Dyslexia. From Diagnoses to Theory
P. Tamboer
The purpose of this thesis was to investigate whether diagnoses of dyslexia can be improved with better a methodology or with self-report questionnaires and brain-imaging techniques. Additionally, we hypothesised that improved diagnostics can contribute to a better understanding of theories of dyslexia, especially regarding the cause or causes of dyslexia.

All conclusions will be discussed thoroughly and not briefly, as is often the case in conclusions of theses, because the methodology of dyslexia is extremely complex. Each study in this thesis only deals with a limited number of issues of this complexity. In each of these studies, we introduced some new points of view regarding diagnoses and theories of dyslexia. Therefore, an extensive overview of the results is warranted for a good understanding of new hypotheses. Moreover, some of my conclusions are based on the overview of results itself.

References to the six separate studies are provided by numbers in the order of appearance in this thesis. Study 1 stands for the first publication (i.e. Chapter 2 in this book), and so on.

1. Methods for diagnosing dyslexia

In Study 1 (Chapter 2), Study 2 (Chapter 3), Study 3 (Chapter 4), and Study 4 (Chapter 5), we found that the methodology of diagnosing dyslexia can be improved in various ways. In Study 1 (Chapter 2), we investigated how dyslexia can best be identified in a large sample of students. We used a new digital battery of tests and a large self-report questionnaire. In Study 2 (Chapter 3), we investigated how many underlying and independent cognitive variables could be distinguished from the whole set of tests and questions, and how these variables are related to dyslexia. In Study 3 (Chapter 4), we investigated predictive and construct validity of the self-report questionnaire in a new sample. In Study 4 (Chapter 5), we compared predictive and construct validity of a short version of the digital test battery and questionnaire with an existing test battery. In the four studies together, we found four improvements for diagnosing dyslexia.

The best statistical analyses

We investigated classification accuracy with regression analyses that determine group membership (i.e. discriminant analysis and logistic regression analysis). These analyses determine the optimal combination of tests and assign a weight to each test that was selected. In Study 1 (Chapter 2), Study 3 (Chapter 4), and Study 4 (Chapter 5), we found high
classification accuracy using these analyses, higher than it could have been accomplished using arbitrarily determined cut-off scores.

Theoretically, using regression scores for determining dyslexia and non-dyslexia could show where the best benefits of different samples lie. In one sample, a spelling test may be the better predictor, while in another sample a phonological or visual test could be the better predictor. Unfortunately, the use of regression analyses is not common practice. It may be even so, that not the quality of the different test batteries determines predictive validity but the method used for analysing the tests.

Pohar, Blas and Turk (2004) evaluated differences between logistic regression analysis and discriminant analysis in various situations. According to these researchers, discriminant analysis should be preferred over logistic regression analysis in the case of small sample sizes, when violations of normality of predictor variables are not too bad and in the case of categorical explanatory variables with four or more answer categories. We analysed this and found confirmation for these findings in Study 1 (Chapter 2) and decided to administer discriminant analysis in Study 3 (Chapter 4) and Study 4 (Chapter 5). In general, each researcher should carefully decide which analysis is most appropriate for the test results at hand.

It is also important to realise that, with discriminant analysis, various choices can be made. For an objective determination of which tests to use as predictors of dyslexia, the stepwise method is preferable over the enter method, because this results in a reduced set of predictors without assigning some predictors higher priority than others beforehand. Setting prior probabilities to all groups equal is also most objective, because prevalence of dyslexia is unknown in a general population, but it is especially unknown in specific samples. A cross-validation procedure by selecting the option leave-one-out classification is highly recommended to prevent that a single case would be classified based partly on itself, and to minimise the effects of outliers.

Finally, we recommend to always carefully interpret classification accuracy. Any classification accuracy is almost meaningless when a sample is not randomly drawn from a certain population or when participants are excluded (e.g. participants with low intelligence, other disorders, etc.). However, even when the sample is random, it is still recommended to present sensitivity and specificity separately. When one group (i.e. the group with no dyslexia) exceeds the other group (i.e. the group with dyslexia), it can happen that overall classification accuracy is high while sensitivity is low. Also, for diagnostic purposes, positive and negative predictive values should be presented when a sample is randomly drawn.
Self-report statements

We found high construct validity and high predictive validity for self-report questions, with predictive validity even higher than predictive validity of tests. In Study 2 (Chapter 3) and Study 4 (Chapter 5), exploratory and confirmatory factor analyses showed that underlying variables of the questionnaire highly correlate with underlying variables of test batteries that measure all well-known symptoms of dyslexia. What explains this success of self-report questions in comparison with test scores?

One reason is that the questions in our studies are specific statements with seven answer categories of a Likert scale, which requires respondents to specify their level of agreement or disagreement on a symmetric agree-disagree scale. The creation of many statements was based on recommendations of Belson (1986). Most statements are long and specific and not short, which is common in many existing questionnaires. Thus, we did not use statements such as ‘I experience difficulties with spelling’, but ‘When I write a word that sounds like another word, I get confused with spelling of the correct letters’. To make statements as specific as possible, we frequently had them start with a condition (‘When I …’) and end with a difficulty. The specific nature of the statements, in combination with seven answer categories, offers the opportunity to respondents to report various specific difficulties as well as strengths with high precision. This is not possible with test items because these usually only have two possible outcomes (i.e. correct or incorrect), which makes them useless for measuring levels of ability. Specific measurement is also difficult to accomplish with sum scores of tests because many test scores represent performances on global abilities, such as ‘spelling’ or ‘phonological awareness’ and not on specific abilities.

A second reason is that some statements enhance recognition. The fact that people with dyslexia usually experience difficulties learning a language is well-known to both researchers and people with dyslexia themselves. It remains unknown, however, what specific differences there are between dyslexia-related difficulties and language difficulties that are experienced by many other people as well. Some self-report statements were found to have high predictive value in all samples investigated in the studies of this thesis. These statements represent combinations of specific difficulties in a context that exactly represents the essence of dyslexia. For instance, one such ‘super statement’ is: ‘When doing a dictation, I almost automatically write down the words without mistakes.’ This statement correlated with seven different factors that were found in Study 4 (Chapter 5) (Table 12). Apparently, this statement represented the exact nature of difficulties that are specific for dyslexia as compared to other,
more general difficulties. Respondents may have recognised themselves especially in this type of statements that combine various specific difficulties.

A third reason is that self-report statements can do what no test can do: measure relative performances. The one thing that all symptoms of dyslexia have in common is that they relate to cognitive abilities. Thus, every test of dyslexia – whether it is a phonological, visual, attentional, or memory test – measures some kind of cognitive performance. Thus, as I argued before, it is almost impossible to make a test that only measures one single cognitive ability. There is always variance explained by general intelligence, schooling background, or motivation to perform well on a test. Smart people, on average, perform better than low intelligent people on every test. The advantage of a questionnaire is that people tend to compare themselves with people from their own social environment. Therefore, that is exactly what we need for reliable predictions. We do not want to know whether a respondent has good spelling abilities; instead, we want to determine whether they have good or poor spelling abilities as compared to people with a comparable background. For instance, classrooms in a primary school, on average, represent children from the same social environment. Classrooms in a secondary school or in higher education represent children or students with comparable intelligence. A child assesses his or her specific abilities – as indicated by specific statements – with children who mostly resemble them. For instance, ‘My friend is just like me, but I make more spelling errors when writing difficult words’. This relative performance reflects the difference between ‘normal errors’ and ‘dyslexia-specific’ errors. Some colleagues of mine put forward the notion that questionnaires cannot be objective. However, what does that even mean? People are generally in the perfect position to evaluate their own abilities. Additionally, in comparison with tests, someone who fills in a questionnaire does not have to be well-rested or perfectly concentrated. There is no need to be nervous, and when a participant is nervous, it will not affect the answers. There is also no reason to lie because, in general, people wish that both their strengths and their weaknesses are acknowledged. Children (but also adults) very much like to answer questions about themselves, mostly because this rarely happens. Teachers and parents tend to give instructions, advice, and recommendations, but they rarely ask children what they think about their own capacities. Of course, all the above must be investigated more thoroughly but it is consistent with very high predictive validity of self-report statements in all samples of this thesis.

Considering the arguments above, self-report statements may provide high predictive validity in all sorts of samples of various ages and various languages. For instance, let us consider the symptom of poor short-term memory. This symptom may express itself in
various languages and ages in very different ways. A child with dyslexia at primary school may, for instance, experience difficulties in learning the capitals of countries for an exam the next day, while an adult with dyslexia can experience difficulties in memorising the tasks that have to be performed at work. An English child can experience difficulties in remembering the spelling of difficult words, while an Italian child can experience difficulties in remembering the rules of grammar. A questionnaire consisting of many statements makes it possible to represent the same symptom in different ways, so that all people with dyslexia are confronted with the specific difficulty they experience. It suffices to adjust the regression formulas in such a way that different statements or the same statements with different weights are selected.

High predictive validity of self-report questions means that questionnaires can be considered as an alternative for test batteries in various situations. Test batteries are used for clinical diagnoses, preliminary screening on schools or institutions, and for classifying participants of samples for studies. In all situations, questionnaires can have an additional value. For screening purposes and for studies, questionnaires might be considered as a full alternative for test batteries. Test batteries are time consuming for a participant, as well as for a psychologist or scientific researcher. In various situations, high costs are required. Questionnaires can be digitalised and subsequently assessed within thirty minutes, they require few costs and hardly any time investment from the psychologist or researcher.

**Measuring as many abilities as possible**

In Study 2 (Chapter 3) and Study 4 (Chapter 5), we found that at least five but probably more cognitive abilities are related to dyslexia. These findings are highly consistent with the findings in a comparable study of Callens et al. (2014). For a theoretical interpretation of these abilities, see Chapter 3. The relevant conclusion here pertains to the methodology: highest predictive validity is achieved when many of these abilities are represented in a predictive regression equation.

The explanation that came forward from this thesis is that the number of variables that is needed in a regression equation for high classification accuracy depends on the homogeneity or heterogeneity of the given sample. Some samples are relatively homogeneous after excluding various participants. This means that the remaining participants within both groups resemble each other. It then makes perfect sense that only a few disabilities characterise the participants with dyslexia. For instance, in a study of Tops et al. (2012), only three tests sufficed for high classification accuracy of students who were recruited from a
specialised dyslexia centre. In our studies, no participants were excluded, apart from fraudulent behaviour on tests. Thus, compared to the study of Tops et al., our sample not only included students with a prior diagnosis of dyslexia and students without any typical difficulties but also students with some typical difficulties without a prior diagnosis of dyslexia. This resulted in a relatively heterogenous sample. What we consistently found is that more variables were needed for high predictive validity when a criterion of dyslexia is more flexible and more heterogenous.

The main conclusion is that, apparently, people with dyslexia are very different from each other, just like people without dyslexia. People differ not only in regard to schooling, additional training, and general intelligence but also in more specific forms of intelligence, such as fluid and crystallised intelligence as well as verbal, numeric, and spatial intelligence, and so on. For people with dyslexia, these individual differences result in various ways of dealing with difficulties resulting from dyslexia. Some people with dyslexia may compensate for some difficulties in different ways, depending on the individual strengths they have. As a result, reliable diagnoses of large and heterogenous samples require measurements of many difficulties. In other words, fishing is easier in a homogeneous pond.

**Flexible criteria and multiple predictions**

We investigated the so-called criterion of dyslexia and non-dyslexia. A criterion means that it is determined beforehand who has dyslexia and who has not. This is, as argued, an arbitrary decision. Usually in diagnostic studies, a strict criterion is chosen: participants of whom we can be sure whether they have dyslexia or not. This is mostly based on former test results, for instance, at an official dyslexia centre. In our studies, we started in the same way. We collected all kinds of biographical information (e.g. former test results, official documentation of dyslexia, history of dyslexic family members, and self-assessment of dyslexia) and categorised all participants in three groups: (1) dyslexia with high certainty, (2) no dyslexia with high certainty, and (3) the remaining. Prediction analyses were performed based on the first two groups, but all participants were categorised.

An important improvement in this standard procedure is to re-evaluate the criterion groups. What we did, was to categorise some of the remaining participants into the groups dyslexia and non-dyslexia, based on the predictions of the analysis. This resulted in more flexible criterion groups. Then, we performed the whole procedure again. The amazing result was higher predictive validity, with more variables in the regression equation; however, this made sense. Strict criterion groups consist of people with severe difficulties, resulting from
dyslexia and super-performing controls. Adding more ‘moderate’ people to the criterion groups requires measuring more variables, but it also allows more people with dyslexia to get ‘recognised’ by the analysis. An objection against this procedure is that it is statistically incorrect because predictions are partly based on previous predictions. In Study 1 (Chapter 2), however, we found that even after repeating this procedure three times, the final classification was highly consistent with the original biographical criterion groups. Thus, no participants from the strict criterion groups were re-assigned to another group. The main change in classification was that participants of the remaining group were added to the group of dyslexia or to the group of non-dyslexia with increased certainty.

Although most participants could reliably be classified in all studies of this thesis, there was always a small remaining group of participants who could not reliably be classified (about 10%). Perhaps some of these participants were highly intelligent and able to compensate for most of the symptoms, while some others were low intelligent people with no dyslexia who were a bit sloppy during the assessment of tests. It is important to realise that in a general population, there will always be people who are difficult to diagnose, no matter what diagnostic procedure is used. Thus, this should further be investigated.

Conclusion

The methodology for diagnosing dyslexia can be improved in four ways. Highest predictive validity is achieved when using self-report statements in combination with test results as possible predictors in regression equations, representing many symptoms of dyslexia, and when predictions are repeated with various criterion groups ranging from very strict to more flexible. Currently, we refer to the improved procedure as the ‘Repeated Criterion Classification Procedure’ (RCCP).

2. Investigating dyslexia with MRI

In Study 5 (Chapter 6) and Study 6 (Chapter 7), we investigated how dyslexia is represented in the anatomy of the brain with Magnetic Resonance Imaging (MRI). Although the methodological interpretation of brain-imaging results is far more complex than that of results obtained from tests or questionnaires, such complexity added many new insights to the diagnostic process of dyslexia and provided theoretical insights in general. The main
conclusion is that every interpretation of structural findings regarding dyslexia depends on the interpretation of what should be considered as statistically significant. Regarding this, there are several important issues.

The first issue is about the methods used for analysing anatomical data. First, anatomical data are usually processed with the automated technique, Voxel Based Morphometry (VBM), but the choices made by researchers regarding the pre-processing of structural images – such as modulation, adjustment of head size, or the choice of smoothing kernel size – vary between studies and may alter the significance of the results (Henley et al., 2010). Second, the significance of the results depends on choices about which technique is used for controlling for confounding variables, such as age, gender, and brain size (Snoek, Miletić, & Scholte, 2018). Third, the significance of the results depends on choices about which technique is used for corrections for multiple comparisons (i.e. Bonferroni, False Discovery Rate, and random fields thresholding), and these vary between the anatomical dyslexia studies.

The second issue is about what it means when a group difference is not significant. Tests of significance with, for instance, a required $p$-value of less than 0.05 were once introduced to prevent researchers from interpreting group differences that could easily be attributed to normal probability distributions. When a $p$-value is below 0.05, this means that there is strong support for an effect. When a $p$-value is above 0.05, there is no strong support for an effect. However, a $p$-value of 0.05 is not a border between ‘true’ and ‘not true’. A $p$-value below 0.05 can still be the result of chance, and a $p$-value of just above 0.05 does not tell us anything about whether a group difference exists or not. For instance, when a $p$-value is 0.052, a group difference more likely than not exists. In ‘normal’ research, this is not relevant because it is relatively easy to replicate findings using large samples. With the limited data of small and different samples available of MRI, however, this issue is very relevant. Thus, the conclusion that group differences do not exist when the $p$-value is just above 0.05 is not justified. Nevertheless, this conclusion may be a leading factor in a journal’s decision to accept or reject an MRI study. Study 5 (Chapter 6) was accepted only when we added significant correlations between various factor scores of symptoms of dyslexia with brain anatomy, which is something we originally planned as a separate study. This raises the question of how many relevant studies were never published. Thus, publication bias should be accounted for when interpreting general findings from MRI studies. For instance, Ramus et al. (2017) suggest that many of the reported differences in small-scale studies may be false-positive results. However, if non-published insignificant results were just a little bit below any
cut-off for significance, these results may, after combining with published results, very well be significant after meta-analysis. Moreover, the fact that various significant correlations were found with brain areas that represented non-significant group differences (in our study and in a study of Pernet et al., 2009a), supports the possibility that these group differences may exist. Only considering a few meta-analytical results as being relevant is a false interpretation of the limited MRI data, which may lead to false conclusions regarding any theory of dyslexia.

The third issue is about samples. Most anatomical studies used small samples of less than 20 participants per group (either dyslexic or non-dyslexic). Most of these studies also reported several areas of significant group differences. In our study with a larger sample, no significant group differences were found, consistent with one earlier study that used a relatively large sample (Pernet et al., 2009a). Two meta-analyses of nine MRI studies showed that hardly any significant group differences exist (Linkersdörfer et al., 2012; Richlan, Kronbichler & Wimmer, 2012). Thus, how should we interpret all of this? Most striking is that low power of small samples results in more significant group differences than high power with large samples or with meta-analyses. Ramus et al. (2017) even found that across 20 published whole-brain MRI studies there is a clear trend in the opposite direction of what would be expected, with small-scale studies contributing disproportionately to the differences reported in the literature. A statistical explanation may be derived from differences between the samples. Dyslexia is characterised by various difficulties. Small samples can be expected to be relatively homogeneous regarding biographical variables (i.e. age, gender, intelligence, level of education, social background, and native language) that affect the severity of various symptoms of dyslexia. Thus, in small samples, some difficulties may be more prominent than others. On the other hand, large samples may be more heterogeneous regarding biographical variables, which might result in more heterogeneity regarding various typical difficulties. Therefore, large samples may also include more people without one specific difficulty, and thus decreasing power for that difficulty. Only small differences regarding heterogeneity between small and large samples may result in decreasing power, especially considering that even the large samples just exceed the minimum of about 30 participants per group which is required for group comparisons to be reliable. Combining small samples to one large sample does not help. The small samples are completely different regarding age, gender, intelligence, level of education, social background, and native language. Moreover, some of the typical difficulties accompanying dyslexia vary to a large extent depending on these biographical differences. Summation of these samples may decrease the power of various results that are only characteristic for specific small samples. This is consistent with conclusions from the
previous paragraph in which I argued that homogenous samples are characterised by only a few specific symptoms of dyslexia, while heterogenous samples are characterised by a large diversity of symptoms across individual participants. Larger diversity of symptoms results in less statistical power for each separate symptom, resulting in no significant group differences.

The fourth issue is about using a classification approach as an alternative for traditional $t$-testing. In Study 6 (Chapter 7), we found a significant classification accuracy of 80%. In a large independent sample, we found a much lower but still significant classification accuracy of 60%. For clinical purposes, these percentages are of course too low. However, another important result of this study is that differences between groups were found using the same sample as in Study 5 (Chapter 6), whereas traditional analyses of group differences found nothing. Three areas of the brain were involved in this classification, and the most stunning result is that these areas were completely different areas than the ones found in Study 5 (Chapter 6). The best explanation is that this represents a more general methodological issue: the difference between measurement and prediction. The combination of small (non-significant) differences may distinguish people with and without dyslexia, while these separate differences may even be too small to detect with analyses of group differences. This confirms three things. First, diagnoses of dyslexia using anatomical MRI cannot be done based on a single area, just as diagnoses with tests or questions require more than one score in a regression equation. Second, group differences cannot be used as a diagnosis. This confirms that regression equations are better predictors of dyslexia than arbitrarily determined cut-off scores. Third, in a relatively large sample, dyslexia is represented by various symptoms. Determining which of these symptoms is the best predictor will depend on the characteristics of different samples. Here, we used a student sample. The second sample was a population sample, probably with some other characteristics when compared with the student sample.

Summarising, we found support for the hypothesis that dyslexia is represented in the brain by various anatomical varieties, using correlational analyses and classification analyses. The interpretation that non-significant group differences mean that there is nothing going on anatomically, is not correct. These findings support that the methodology of dyslexia research is extremely complex. Furthermore, these results support that dyslexia is characterised by many symptoms that vary between small and homogenous samples to a large extent.
3. Dyslexia and theoretical conclusions

From results to conclusions
The exploratory study of diagnostic methods in this thesis resulted in the conclusion that dyslexia is characterised by many different symptoms that vary between individuals to a large extent. So, what does this mean for theories of dyslexia? What else did we learn from the results presented in this thesis? Can we draw more conclusions? Before discussing this, I believe it is warranted to emphasise various aspects of drawing theoretical conclusions about dyslexia in general.

When something is fully unknown, such as the cause or causes of dyslexia, this always results in many theories. Thus, it is quite possible that no area of research of the human mind yielded so many different theories as dyslexia, with maybe intelligence as the only exception. On first sight, this seems very positive. There are, however, adverse effects. The existence of many theories makes it almost impossible for any individual researcher to keep an overview of all new theories and hypotheses and, at the same time, mirror his or her new research data to all of them. This results in islands of research groups, usually nested in different countries, with each group focussing on only a subset of theories. In England, for instance, dyslexia research focused mainly on phonological aspects of dyslexia, while dyslexia research in Italy also focused on visual and attentional difficulties. In many scientific papers about dyslexia that were published in leading journals, competing theories were not mentioned at all. How then can these different insights be combined into one universal model of dyslexia?

At present, the situation is completely unclear. New theories of dyslexia are proposed every year. Many completely different definitions of dyslexia circulate across publications. There are even researchers who do not mention the word ‘dyslexia’ anymore but replaced it with ‘reading disorder’ (e.g. Black, Xia, & Hoeft, 2017; Xia, Hancock, & Hoeft, 2017). The chaos is now complete. In this situation, some theories are declared sacred, despite contradicting evidence. This has been the case with the theory of impaired phonological awareness, which is still generally considered as the key theory of dyslexia, even though some serious objections have been proposed. After a while, it has become impossible for researchers not to look through coloured glasses anymore.

Admissions of ignorance and temporary mystification
As stated in the introduction, we wanted to avoid an initial discussion about the different theories because of the danger that this could distract us from clear methodological reasoning. In the separate chapters of this thesis, however, we evaluated many theories of dyslexia based
on the methodological results. In this conclusion, I want to present a clear overview of these evaluations, and even introduce a new theoretical perspective.

Generally, there are two ways to develop a new theory. One way of developing a new theory is by using the inductive or bottom-up approach. This means that a theory is built upon existing knowledge. A common procedure is: (1) data collection, (2) formulating a hypothesis, (3) testing this hypothesis in a new sample, (4) rejecting, accepting or adjusting the hypothesis, and so on. Regarding dyslexia, the problem with this method, so far, is that the accumulating amount of data has resulted in many competing hypotheses. There is still no single hypothesis or theory that can explain all the data. Each hypothesis or theory can be rejected based on existing data, although it will always remain a topic of debate. Moreover, as explained before, no single theory can predict who has dyslexia and who does not. Of course, we can always continue this way. However, we do not know how long the road to salvation is, nor do we know whether salvation will come in the end. Maybe the origins of dyslexia are too subtle to detect with the current methods. Then again, this strategy of developing theories might just as well end in a complexity that is beyond our comprehension.

A second way of developing a new theory is by using the deductive or top-down approach. This means that a theory is built based on an intuitive idea that encompasses the core problems of a topic. In the case of dyslexia, this should be an idea that explains that dyslexia is characterised by a variety of symptoms that differ on an individual level, without one symptom being symptomatic for all people with dyslexia. The main disadvantage of this strategy is that the proposed theory could be complete nonsense, even when it explains many of the symptoms. The advantage is that it searches for an explanation directly on a deeper level.

In this conclusion, I will use a combination of both strategies to develop a new theory. First, I will present five general theoretical propositions that are crucial for understanding further steps in theory development. All propositions are based on the studies of this thesis, in combination with existing knowledge from literature, and on the fact that, despite this knowledge, we still have no clue about what causes dyslexia. Admitting that our knowledge is very limited may in fact be a crucial step for embracing completely new insights (admissions of ignorance). These propositions may lead to a theory that, based on the data that are currently available, or will be in the near future, and can neither be proven nor falsified (temporary mystification) but may inspire us to further insights and research.
Theoretical proposition 1:

Dyslexia has an unknown cause or causes, but many symptoms

All researchers agree that dyslexia is characterised by more than one symptom. Moreover, most researchers agree about the existence of impaired phonological awareness, impaired spelling abilities, reduced short-term memory, poor rapid naming abilities, and that various aspects of visual attention may be impaired. Disagreement exists, however, about the exact number of the symptoms, the severity of the symptoms, the causal nature of the symptoms, the relations between the symptoms (subtypes of dyslexia), and individual variation regarding the various symptoms. In many studies, relations were investigated between various abilities related to reading and underlying symptoms such as impaired phonological awareness and rapid naming (e.g. Hulme et al., 2015; de Jong & van der Leij, 1999; Lervåg, & Hulme, 2009; van Viersen et al., 2018). However, only a handful of studies contained analyses of relations between underlying symptoms, such as phonological, visual and attentional symptoms (e.g. Bosse, Tainturier & Valdois, 2007).

In Study 2 (Chapter 3) and Study 4 (Chapter 5), we conducted various explorative and confirmative factor analyses on both test results and the questionnaire, with Study 4 (Chapter 5) being an extended replication of Study 2 (Chapter 3). An important outcome in Study 2 (Chapter 3) was that latent variables of the tests highly correlated with latent variables of the questionnaire with the same interpretation. Furthermore, the outcomes of the analyses of the two studies showed both similarities and differences. In short, we found that the number of ‘independent’ variables that characterise dyslexia is at least five, but probably more, maybe even ten or so. Some variables came up in all analyses: spelling, phonology, and short-term memory. The main difference between the numerous analyses was that some variables were taken together in one analysis but separated as independent factors in other analyses, such as spelling and rapid automated naming. We found support for eight latent variables: spelling, reading, phonology, rapid automated naming, short-term memory, attention, confusion (rhyme), and complexity (whole-word-processing). Callens et al. (2014) found similar results: seven latent variables with high-effect sizes were distinguished from 53 tests, using exploratory factor analysis.

The best conclusion is that variables underlying dyslexia are not independent from each other. Some may seem independent in the analyses, but the analyses only describe phenotypical outcomes. The main difference between people with dyslexia and those without is that those with dyslexia suffer from relatively more impairments than those without dyslexia. We also found that none of these latent variables by itself could distinguish people
with dyslexia from those without, where the combination of variables resulted in very high classification accuracy. People with dyslexia suffer from many symptoms, but not necessarily all. Attempts to distinguish subtypes of dyslexia failed in this thesis. No subtypes such as phonological versus visual were found, but the samples may have been too small for the detection of subtypes.

The first theoretical proposition is that dyslexia is caused by something unknown, but with many consequences. These consequences vary on an individual level depending on age, gender, intelligence, schooling, additional training, native language, social background, motivation, and so on. Relations between different symptoms are complex and influenced by different additional variables.

**Theoretical proposition 2:**
**Dyslexia has probably a single cause**

The proposition from the previous paragraph is that neither of the latent variables that were found in this thesis can be considered to represent a cause of dyslexia on its own. The next question to address is why most people with dyslexia suffer from many, but not all symptoms of dyslexia. A logical explanation is that symptoms of dyslexia result from an underlying cause in different ways among individuals, or that some individuals can compensate for some of the symptoms because of additional training, good schooling, or high intelligence. Another view is the multiple deficit theory (MDT) of dyslexia, as proposed by Pennington (2006), which assumes that there is no single deficit causing dyslexia but declares that dyslexia is the outcome of multiple causes.

In recent years, the MDT has become increasingly popular (e.g. van Bergen, van der Leij & de Jong, 2014; de Jong & van Bergen, 2017; Peterson & Pennington, 2015). The MDT defines dyslexia as poor reading that results from the interplay between risk factors and protective factors. For instance, impaired phonological awareness is, according to the MDT, not only a symptom of dyslexia but also one of the possible causes or risk factors that can lead to dyslexia. According to this view, for instance, poor reading (dyslexia) can be the result of poor phonological abilities while rapid naming is unimpaired, or poor reading (dyslexia) can be the result of poor rapid naming abilities while phonological abilities are unimpaired. The basic question here is as follows: Is there one single cause of dyslexia, or should dyslexia be defined as being the outcome of the interplay between various factors? Although none of these views can be proven right or wrong with the data currently available, I will argue based
on the present thesis that the view of a single cause prevails over the view of multiple causes. There are five issues regarding the two competing views, which are evaluated below.

The first issue is that a single cause of dyslexia has not yet been identified. Some have argued that this is one of various general shortcomings of any single cognitive deficit model of dyslexia (e.g. van Bergen, van der Leij & de Jong, 2014), or even one of the key reasons for rejecting these models (Pennington, 2006). However, that something has not yet been found does not mean that it does not exist. Much is unknown about the human brain and we just started to investigate it. That much is unknown was confirmed in a study of Van Bergen et al. (2015) which investigated parental reading influence on children’s reading. It was found that about half of the genetic risk of dyslexia was mediated by known cognitive causes. Thus, the other half of the genetic risk should be mediated by cognitive correlates that are to date unknown (de Jong & van Bergen, 2017). This is consistent with an earlier conclusion regarding developmental disorders in general: that the multiple deficit model is universally applicable to developmental disorders but, therefore, remains abstract, and that it is not specified which etiological factors, neural systems, and cognitive processes interact to produce a given disorder (van Bergen, van der Leij, de Jong, 2014). What does this mean? Should we keep looking for other possible causes of dyslexia, but forget about a single cause? I believe that it is too early to decide this. There are so many unknown symptoms that can accompany dyslexia; therefore, it would be premature to state that neither of those may represent a key feature of dyslexia, at least not before this has been thoroughly investigated, no matter how difficult this is and how long this search will last. As I will argue further on, there are reasons to believe that a single cause of dyslexia exists.

The second issue involves the number of underlying cognitive variables that has been proposed so far. In this thesis, it was shown that at least eight cognitive variables are involved in dyslexia: spelling, reading, phonology, rapid automatised naming, short-term memory, attention, confusion (rhyme), and complexity (whole-word-processing). To my knowledge, confusion and complexity have not been reported before, whereas the other six cognitive variables are well-known. In the literature of dyslexia, many theories have been proposed and, as described in the introduction of this thesis, at least 28 symptoms were described, including various visual and attentional deficits or, for instance, impaired reading of music notes (Hébert et al., 2007; Miles, Westcombe & Ditchfield, 2008; Tunmer & Greaney, 2010). However, in studies that propose the MDT as an alternative for single deficit explanations, visual and attentional theories of dyslexia were hardly considered relevant (e.g. Peterson and Pennington, 2015). This is inconsistent with the large number of theories and symptoms of
dyslexia that were described in the literature. For instance, it is found that impaired phonological awareness cannot be the central mechanism that explains all characteristics of dyslexia; yet, that does not mean other possible central mechanisms should be discarded. In the studies of the present thesis it became clear that some underlying variables of dyslexia cannot be entirely independent from one another. Various exploratory factor analyses showed that certain abilities loaded on one latent variable in one analysis but on two latent variables in another analysis. The existence of interrelations between many cognitive variables justifies the assumption that there must be something more elementary that connects these variables, an elementary single cause maybe, as the g-factor in intelligence research. The question is then: Does this elementary factor exist, or does it merely represent the statistical outcome of interrelations between various variables related to dyslexia?

The third issue is about defining dyslexia. According to the International Dyslexia Association (IDA) (2002), dyslexia is defined as follows: ‘Dyslexia is a specific learning disability that is neurobiological in origin. It is characterized by difficulties with accurate and/or fluent word recognition and by poor spelling and decoding abilities. These difficulties typically result from a deficit in the phonological component of language that is often unexpected in relation to other cognitive abilities and the provision of effective classroom instruction. Secondary consequences may include problems in reading comprehension and reduced reading experience that can impede growth of vocabulary and background knowledge.’ Based on this definition, many researchers consider dyslexia as a (word) reading disorder, which resulted in using ‘dyslexia’, ‘reading disorder’, and ‘poor reading’ interchangeably across studies. Where the definition of the IDA only mentions a phonological deficit as underlying cause, the MDT proposes that many underlying causes are possible. However, despite the number of causes, the definition of the IDA and the use of terms like ‘poor reading’ imply that dyslexia, in fact, represents the low end of a continuous and normal distribution of a continuous disorder. Moreover, in order to diagnose dyslexia, a somewhat arbitrary cut-off must be set on a continuous variable that makes a threshold between affected and unaffected rather arbitrary (van Bergen, van der Leij & de Jong, 2014; Peterson & Pennington, 2015). In some studies, for instance, categorisation as either dyslexic or non-dyslexic is based on performances below or above the 10th percentile cut-off on task of word reading fluency (e.g. van der Leij et al., 2013). This distinction between people with dyslexia and those without has some strange consequences. Assume that a child has been diagnosed with dyslexia at the age of ten years because his or her reading performance was just below the threshold for dyslexia. Based on this diagnosis, this child starts to practice extensively
under the supervision of teachers, remedial teachers, and parents. After a year, his or her reading performance has improved to a level just above the threshold for dyslexia. Does this child have dyslexia or not? This means that, for some people, a diagnosis of either dyslexia or no dyslexia will never be possible because their performances may vary just around the threshold throughout their lives. Another consequence is that people without reading difficulties have no dyslexia per definition. In fact, this is the key difference between the single-cause and the multiple-cause views of dyslexia. When multiple causes are involved, a condition such as dyslexia is by definition the low end of a continuous distribution. A single cause of a condition should be defined by the cause and not by one of many possible results of that cause, even when this cause is still unknown. For example, what happens when someone has dyslexia but does not suffer from reading difficulties, but that person does suffer from other difficulties? Some children in the Netherlands with early reading difficulties managed to overcome most of these difficulties in an early stage of the primary school; however, they still experienced major difficulties all over again in secondary school when they started to learn English, Greek, mathematics, or reading music notes. These children will never understand why they experience such difficulties. In fact, children with dyslexia who tried their very best learning to read and write on primary school were punished in comparison with children who did not practice a little extra. Only the lazy children will then be rewarded with extra time during exams in secondary school or at a university. That some people with dyslexia do not suffer too much from poor reading does not mean that their dyslexia disappeared, but only that other symptoms may be more prominent. In short, people are not very well supported by defining a disorder based on an arbitrarily chosen threshold on only one task (reading), just because underlying causes are unknown.

In this thesis, something was found that even contradicts the continuous character of dyslexia. In Study 1 (Chapter 2), the severity of dyslexia was expressed by a score, which was the outcome of the regression formula that had highest classification accuracy. The frequency distribution is presented in Study 2 (see Chapter 3, Figure 1). This score represents many symptoms of dyslexia with different weights for each regressor (with each regressor representing one or a combination of symptoms). According to the definition of the IDA and according to the MDT, a normal distribution should be expected. However, the distribution of this score shows two separate normal and continuous distributions, which do not overlap; one representing people with dyslexia and the other representing people without dyslexia. This strongly supports that dyslexia is only continuous within the separate groups of people with dyslexia and those without.
The fourth issue is about the genetic difference between dyslexia and impaired 'normal reading skills'. Both are familial and moderately heritable; more specifically, however, the neuropsychological deficits associated with dyslexia are considered to be heritable (Christopher et al., 2013; Peterson & Pennington, 2015). Not more than ten candidate genes have been identified in relation to dyslexia (Carrion-Castillo, Franke & Fisher, 2013; Darki et al., 2012; Gialluisi et al., 2014; Kere, 2011; Scerri & Schulte-Körne, 2010; Scerri et al., 2011). Some of these genes were found to affect neuronal migration during prenatal processes in rodents (Kere, 2011). However, none of the studies that related genes to dyslexia have convincingly been replicated. Thus, although some of these genes may be involved in the development of dyslexia, it is premature to draw conclusions regarding the cause or causes of dyslexia. If we assume that dyslexia is in fact poor reading, and some genes exist that are related to reading, those genes must code cognitive functions that were present long before we started to read on a large scale. A study of Van Bergen et al. (2014) showed that, in children with dyslexia, verbal intelligence and nonverbal (arithmetic) intelligence are indeed affected as well. An explanation is that the set of genes involved in dyslexia has pleiotropic effects. These genes are involved in neuronal migration during early brain development and, as a result, also affect the development of other abilities (Plomin & Kovas, 2005; Kovas et al., 2007). However, are we now still talking about dyslexic genes? What about the consensus that dyslexia is independent from general intelligence?

In summary of this issue, there are numerous genetically determined cognitive functions underlying reading, dyslexia, and (verbal) intelligence. However, most of these functions are unknown. For example, rapid naming cannot be such a function, because this task involves reading, which we started to do only recently on an evolutionary scale. The same argument can be used for phonological awareness. Therefore, candidate genes must code for more elementary functions. Reading involves various cognitive abilities, some of which were present long before people started to read. These functions may very well be genetically determined. However, if dyslexia is defined as an unknown underlying single deficit instead of a reading disorder, findings about genes that are involved in (poor) reading cannot be used as an argument for the probability of multiple causes of dyslexia.

The fifth issue is about the comorbidity between dyslexia and for instance Attention Deficit Hyperactivity Disorder (ADHD). The MDT claims that this comorbidity is easier to explain with a multiple deficit model than with a single deficit model because this comorbidity is mediated by shared etiologic and neurocognitive risk factors (Boada, Willcutt, & Pennington, 2012; Peterson & Pennington, 2015; van Bergen, van der Leij, & de Jong,
2014; Willcutt et al. 2010). It is estimated that 15–40% of children with dyslexia are also diagnosed with ADHD, and 25–40% of children with ADHD also have dyslexia (Eden & Vaidya, 2008; Purvis & Tannock, 1997; Willcutt, Pennington, & DeFries, 2000a). According to the DSM-V (APA, 2013), ADHD is characterised by a persistent pattern of ‘inattention and/or hyperactivity-impulsivity that interferes with functioning or development’. ADHD is also familial and significantly heritable. Furthermore, a distinction is made between three subtypes: the predominantly inattentive type, the predominantly hyperactive or impulsive type, and the combined type. For a diagnosis of each type, children must meet criteria for at least six of the nine symptoms. An alternative explanation for the comorbidity between ADHD and dyslexia may be that people with the inattentive subtype of ADHD are people with dyslexia who suffer from visual or attentional impairments. Some findings seem to be consistent with this. For instance, in various twin studies, it was found that most of the phenotypic covariance between reading difficulties and inattention was explained by common genetic influences, whereas phenotypic covariance between reading and hyperactivity-impulsivity was less explained by common genetic influences (Boada, Willcutt, & Pennington, 2012; Willcutt, Pennington, & DeFries, 2000b; Willcutt et al., 2007). This raises the question whether ADHD represents one disorder, or two disorders with one of them being dyslexia. Another explanation for the comorbidity between ADHD and dyslexia may be that ADHD might be over-diagnosed whereas dyslexia might be under-diagnosed. We must keep in mind that diagnoses of ADHD are frequently based on symptom ratings obtained from parents or teachers, who might exaggerate the severity of some symptoms. More importantly, however, some symptoms of ADHD may just be the result of dyslexia. Children with dyslexia who are not able to read, or spell, may become frustrated, especially when teachers do not acknowledge that these children might be dyslexic, but instead tell them that they are stupid, something which is still common in many schools. This can lead to a lack of motivation and impaired concentration at school. These children may start to show either internalised or externalised behaviour (Terras, Thompson, & Minnis, 2009). The internalised behaviour can lead to a diagnosis of the inattentive type of ADHD, and the externalised behaviour can lead to a diagnosis of the hyperactive or impulsive type of ADHD. Other comorbidities can easily be explained as well. For example, approximately 30% of children with early language or speech problems go on to develop dyslexia (van Bergen, van der Leij, & de Jong, 2014). However, when we assume that dyslexia is a single heritable trait, whether or not it leads to poor reading, these early language or speech problems can also be caused by dyslexia. In the remaining 70% of the children, these problems may result from something
else, such as hearing problems or low intelligence. However, it is possible that these children have dyslexia as well, although the severity of their reading problems is not sufficient for a diagnosis of dyslexia based on the MDT. Summarising, comorbidity between dyslexia and ADHD can be explained by the MDT. However, a single deficit model of dyslexia can explain this comorbidity as well. For all models, though, it should be kept in mind that the prevalence of this comorbidity depends on unknown over- or underdiagnoses of both dyslexia and ADHD, as well as on the various definitions and subtypes of these conditions.

In summation of this theoretical proposition, there are no data or convincing arguments that make a multiple deficit explanation of dyslexia more likely than one that assumes a single underlying deficit, even knowing that a single deficit still must be identified. In a study by Pennington et al. (2012), a multiple deficit model and various single deficit models were tested on diagnostic power, but none of the models could reliably predict dyslexia. Defining dyslexia as poor reading or reading disability on a continuous scale is arbitrary and only based on the assumption that dyslexia has multiple causes, and its clinical implications are not helpful for some of the children who experience serious difficulties. Evidence from genetic studies is weak because most findings could not be replicated. Furthermore, on a behavioural level, a single deficit model of dyslexia can explain comorbidity just as well as the MDT. Most importantly, in this thesis, it was found that a regression score representing severity of dyslexia was characterised by two separate normal distributions. Actually, the MDT represents the traditional bottom-up approach of developing a new theory. A single deficit model can be developed using a top-down approach, as will be explained in the paragraphs to follow.

The second theoretical proposition is that dyslexia probably has a single underlying but unknown cause. Symptoms of dyslexia result from this unknown cause in different ways among individuals, depending on the ability to compensate for some of the symptoms as a result of additional training, good schooling, motivation, or high intelligence. This results in a severity of dyslexia being normally distributed but separated from a normal distribution of people without dyslexia.
Theoretical proposition 3:

Anatomical variety results from training differences

The proposition that dyslexia is characterised by many symptoms is consistent with our findings regarding the diagnosis of dyslexia using MRI (chapter 2 of this conclusion). In Study 5 (Chapter 6) and Study 6 (Chapter 7), we concluded that dyslexia is represented in the brain by various anatomical varieties that vary between different small and homogenous samples. Thus, there may be something that causes dyslexia, which has many consequences, both on an anatomical level and on a phenotypical level.

In chapter 2, we discussed the results of MRI studies regarding sample size and significance. Yet, we should further question what it means when people with dyslexia have a different volume of grey matter in a specific area of the brain than people without dyslexia. In the introduction, we already introduced this issue and suggested that anatomical variations regarding dyslexia may be induced by genetics but may also result from training differences. Seeing that dyslexia is genetically determined, it already plays a factor in the earliest stages of cognitive development. Depending on the variables mentioned in the previous paragraph (i.e. age, gender, intelligence, schooling, additional training, native language, social background, and motivation), children may intuitively use their strengths to compensate for their weaknesses and, thus, develop different strategies when dealing with dyslexia. This may result in many differences in the severity of symptoms and in many different anatomical variations.

Maybe what we are seeing here are not genetically induced variations at all. Maybe we are only seeing the effects of training. Many areas are hardly used because they are involved in some weaknesses, and other areas are used intensively for compensation. The area that is most actively involved in training and automaticity is the cerebellum. Especially this area of the brain shows very different results between studies, with people with dyslexia in one study showing more grey matter volume in one particular area of the brain but, in a different study, showing less grey matter in another area of the brain (for good overviews of results, see Black, Xia & Hoeft, 2017; Ramus et al., 2017; Xia, Hancock & Hoeft, 2017). Most of the results of Study 5 (Chapter 6) and Study 6 (Chapter 7) support this view. For instance, a factor related to performances in spelling correlated negatively with grey matter volume in both the left and right occipital fusiform gyrus and the left posterior cerebellum. This may imply that reduced spelling abilities lead to more training and, thus, to augmented grey matter volume in those areas.
The third theoretical proposition is that the brain displays an anatomical variety resulting from training differences. Various symptoms result in additional training of these symptoms or, instead, of abilities that might compensate for such symptoms. On an individual level, this anatomical variety depends on age, gender, intelligence, schooling, additional training, native language, social background, motivation, and so on. Anatomical variety, resulting from genetical influences, cannot be excluded but may very well be too small to detect.

**Theoretical proposition 4: The cause of dyslexia is subcortical**

The previous propositions were used to argue that dyslexia probably has a single cause that results in phenotypical and anatomical variety, with training effects as an underestimated factor. However, what could be the cause? Moreover, what could be the origin of inflammation that leads to this widespread fire?

One hypothesis is that there is something wrong with the functional connectivity in specific pathways of the brain, caused by reduced white matter density. Indeed, there are many studies supporting this hypothesis (e.g. Vandermosten et al., 2012). Another hypothesis is that the key variation is a reduced folding of grey matter (e.g. Płoński et al., 2017). However, these hypotheses do not necessarily provide a causal explanation. Reduced connectivity or folding may result from reduced functioning of separate areas in the brain and may just as well be caused by something more fundamental.

Throughout the literature of dyslexia, based on MRI or fMRI, the reported areas are located in almost the entire cortex, thus, in the cerebellum, occipital lobe, temporal lobe, parietal lobe and frontal lobe, and in both hemispheres. Until recently, however, no studies were published about possible relations between dyslexia and subcortical functioning. In Study 5 (Chapter 6), we found that within the group of people with dyslexia, a variable related to performances in Dutch-English rhyme words correlated positively with GM volume in the left and the right caudate nucleus. In another recent study, a reduction of grey matter was reported in the left thalamus (Jednoróg et al., 2015). The thalamus is involved in the distribution of sensory information to the cortex. The caudate nucleus is involved in several executive control functions, and in the processing of information. Thus, both areas are involved in processes that affect various specific functions throughout the brain.

The question now is whether anatomical variations in these subcortical areas result from training differences as well. This could be so, but if something fundamental causes
dyslexia, it is more likely to be found subcortically than cortically. Only a subcortical variation can have widespread effects, such as those found in dyslexia. Furthermore, it is possible that subcortical variations result in specific effects, without affecting all functions. General and specific forms of intelligence may be spared. See Chapter 4 for a further discussion of the functionality of the thalamus and caudate in relation to dyslexia.

A subcortical variation may be too small to detect in small samples, but it can be detected in large samples. We argued that small samples lead to more significant results than large samples because small samples tend to be more homogenous. However, if a cause of dyslexia is to be found subcortically, it should be common for all people with dyslexia and power should accumulate with larger samples. This is exactly what was found. Both Study 5 (Chapter 6) and the study of Jednoróg et al. used relatively large and heterogenic samples. The sample of Jednoróg et al. even consisted of various subsamples from different countries with different languages. Very recently, a new study (Jagger-Rickels, Kibby & Constance, 2018) confirmed involvement of the caudate nucleus in dyslexia and ADHD, while thalamus involvement was found for a comorbid dyslexia and ADHD group.

The fourth theoretical proposition is that dyslexia is nested somewhere in the subcortex, but differences between people with and without dyslexia are too small to be detected in small samples. In large samples, anatomical effects in the caudate and thalamus are sometimes visible. The subcortical cause of dyslexia causes widespread anatomical effects that influence specific cognitive functions while general and various specific forms of intelligence remain intact.

Theoretical proposition 5:

Dyslexia exists, is not a disorder, but a dichotomous perceptual variation

In summary of the first four propositions, the cause of dyslexia is unknown and maybe too small to detect, but with widespread effects throughout the brain which results in a large variety of symptoms. About the same could be stated about (poor) intelligence; but then, would that classify dyslexia as a specific form of intelligence? Does dyslexia exist at all? These questions were raised in an impressive overview of studies on dyslexia by Elliot and Grigorenko (2014). What can we conclude from this thesis regarding such questions?

In ‘Theoretical proposition 2’, I discussed the findings of Study 1 (Chapter 2), indicating that a severity score of dyslexia showed two separate normal and continuous distributions. The existence of two separate normal distributions instead of one, supports the notion that dyslexia exists and is a dichotomous condition, and not that dyslexia is the utter
left side of a normal and continuous distribution that represents some kind of cognitive ability, such as reading. Variations within both distributions are easily explained by variations regarding age, gender, intelligence, schooling, additional training, native language, social background, motivation, and so on. The distribution of this score shows two normal distributions that do not overlap: one representing people with dyslexia and the other representing people without dyslexia.

The idea that dyslexia is a dichotomous condition is not strange. There are more dichotomous conditions that originate from the brain, such as hand preference and sexual preference, although some people are ambidextrous or bisexual. Thus, these human traits are divided into three groups. Estimations of prevalence of these groups are not very reliable in the literature. However, it is striking that these estimations are about the same for dyslexia. For these three traits, there is a majority group of about 75–90% of all people (i.e. heterosexual, right-handed, and no dyslexia), a small group of about 5–15% of all people (i.e. homosexual, left-handed, and dyslexia), and a very small group of about 3–8% (i.e. bisexual, ambidextrous, dyslexia, or no dyslexia is unclear). Of course, this proves nothing, except that dichotomous traits with one subgroup being much larger than the other, are common in the brain. Despite decades of research, it is still unresolved what causes dichotomous traits, such as hand and sexual preferences, just like with dyslexia. However, let us not forget that brain research is still in its infancy. So far, we were looking at a large forest, hoping to see the trees in the middle of it.

If dyslexia is indeed a dichotomous condition, it also can be ruled out that dyslexia is a specific form of intelligence, such as spatial intelligence or arithmetic intelligence. All these specific forms of intelligence are abilities with normal distributions. Another possibility is that dyslexia is not a cognitive but a perceptual condition. Support for this can be found in Study 2 (Chapter 3) and Study 4 (Chapter 5). In these studies, we found various well-known cognitive variables that are often impaired in people with dyslexia, such as spelling and reading abilities and short-term memory. However, other variables – such as phonological abilities, automatised rapid naming, attention, and confusion – may not represent cognitive but more perceptual processes (see Chapter 4).

So far, I have argued that dyslexia is probably a dichotomous perceptual condition without knowing what causes dyslexia. One thing all researchers agree on is that dyslexia has a genetic origin. The offspring of a parent with dyslexia will, depending on the cut-off, have a chance of about 30–65% to have dyslexia as well (Snowling, & Melby-Lervåg, 2016). If dyslexia is genetically determined, it must already exist for a long time, much longer than
when people started to write and read. This has been stated by other researchers as well, however, without drawing any clear conclusions. Taken one step further, it can be argued that dyslexia is not a disorder at all. Dyslexia is a genetic condition with a relatively high prevalence for a disorder. One could argue that anything that results in a disadvantage, whether it is impaired reading or slow naming of numbers, should be considered as a disorder. Regarding homosexuality, however, most scholars would not argue in the same way, although the natural disadvantage of being homosexual is clear (unlikely to produce offspring). As long as we do not know what causes dyslexia, prevalence should go to considering dyslexia as a genetic variation, resulting in a perceptual dichotomy. This variation has disadvantages but may just as well have advantages. The disadvantages arose only when people started to write and read, so evolution had no reasons to let it disappear.

For years, I have been intrigued by a study of Lachmann & Van Leeuwen (2007). They introduced a Functional Coordination Deficit Model, proposing that dyslexia reflects the inability to suppress symmetry of letters. They suggested that only people without dyslexia learned to suppress symmetry. This might be an explanation for confusion between the letters [p] and [b]. People with dyslexia may tend to perceive these letters as the same, which can be beneficial in certain tasks. The results of this study are consistent with dyslexia as a genetic, dichotomous and perceptual condition that has disadvantages and advantages. When I spoke with a colleague about this (Kretzschmar, 2017), he proposed, as a joke, that if this were true, dyslexia may never have been a genetic adaptation, but instead, the adaptation was evolving away from dyslexia. By now, I think this joke might be true. People with dyslexia are the original people and getting rid of dyslexia was a variation with benefits for not getting confused. It would offer a perfect explanation for the existence of the variable confusion as posited in this thesis, which as far as I know is for the first time in the literature.

Perception and cognition evolved thousands of years ago in ways we do not understand, and we can only have an educated guess about it. A possible educated guess is that, alongside with cognitive development of intelligence, a variation evolved that made it possible to perceive small details and symbols without getting confused. That not all people acquired this ability was not a large disadvantage for group survival. Only centuries later, these people have difficulties in the complex and specified abilities that are, for instance, needed to learn to write and read.

The fifth theoretical proposition is that dyslexia is a dichotomous, perceptual, and genetic variation that should not be considered as a disorder. It affects various cognitive processes, such as learning to write and read, but it is not part of cognition itself.
4. Theory of impaired inhibition and excitation

From knowledge to theory

In Chapter 3, I presented five propositions that can be summarised in one sentence: Dyslexia should not be considered as a disorder but as a dichotomous, perceptual, and genetic variation with an unknown cause in the subcortex, resulting in widespread effects on various perceptual and cognitive functions and displaying a high variability between individuals depending on intelligence, schooling, additional training, native language, social background, and motivation. Throughout this conclusion, I argued that all aspects of this hypothesis follow directly from the results of this thesis in combination with existing knowledge.

Although the purpose of this thesis was to study methods for diagnosing dyslexia, I hypothesised that it might also result in conclusions of theoretical importance. The above summary of conclusions is based on this thesis as a whole. In the separate studies though, we discussed various results with existing theories, putting forward various objections against some of them and suggesting various new interpretations. Here, I could give a summary of this. However, when I evaluated these objections and suggestions, I found support for something that is shared by all theories. Therefore, I decided to present it as a new theoretical perspective of findings; a new theory, so to say, that encompasses all theoretical conclusions of this thesis.

Any new theory of dyslexia though, as I argued above, must adhere to some general requirements. In the case of dyslexia, so many theories have been proposed; thus, it seems pointless to propose yet another theory that opposes aspects of other theories. A better solution is to use a top-down strategy by developing a theory that encompasses all other theories. At the same time, it is paramount not to speculate but to respect the limits of our knowledge (admissions of ignorance). We must also accept that a broad perspective may not be put into use easily, seeing that a broad perspective may not be falsifiable directly with the scientific tools available at present (temporary mystification). The only way to test whether any theory of dyslexia is correct is to combine the top-down strategy with the bottom-up strategy by verifying that a new theory is consistent with all available data.

According to my conclusions, a theory of dyslexia must be a perceptual variation that originates in the subcortex, for instance, in the areas that were found to be involved in dyslexia: the thalamus and the caudate nucleus. The thalamus is usually described as a relay station where sensory information is filtered and transferred to the cerebral cortex, received
back from the cerebral cortex and sent back again, and so on. As was described in Study 5 (Chapter 6), the caudate nucleus is implicated in several executive control functions and language functions, such as language switching in bilinguals, second language learning, and suppression of irrelevant words. A full quote from Study 5 (Chapter 6) will explain it best: ‘In relation to these findings, the relation between the caudate nucleus and the test Dutch-English Rhyme Words, which requires fast switching between languages, makes perfect sense. This is also the case with the confusion reported via self-report questions, which represented typical mistakes, such as exchanging letters within words and exchanging words within sentences – mistakes that might result from impaired cognitive control of attention. We think that the possibility exists that reduced grey matter volume in the caudate nucleus in relation to rhyme/confusion might represent a more fundamental dysfunction of dyslexic people, which might encompass various difficulties of confusion, such as exchanging letters or words.’

It is not perception itself that is altered in dyslexia, but it is the higher processing of incoming sensory information, whether it is visual or auditory. The involved key functions are as follows: control of attention, parallel processing, switching, suppression, inhibition, and excitation. Suppression of symmetry in the study of Lachman and Van Leeuwen (2007) is fully consistent with these key functions. More in general, the perceptual variation might have something to do with both suppression or inhibition and excitation of all kinds of sensory information. People with this variation in perception, such as people with dyslexia, may have a different way of looking and listening at things. When irrelevant information is not suppressed, these people have more information to process at the same time, thus having a more global way of perceiving things. For example, this quality might be beneficial for architects. However, this global view has disadvantages when cognitive tasks are performed, such as reading, which require fast switching between suppression and excitation and between relevant and irrelevant information. Reading requires the processing of so much sensory information at the same time; therefore, people with dyslexia get confused about what is relevant and what is irrelevant.

The theory I propose is that, originally, people perceived sensory information in a global way. Alongside cognitive development, a genetic variation benefitted a more specific way of processing information. This variation is related to inhibition and excitation of relevant versus irrelevant sensory information. The variation involves a sort of on and off button in the brain. This has widespread effects on various perceptual and cognitive functions. Nowadays, advanced cognitive functions are required for, for instance, reading. Nature was
not aware that people were ever going to do something that is so complicated. Thus, unfortunately, in modern times, disadvantages are more prominent than advantages.

This theory might explain all other theories of dyslexia because it focuses on more fundamental traits. It is not necessary at this stage to specify where exactly in the subcortex this perceptual variation is nested. It is not possible to describe all details of this variation in this conclusion. It is a theory that comes forward from the results in this thesis. However, as stated above, it is required to explain existing data from this thesis and all other research available, both theories and symptoms. This will be done extensively in a separate manuscript. Here, we only highlight the most important findings regarding the theory of inhibition and excitation and existing theories of dyslexia.

In one sentence, the new theory can be summarised as follows: Dyslexia is a dichotomous, genetic variation, originating in the subcortex, which involves higher processing of sensory information through an on and off-button (inhibition and excitation) that is crucial for the control of attention, which has widespread effects on various perceptual and cognitive functions, with high variability between individuals depending on intelligence, schooling, additional training, native language, social background, and motivation.

**Testing the theory of inhibition and excitation**

*Dyslexia as a language disorder*

According to most definitions, dyslexia is a language disorder, predominantly in the domain of reading. However, the exact nature of the language disorder has never been described. Reading is an extremely complicated process that involves many separate cognitive and perceptual functions. A disorder in only one of them can easily disturb the whole learning process of reading.

At a very early stage of cognitive development (about five or six years), the human brain receives the assignment to learn reading, while during evolution, the human brain never had the opportunity to prepare itself for such a complex task. Mastering this ability requires years of practice, while general cognition has hardly been developed. During this period the brain develops a reading network based on many separate functions that were originally meant for entirely different tasks. While spoken language had a chance to develop in the brain on an evolutionary scale, resulting in various specified areas (e.g. Broca’s area and Wernicke’s area), there is no specific reading area in the brain.

It is paramount to realise that the first developmental stages of reading involve visual processes. Large amounts of letters, words, and sentences enter the brain as visual sensory
information with high speed. Quick decisions must be made, which requires a perfect control of attention. Which letters, words, and sentences are crucial for understanding a text? When irrelevant letters or words are not inhibited, confusion arises: letters and words get mixed up and letters and words that resemble the ones already processed are added, replaced or forgotten. If there is no working control mechanism, the brain gets overloaded with sensory information. To make things even more confusing, sometimes identical letters represent different sounds in different words, and visually resembling words can have a completely different pronunciation. On the other hand, the same sound can be represented by different letters, and words that sound similar can have completely different writing. This is probably the reason that English is considered to be the most difficult language to learn for people with dyslexia.

A more specific explanation can be derived from studies of noise exclusion and visual crowding. Various deficits of noise exclusion are reported in the literature (Benassi et al., 2010; Sperling et al., 2005; Sperling et al., 2006). This is fully consistent with a lack of control due to too little inhibition and too much excitation. Noise is not inhibited, but it remains active or even becomes more excited, which leads to interference with relevant stimuli. The same mechanism may be happening during visual crowding. Visual crowding is a form of masking, in which single-letter identification is compromised by the presence of additional letters or other simple visual forms in close proximity (e.g. Crutch & Warrington, 2007; Levi, 2008; Pelli & Tillman, 2008). In one study, 60% of dyslexics’ slowness in word analysis was explained by crowding effects (Martelli et al., 2009). Visual crowding is a key process of reading. During reading, foci of attention quickly shift from point to point with regular intervals, and a so-called ‘crowding window’ moves alongside these foci. This crowding window is an area around the focus of attention, in which everything can be identified. A disturbance of normal shifting between inhibition and excitation may have various effects on the crowding window. It might become larger, resulting in overlap between succeeding windows. Also, the distance between succeeding foci of attention may be smaller or larger, resulting in overlap or skipping letters or words. Any disturbance of these processes may result in impaired control of attention and, thus, in slow and inaccurate reading.

In summary, it is important to realise that when people with dyslexia are learning to read, this not only involves the development of phonological abilities but also visual abilities. If certain perceptual processes are different in people with dyslexia, these processes may affect both visual and phonological abilities required for reading.
The phonological deficit theory is by far the most frequently proposed to be a causal theory. This theory posits that dyslexia is caused by impairments in phonological information processing, probably caused by problems in the access to or fuzziness of phonological representations of words in the phonological lexicon (e.g. Vellutio et al., 2004; Shaywitz & Shaywitz, 2005; Snowling & Hulme, 2005). An important finding is that, in an fMRI study (Boets et al., 2013), no differences between people with and without dyslexia were found regarding phonetic representations, but only deficient access to phonological representations. This clearly supports the idea that there is something going on during the processing of phonological information, which is an idea also suggested by Blomert, Mitterer and Paffen (2004).

Explaining the phonological deficit theory with an on and off button requires acknowledgement of the many forms of resemblance that exist in languages. Many letters and words resemble other letters and words, either visually or auditorily, depending on variety between languages. So, what is happening? When you read a word, a message is sent to the phonological lexicon. In that lexicon, various sounds are activated that may represent the correct pronunciation of the word and are sent back to, for instance, the working memory. Then, the incorrect pronunciations must quickly be inhibited, and the correct one activated. When this inhibition is too slow or even absent, confusion arises about the correct pronunciation. With letters, an additional problem can arise. If the symmetry of letters is not correctly inhibited, then reading the letter [p], for instance, may activate all the sounds of [p], [b], [d], and [q] simultaneously. Deciding which one is the correct one then becomes exponentially more complex. Sometimes an identical letter can have different pronunciations, depending on the word; however, different letters can also share the same pronunciation. These processes are probably far more complex than we can imagine, but clearly, any lack of control of inhibition and activation will affect the entire process.

According to the allophonic speech perception theory (Serniclaes et al., 2001; Serniclaes et al., 2004; Bogliotti et al., 2008; Dufor et al., 2009), people with dyslexia are characterised by poor discrimination between phoneme categories. According to this theory, people with dyslexia maintain a higher sensitivity to acoustic differences within one phoneme category. For example, the letter [p] is perceived by dyslexics as a wide range of sounds that overlaps the range of sounds of the letter [b]. Normally, young children lose this sensitivity, which leads to categorical perception of phonemes. However, this may not happen to people with dyslexia; thus, as a result, they remain more sensitive to differences within one phoneme.
category. They perceive allophones, which are contextual variants of phonemes. Somebody with dyslexia, who perceives an allophone, will have problems with attributing the same written symbol to sounds of different categories. These findings are easily explained by poor inhibition. As a child, people with dyslexia did not learn to inhibit the overlapping sounds between letters. This may have contributed to difficulties in the pronunciation of the correct letters in complex words, or to activation of the wrong letters when reading a letter with a resembling sound, as is the case with the [p] and the [b].

In short, poor inhibition affects all reading and speaking processes that involve both visual and auditory resemblance. This view explains more symptoms of dyslexia than the phonological deficit theory can. For instance, confusion between the letters [p] and [b] can be attributed to a phonological deficit, but visual confusion between letters cannot be explained by this theory. As Greek school teachers told me, in the Greek language a typical confusion of people with dyslexia is between the number ‘3’ (pronounced as /tria/) and the letter epsilon ‘ε’ (roughly pronounced as the ‘e’ in the English word bet). In Greek, there is no auditory resemblance at all. This can be explained by poor inhibition of symmetry, but not by the phonological deficit theory.

**Impaired automatized rapid naming**

Impaired automatized rapid naming is consistently reported as one of the main symptoms of dyslexia (e.g. Jones, Branigan, & Kelly, 2009), especially regarding the naming of letters and numbers but also of pictures and colours. How to explain this with the on and off-button? What happens during rapid naming? Five different letters (or numbers, pictures, or colours) are presented on a paper in columns in a random order and must be read out aloud as quickly as possible without making mistakes. It has been suggested that impaired inhibition of preceding items causes a delay in serial rapid naming (Jones, Snowling, & Moll, 2016). This is consistent with the idea of the on and off-button.

What happens is the following: you see the first letter, and while you are pronouncing this, you look at the next letter. Still pronouncing the first letter, you must remember the second letter because your eye is already going to the third letter. Maybe, your eye is already going to the fourth letter because you can easily remember the second and third letter. However, you must pronounce the second letter before the third letter. Thus, you must inhibit the third letter temporarily and activate the second letter, while reading the fourth letter. After that, the second letter must be forgotten and the third letter, which is still held in memory, must be activated. Meanwhile, your eye has already progressed to the fifth and sixth letter,
which must be temporarily inhibited again. This clearly requires a perfect control of attention to the right letter for pronunciation. It is a process of fast switching between inhibition and excitation. One small mistake of inhibition or excitation leads to an error or total confusion.

**Impaired short-term memory**

Another well-known symptom of dyslexia is impaired short-term memory, usually measured with a test of digit span. Digit span tests mostly consist of numbers with an increasing number of digits. All must be memorised and pronounced in the correct order. To my knowledge, there are no reports of poor long-term memory or poor short-term memory for episodic events. Therefore, the question arises whether there is something wrong with the memory or with something else. Numbers may trigger all kinds of associations with, for instance, birth dates, age of a sister, and so on. All of this must be inhibited. During the repeating of the digits, there are also processes of inhibition and excitation, which are required to keep track of the correct order of the digits. In fact, a study of Hachmann et al. (2014) showed that people with dyslexia tend to remember digits in the incorrect order; however, they do not perform poorer than other people in tests that require remembering digits without the need of a specific order.

**Explanation of other symptoms**

Evaluating all symptoms of dyslexia with the on and off-button would require a separate thesis. There are many symptoms that must be explained by this button. For instance, poor concentration may be explained by poor inhibition of surrounding noise. Pianists with dyslexia experience difficulties in reading music notes on two staffs at the same time. This might be explained by poor inhibition and excitation during quick shifting between the staffs because notes in the same position on separate staffs denote a different meaning. There is lot more to say about this theory and the symptoms that were evaluated shortly in the above paragraphs.
5. Conclusion

The main conclusion of this thesis is that the study of the methodology of diagnosing dyslexia provided both suggestions for improvements as well as several new theoretical perspectives. Beforehand, the assumption was that diagnoses can only be improved without any preference for a specific theory of dyslexia. This was supported by the results of this thesis. Based on these results, we developed a new theoretical idea. The main reason for this was to show that a theoretical idea that does not exclude other theories will improve the explanations of every complex issue that accompanies the diagnoses of dyslexia.

The final definition of dyslexia, based on this thesis, is as follows. Dyslexia is a dichotomous, genetic variation, originating in the subcortex, involving higher processing of sensory information through an on and off-button (i.e. inhibition and excitation) that is crucial for the control of attention, causing widespread effects on various perceptual and cognitive functions and displaying high variability between individuals, depending on their intelligence, schooling, additional training, native language, social background, and motivation.

This definition explains why self-report statements are more successful in diagnosing dyslexia than tests. Self-report statements address the relative abilities of a large variety of cognitive demands, considering that people with dyslexia vary on various other characteristics, such as intelligence. This definition also explains the relation between the findings of tests and self-report statements with anatomical variations in the brain.

The main characteristic of this definition is that it can be a basis for more improvements in diagnosing dyslexia. The relevance of this new theory of dyslexia in the current thesis is to show that it is thinkable that there is a common cause that encompasses all existing theories, because it is the only way to understand the results of this thesis. Dyslexia was once a perceptual variation that, in the modern human being, initially without intention, causes various difficulties during cognitive learning that vary between individuals to a large extent. If diagnoses of dyslexia are only based on a few specific impairments, they will always lead to misdiagnoses. Only if diagnoses of dyslexia are based on the new broad view that was presented in this thesis, will they be independent from any differences in intelligence, schooling, or between languages.


