-color pairings. For instance, in English the letter 'Y' is often associated with yellow because of the color name. In Dutch, the color name yellow is 'geel'. Therefore, the 'Y' is not often associated with yellow for Dutch synesthetes. Also, grapheme frequencies of both languages differ. This means that Dutch training material should be based on grapheme-color regularities observed in Dutch synesthetes.
- Moreover, the specific grapheme-color pairings (e.g. A=Red) in the training material should also vary slightly in presented color (e.g. different shades of red). During the course of the intervention, colors may become more fixed according to regularly adjusted personal preferences. Firstly in general color (i.e. A= red/yellow/white → A= red) and later in a more specific color (e.g. A=scarlet red). This process may allow for more color subtleties to develop; multiple letters may start with one basic color but diverge over time (e.g. A/K/R= red → A= scarlet red, K= firetruck red, and R= wine red).
- A grapheme-color consistency test should be regularly administered for two reasons. Firstly, to adjust the colors presented in training material to these updated preferences. Secondly, to study and monitor whether associated colors actually gain in number and consistency.
- The method to adjust the color scheme is an obstacle which admittedly this thesis only has some considerations for. Adjusting the color of presented graphemes in the training material should be based on the outcomes on the grapheme-color consistency test. Typically, during a grapheme-color consistency test participants are asked three times to select a color for a grapheme. However, it wouldn't be sensible to simply change the presented color for a grapheme by taking the average of euclidean distance in CIELUV color space (e.g. Bor et al., 2014) for that grapheme. If the associated

colors for a grapheme aren't (yet) consistent, then the adjustment would be a color the participant never agreed with. This could partly be resolved by taking the average of two out of three 'most similar colors' in terms of CIELUV disparity. However, the same problem remains when even those two are very different. Therefore, perhaps adjustments should only be made when a participant has a fairly consistent score for a grapheme. Moreover, in the beginning, a grapheme has a probabilistic chance of being one color or another. It would make sense to adjust this probability according to answers on the consistency test, even if the answers aren't all that consistent. For example, the 'A' starts with an 80% probability of being red and 20% of being yellow. If a participant indicates 'red', 'yellow', and 'yellow' for 'A' on the consistency test, it would be reasonable to increase the probability of encountering a yellow 'A'. However, what if the participant would have indicated 'red', 'red', and 'yellow'? On the one hand, the ratio of yellow is still higher (i.e. 33%) than the ratio of yellow A's in the training material. On the other hand, personal preference is clearly skewed to a red A.

With these guidelines, synesthetic pairings may be steered into a natural and idiosyncratic scheme and may best reflect the normal development of synesthesia. Also, two other recommendations unrelated to the training material are:

- To avoid exposure to incongruent associations, colored reading material (e.g. books with colored letters) other than provided by the intervention should be avoided as much as possible. Nevertheless, insofar it cannot be avoided, it is good to realize that in congenial synesthetes this occasional incongruency also did not prohibit the development of synesthesia.
- Besides exposure to colored letters, children should be taught a wide variety of color terms. Again, • GC-synesthetes use a significantly broader and more detailed set of color terms to describe their color associations (Simner et al., 2005). They also have a superior color working memory (Terhune et al., 2013) and are better at color discrimination compared to non-synesthetes (McCarthy & Caplovitz, 2014). These effects may be caused by synesthesia. However, a feedback mechanism might also be at play. Color knowledge influences color perception, which in turn may influence synesthetic perception. Having a unique label (name or concept) for a color has an effect on the perception of that color. For instance, the language of the Himba tribe in Namibia doesn't have a separate word for the color blue. They have no linguistic distinction between green and blue. Indeed, they find it difficult to discriminate a blue square among an array of identical green ones (Goldstein et al., 2009). For most of us this is a no-brainer: the blue square just pops out. Interestingly, the Himba have more distinctive color names for different shades of green. Reversely, they are able to discriminate a slightly different green square among an array of green squares, while most of us do not perceive any difference. For this reason, knowing more distinctive color labels may help building up a more subtle and diverse color scheme.

7 SUMMARY AND CONCLUSION

A lot of information has been given on the topics of dyslexia and synesthesia. In order to better understand why synesthetic training might benefit dyslexic children, it might be helpful to begin this summary with a short recap of the underlying problem of dyslexia. The second chapter discussed how our brain is not specifically evolved for reading and learning to read implies massive changes of the brain. Brains are differently susceptible to a variety of strategies in dealing with these rather novel demands, such as the ability to create and automate certain cross-modal representations and not others, as well as the ability to reassign parts of the brain to process written script. Differences in exposure and educational methods will foster different strategies the brain may utilize in order to make sense of the data. In the course of literacy acquisition dyslexics partly fail to employ otherwise successful strategies of dealing with script and fail to develop an efficient reading network in the brain. The inability to form an efficient reading network seems to a certain extent due to genetic predispositions. In people prone to be dyslexics parts of the reading network and connections between them respond and develop differently to traditional strategies of learning to read. It seems the *explicit* strategies our education utilizes, which mainly entails the conversion and automation of graphemes to phonemes, isn't a viable *implicit* strategy for this subset of brains, resulting in the development of dyslexia. In other words, a dyslexic brain has failed to successfully change or re-assign what in good readers has become the reading network, because that type of brain is predisposed to be less suitable for that particular strategy that changes these particular areas and the connections between them. Thus, the traditional way to learn to read doesn't resonate with the (looming) dyslexic brain. It could of course well be that such a predisposed brain will never be able to develop an efficient reading network and will never learn to read accurately and fast. It almost certainly seems it will not develop into a reading network exactly like normal readers. However, the 'traditional' reading network might not be the only possible configuration that results in skilled reading.

The dyslexic brain may be predisposed to be more suitable for applying other strategies that address other parts of the brain, other modalities and strengthen other connections in order to eventually form a slightly different, but efficient reading network. Moreover, these other strategies may not have to completely replace traditional (grapheme-phoneme) strategies, but could work in addition to them, subjugating other parts of the brain to be part of the reading network and strengthening different functional connections in order to overcome their predisposition of failing to develop an efficient reading network the traditional way. This proposition may seem rather out of bounds and far-fetched, but there is another subset of people that seem to do exactly this.

As reviewed in the third chapter, people with synesthesia seem to implicitly employ different learning strategies, create and automate different forms of cross-modal representations and address nontypical modalities in response to certain stimuli such as graphemes. Moreover, these additional strategies develop during the acquisition and mastering of these categorical stimuli and are therefore thought by many to aid in

the successful processing of these novel stimuli. In other words, (GC-)synesthetes employ a different strategy in developing a reading network suitable for a differently predisposed brain. The fact that synesthesia is also at least partly hereditary suggests there is some hardwired level of susceptibility for picking up on crossmodal cues in our environment and the ability to bootstrap these associations into an idiosyncratic system for novel purposes. However, there are no reasons to suggest that this ability is unique to synesthetes. Moreover, these associations must still be learned. While this happens implicitly in developmental synesthesia, recent research discussed in the fifth chapter suggests this can also be achieved explicitly in nonsynesthetes.

Unfortunately, the findings presented in fourth chapter are inconclusive whether the prevalence of dyslexia is actually lower among GC-synesthetes. While the biggest dataset (i.e. the synesthesia battery) strongly suggests a significantly lower prevalence of dyslexia among GC-synesthetes compared to those who are not, both the GNO study as well the study by Carmichael et al. (unpublished) failed to find this inverse relation. However, the fact that a subset of GC-synesthetes do report dyslexia has opened up a potential new and interesting line of inquiry as to the phenomenological nature of their conditions. Moreover, it also implies that dyslexics can still acquire the strong grapheme-color associations this study proposes.

Altogether, this suggests that training synesthetic associations may be a viable alternative or an useful addition to current remedial tools for dyslexics. More specifically, considering the seemingly critical period in which synesthesia develops and reading problems become apparent, training synesthetic associations may be used as a preventive strategy at a young age for those with a familial disposition towards dyslexia. Hopefully one day, the specific methods and materials recommended in this study may provide a valuable framework for future studies into this fascinating topic which might relieve dyslexic children from their handicap as well as potentially provide valuable new insights into the curious workings of synesthesia.

8 ACKNOWLEDGEMENTS

I would like to thank Maarten Lamers for his guidance, patience and positivity during this long project and Tessa Verhoef for her willingness to scrutinize my work. I also would like to specially thank Josh Jackson, Sean Judge and Scott Novich from Eagleman's lab, Dr. Tessa van Leeuwen from the Donders Institute for Brain, Cognition and Behaviour, and Dr. Duncan Carmichael from the University of Sussex for sharing their (preliminary) data and extensively answering all my questions. Moreover, the time, effort and expertise Youri Feenstra has put in helping me with the data analysis of the Synesthesia Battery has been quintessential in sorting out the relevant data. Further, I am grateful for all the professional advice and insights from Olympia Colizoli, Romke Rouw, Nicolas Rothen, and Gori Geiger on the topic of synesthesia. Lastly, I would like to specially thank my friends and family for reading and correcting my work and helping me to finish this enormous project.

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• Page. 5: Fig. 1. the kiki-bouba effect;

https://en.wikipedia.org/wiki/Bouba/kiki_effect accessed February 23th, 2017.

- Page 8: Fig. 2. Modified picture, original from L. Flowers: https://reading-interventions-info. wikispaces.com/ Neurological+Research)
 Retrieved July 12, 2017
- Page 43: The Synesthesia Battery: http://www.synesthete.org
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