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Reading in dyslexia across literacy development: A longitudinal study of effective connectivity

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ABSTRACT

Dyslexia is a literacy disorder affecting the efficient acquisition of reading and writing skills. The disorder is neurobiological in origin. Due to its developmental nature, longitudinal studies of dyslexia are of essence. They are, however, relatively scarce. The present study took a longitudinal approach to cortical connectivity of brain imaging data in reading tasks in children with dyslexia and children with typical reading development. The participants were followed with repeated measurements through Pre-literacy (6 years old), Emergent Literacy (8 years old) and Literacy (12 years old) stages, using Dynamic Causal Modelling (DCM) when analysing functional magnetic resonance imaging (fMRI) data. Even though there are a few longitudinal studies on effective connectivity in typical reading, to our knowledge, no studies have previously investigated these issues in relation to dyslexia. We set up a model of a brain reading network involving five cortical regions (inferior frontal gyrus, precentral gyrus, superior temporal gyrus, inferior parietal lobule, and occipito-temporal cortex). Using DCM, connectivity measures were calculated for each connection in the model. These measures were further analysed using factorial ANOVA. The results showed that the difference between groups centred on connections going to and from the inferior frontal gyrus (two connections) and the occipito-temporal cortex (three connections). For all five connections, the typical group showed stable or decreasing connectivity measures. The dyslexia group, on the other hand, showed a marked up-regulation (occipito-temporal connections) or down-regulation (inferior frontal gyrus connections) from 6 years to 8 years, followed by normalization from 8 years to 12 years. We interpret this as a delay in the dyslexia group in developing into the Pre-literacy and Emergent literacy stages. This delay could possibly be detrimental to literacy development. By age 12, there was no statistically significant difference in connectivity between the groups, but differences in literacy skills were still present, and were in fact larger than when measured at younger ages.

1. Introduction

Dyslexia is a developmental disorder affecting the efficient acquisition of literacy skills, present in 5–17% of the population (Gabrieli, 2009). It influences reading accuracy and fluency (Lyon et al., 2003), as well as spelling and composition skills (Berninger et al., 2008). With targeted intervention, many persons with dyslexia can achieve functional or normal reading skills, although fluency problems are generally harder to remediate than accuracy problems (Alexander and Slinger-Constant, 2004). Problems with writing are comparatively more resistant to remediation, and will often persist for much longer than reading difficulties (Berninger et al., 2008). The disorder is primarily of neurobiological origin (Lyon et al., 2003), but it also has correlates at the cognitive and behavioural levels (BDA, 2007). Dyslexia is not caused by factors in the environment, but its expression may still be influenced positively or negatively by circumstances in the home, school/workplace and by the general literacy environment (Samuelsson and Lundberg, 2003). Importantly, dyslexia is not a matter of general IQ (Lyon et al., 2003; Tanaka et al., 2011).

For many years, the central hypothesis has been that dyslexia is chiefly a consequence of a deficit in the phonological system (Hugdahl et al., 1998; Melby-Lervåg et al., 2012; Vellutino et al., 2004). However, in line with a general shift in the view of developmental disorders toward more multidimensional models emphasizing synergistic effects

Abbreviations: DCM, Dynamic Causal Modelling; IFG, inferior frontal gyrus; IPL, inferior parietal lobule; OT, occipito-temporal cortex; Pre-G, precentral gyrus; STG, superior temporal gyrus.

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(Moll et al., 2013), acceptance is growing for a multifactorial and dimensional view of dyslexia and related disorders (Bishop and Snowling, 2004; Pennington and Bishop, 2009; Ramus et al., 2013; Snowling and Hulme, 2012). In this view, it is recognized that, apart from the phonological component, dyslexia is associated with a number of cognitive benchmarks, like deficits in rapid automatized naming (RAN) (Norton and Wolf, 2012; Warmington and Hulme, 2012; Wolf and Bowers, 1999), verbal short term memory (Beneventi et al., 2009; Kibby, 2009; Trecy et al., 2013), working memory (Beneventi et al., 2010; Helland and Asbjørnsen, 2004; Smith-Spark and Fisk, 2007), long term memory (Menghini et al., 2010), visual skills (Bosse et al., 2007; Vidyasagar and Pammer, 2010) and executive skills (Beneventi et al., 2010; Helland and Asbjørnsen, 2000). The expression of these benchmarks varies from individual to individual. Hence, it is becoming clear that dyslexia is a complex disorder, where it is likely that specifically and individually adapted training schemes are necessary to release the reading potential of the individual.

Reading development typically goes through successive stages. Frith (1985) described three distinct phases learning to read; the logographic phase, the alphabetic phase and the orthographic phase, corresponding to the Pre-literacy, the Emergent literacy and the Literacy stages of reading development. At 6 years of age the participants in our study were at the Pre-literacy stage. This was before formal literacy training had started. Nevertheless, a few participants were able to read a few simple words, but most were at the stage where they were able to recognize logos, but not decode regular printed text, which fits Frith's description of the logographic phase. The Emergent literacy stage corresponds to our 8-year-olds. At this point in development children are mostly able to decode printed text via an alphabetic strategy, identifying single letters and synthesizing them into meaningful words. Hence, their reading skills are in the alphabetic phase. Finally, at the age of 12, they should have reached the Literacy stage, and be largely capable of decoding efficiently via an orthographic strategy, similar to what is seen in adults who largely decode whole words or chunks of text directly without going via phonological synthesis. In dyslexia reading phases can be prolonged, or the child may not follow the expected successive development (Frith, 1985).

At a neurobiological level, it has become increasingly clear that an important perspective in analysing brain function is on networks and connectivity, as opposed to the identification of isolated areas showing changes in neuronal activation. In this study we have chosen Dynamic Causal Modelling (DCM) (Friston et al., 2003) as an analysis approach to our functional magnetic resonance imaging (fMRI) data. The basic idea behind DCM is to create generative models to investigate how neuronal activity in different brain regions is interdependent. Even though interconnections cannot be directly observed from fMRI data, the principle is to analyse the time series from the different regions, and infer the responses after some form of perturbation to the system. From here, the effective connectivity between the brain states is estimated (Friston et al., 2003).

The classical model of the reading network describes two (McCandliss and Noble, 2003) or three (e.g. Sandak et al., 2004) separate but interacting cortical networks. Sandak et al. (2004) identified a dorsal, a frontal and a ventral reading system network, all in the left hemisphere. The dorsal network subsumes the angular and supramarginal gyri, as well as posterior parts of the superior temporal gyrus. This network is thought to be active in phonological analysis and the mapping between print, sound and meaning. Along with the dorsal network, the frontal network, centring on posterior parts of the inferior frontal gyrus, is held to be especially important in beginning reading. In general, hyperactivity in frontal reading areas is often found to reflect different forms of compensatory activity in dyslexia (Brunswick et al., 1999; Richlan et al., 2009). Finally, the ventral network, part of which was termed the “occipito-temporal skill zone” by Sandak et al. (2004), is more important for advanced reading and semantic processes, and includes the inferior occipito-temporal/fusiform area, as well as parts of the middle and inferior temporal gyri. These networks are also critically involved in the same cognitive processes, described above, which are thought to be affected in dyslexia. The classic model has, however, recently been challenged in a series of studies and meta-analyses from Richlan, Wimmer and colleagues. They have repeatedly shown that orthographic depth is an important dimension in reading in general and in dyslexia in particular. (Richlan, 2014; Richlan et al., 2009, 2010, 2011; Wimmer et al., 2010). There is an ongoing debate about the effects of different linguistic and orthographic conditions upon the expression of dyslexia in different languages, and hence upon the cortical demands posed by reading tasks (Hadzibeganovic et al., 2010; Landerl et al., 2013; Wimmer et al., 2010).

In two recent studies, Richlan (2012, 2014) proposed an extended version of the classic three-network model, sub-dividing the frontal network into the inferior frontal gyrus (IFG) and the precentral gyrus (Pre-G), and the dorsal network into the inferior parietal lobule (IPL) and the superior temporal gyrus (STG), in addition to the ventral network (the occipito-temporal cortex (OT)). The OT is the same region that has been termed the Visual word form area by Dehaene and Cohen (Cohen and Dehaene, 2004; Dehaene, 2009; Dehaene and Cohen, 2011), and which is thought to be specialized for decoding print. Richlan (2014) went on to show that the new and extended model makes better predictions for the modulation of cortical activity in response to reading tasks, when taking orthographic depth into account. It should be noted that this extended version bears some resemblance to Hickok and Poeppel's (2007) well-known model of speech-processing. The route from the OT to the STG, IPL and Pre-G would then be parallel to the dorsal pathway, thought to serve the conversion from signal to articulatory output. Similarly, the route from the OT to the IFG would correspond to the ventral pathway, contributing to the translation from signal to semantics.

Few studies have employed DCM in the study of dyslexia, and none have used DCM in a longitudinal dyslexia study. The few studies investigating the development of effective connectivity in reading have only looked at the development of typical reading skills (Bitan et al., 2007, 2009; Booth et al., 2008). Based on a rhyming task, Bitan et al. (2007) found that the coupling between the dorsal inferior frontal gyrus and other selected regions (lateral temporal cortex, ventral inferior frontal gyrus and anterior superior temporal gyrus) increased with age, whereas connectivity to and from the superior temporal gyrus decreased with age. They concluded that there is reduced involvement of primary sensory processes over the course of development as a result of maturation and increasingly efficient processing. Booth et al. (2008), on the other hand, used both a visual and an auditory spelling task, and found developmental increases in connectivity that were especially pronounced from the calcarine sulcus to the STG (visual) and from Heschl's gyrus to the dorsal IFG (auditory). Furthermore, contrary to what was expected, they found no developmental effects in the IPL. Finally, using a rhyming task including a conflict element (words that rhyme despite having different spelling patterns), Bitan et al. (2009) reported developmental increases in the connections from the inferior frontal gyrus and the fusiform gyrus to the lateral temporal cortex. This was discussed in terms of the development of bottom-up and top-down processing, and the authors concluded that the observed changes in connectivity reflected a developmental increase in top-down control mechanisms, which was suggested to be primary to the decrease in bottom-up processing.

In dyslexia research, such a developmental perspective is essential. Hence, longitudinal studies are of great importance. Goswami (2003) stressed the need for developmental designs in order to disentangle some of the inconsistencies found in dyslexia research. In a different study, we have shown that even though the difference in literacy skills between children with and without dyslexia increase with age, the difference in a number of related cognitive skills in fact decreases (Helland and Morken, 2015). Furthermore, other studies have shown that the brain networks involved in reading and language actually change as a consequence of literacy acquisition itself (Carreiras et al., 2009; Dehaene et al., 2010). Still, longitudinal studies of dyslexia are a difficult endeavour for a number of reasons. For one, they are very resource demanding, and second, there is a constant balancing between collecting the desired amount of data and not over-using the subjects, who are often young children, with repeated measurements over an extended time period. It can also be challenging to recruit a sufficient number of participants for longitudinal studies. Even so, there are a few well-known longitudinal studies in the field, such as the Jyväskylä study (https://www.jyu.fi/ytk/laitokset/psykologia/huippututkimus/en/research/JLD_main), the Colorado Twin study (http://ibgwww.colorado.edu/lts/) and the Connecticut Longitudinal study (Shaywitz et al., 1990). The Bergen Longitudinal Dyslexia study, of which this study is part, distinguishes itself from these studies by taking an endophenotypical approach to participant recruitment, rather than using genetically or clinically based samples. Please refer to Helland et al. (2011a) and the methods section below for a more detailed description of the recruitment and selection procedures in this study.

Based on previous research indicating that frontal regions are important in beginning reading, whereas occipito-temporal regions are increasingly recruited with proficiency (Sandak et al., 2004), we hypothesized that the connectivity to and from the OT region would get stronger as a function of age and literacy stage. We also expected this effect to be weaker in the dyslexia group, since their skill level is often lower than typical readers. We further hypothesized that connectivity to and from the frontal regions would be steadily present in typical readers since these regions are thought to be essential from the start of reading acquisition (Sandak et al., 2004), but comparatively weaker in readers with dyslexia. Finally, we expected these effects to be reinforced by increased reading processing demands.

2. Materials and methods

The present study was part of the Bergen Longitudinal Dyslexia study, seeking to assess children at risk of developmental dyslexia through an extensive battery of literacy and cognitive tests (Helland and Morken, 2015; Helland et al., 2011a, 2011b; Specht et al., 2009). Additionally, a subgroup of the participants went through fMRI at 6, 8 and 12 years of age. This is the focus of the present study.

The Bergen Longitudinal Dyslexia study was approved by the Regional Committee for Medical Research Ethics (REK-Vest) and the Norwegian Social Science Data Services (NSD).

2.1. Participants

The original group of participants was selected as follows: Four municipalities in Western Norway were contacted and agreed to participate. The school authorities in these municipalities identified altogether nine preschools with a total of 120 children in the appropriate age group (5 years old, and attending their last year of preschool). All 120 children were invited to participate in the study, and the parents of 109 returned signed forms of informed consent. A risk index questionnaire (RI-5) (please refer to Helland et al. (2011a) for further details) was distributed to both parents and preschool teachers of these 109 children. Inclusion criteria were; no impaired sight (uncorrected) or hearing, native Norwegian speakers, and no known neurological disorders (e.g. ADHD) as reported by parents. Four children were excluded because they did not meet the inclusion criteria. Of the remaining 105 children 25 were identified as at risk for developmental dyslexia based on the results on RI-5. These constituted the Risk group. A matched Control group (N=24) was identified, leaving a group of 53 children who were not further assessed. For further information on the selection process, please refer to Helland et al. (2011a). At age 12, the participants were re-classified into a group with typical literacy development and a group with dyslexia. The dyslexia assessment consisted of four different literacy measures, all from standardized Norwegian literacy tests: the three tests non-word reading, real word reading and real word spelling were taken from the Standardisert test i avkoding og staving (STAS) [Standardized Test of Decoding and Spelling] (Klinkenberg and Skaar, 2001), silent text reading fluency and comprehension was tested by the age-appropriate Carlsten reading tests (Carlsten, 1982) which are cloze tests. A detailed description of the assessment materials can be found in Helland et al. (2011a).

It should be pointed out that the participants received preparatory literacy training from age five to seven (please refer to Helland et al. (2011b) for details on the training scheme). This was done in response to the request of the ethical committee approving the study.

All selected participants were invited to participate in the fMRI data acquisition sessions. This assessment required a separate informed consent, and only a subgroup of the participants in the study attended fMRI. For the purpose of the longitudinal DCM analysis we excluded participants who did not show activation or deactivation in all five selected regions (see below). The exclusion procedures were carried out for each data acquisition session separately in order to retain a satisfactory number of participants to be able to go through with the analyses. This meant that the number and identity of the participants varied between data acquisition sessions. One participant in the group of 6-year-olds (girl, control) and one participant in the group of 8-year-olds (boy, control) did not participate in the last round of assessments. Hence, these participants could not be classified into dyslexia/typical, and were therefore excluded from the analyses. Please refer to Table 1 for an overview of the number of participants in each group and their mean age at the different data points. Twelve participants took part at both ages six and eight. Twenty-four participants took part at both age 8 and 12 years. Eleven participants took part at all three data collection sessions. Details of the dyslexia assessment are presented in Helland et al. (2011a).

2.2. Stimuli

The paradigm for the fMRI data acquisitions (Specht et al., 2009) was constructed to follow the different phases of learning to read. An fMRI session started with a picture recognition condition to make sure the task was understood. This was followed by three literacy conditions with increasing processing demands. The easiest condition was constructed to require logographic processing. In this condition, the participants were shown the logos of familiar brands (like The Coca Cola Company™ or Lego™), which would not require alphabetic decoding to be identified. This condition was administered at ages six and eight. The next stage was alphabetic processing, and consisted of short and regular words, allowing an alphabetic reading strategy. This condition was administered at all three data acquisition sessions. This was followed by an orthographic condition, with longer and more irregular and complex words, requiring an orthographic reading strategy. This was also administered at all three data acquisition sessions. Finally, when the participants were 12 years old, a sentence condition was added to accommodate the more advanced reading level of the participants and further strain the reading processing mechanisms. Please see Fig. 1 for an overview of the paradigm with examples. As only alphabetic and orthographic literacy processing conditions were used across all three data acquisition sessions, the analyses in the

Table 1
Participants fMRI.

Age	Total	Dyslexia/Typical	Mean age Dyslexia/Typical	*p*-value
6	18	6 (M1, F5)/12 (M7, F5)	6:8/6:6	< .38
8	30	10 (5M, 5F)/20 (12M, 8F)	8:6/8:6	< .84
12	27	10 (M4, F6)/17 (M9, F8)	11:10/11:8	< .09

Ages	Processing level	Example
6 - 8 - 12	Object recognition	
6 - 8	Logographic processing	LEGO Bob the Builder Enjoy Coca-Cola
6 - 8 - 12	Alphabetic processing	snop
6 - 8 - 12	Orthographic processing	lørdagsgodt
12	Sentence processing	Har vi kake til festen?

Fig. 1. Paradigm overview with stimulus examples.

present study are based on these two conditions.

2.3. fMRI procedure

Stimulus presentation, synchronization with trigger signals from the MR-scanner, and response recording was done with the E-prime software (Psychology Software Tools, Pittsburg, PA: www.pstnet.com). The experiment used visually presented stimuli in a block- design, presented via scanner-compatible goggles (www.nordicneurolab.com). As described above, the paradigm had four different conditions at each data acquisition session, but which conditions were included varied slightly because we wanted to adapt to the skill level of the participants, as described above. However, picture recognition, alphabetic and orthographic processing were administered at all three fMRI data acquisition sessions. Of these, the two reading conditions went into the present analyses. The stimuli were sorted into four categories: “things to drink”, “things to eat”, “things to play with” and “things to watch on TV”. One of these was the target category. The participants were randomly assigned to a target category, and the target for each child was the same for all the conditions within one data acquisition session, but varied between sessions. Each condition had one run, with four ON-blocks and four OFF-blocks per run. In the ON-blocks, stimuli were presented in a randomized fashion, and the task was to press a button on the hand-held response grip (www.nordicneurolab.com) provided whenever the target category appeared. The participants were trained outside the scanner on a similar, but separate set of stimuli. Each stimulus appeared for 5 s, followed by a 1 second blank screen. There were 4 stimuli per block, of which one was the target. This resulted in ON-blocks of 24 s. The OFF-blocks were of equivalent length, but consisted only of a blank screen. Thus, one run lasted for 192 s, with four runs per session totalling to 12.8 min. The full MR-protocol for a single session lasted about 45 min, including participant preparations, task instructions, and 3D anatomy scanning. The whole study finally, consisted of three data acquisition sessions, one at age six, one at age eight, and one at age 12.

2.4. MR image acquisition

The MR-scanner was a General Electric Signa 3.0 T with 40 mT/m TwinSpeed gradients and Quiet Technology. For anatomical data we used a 3D T1-weighted Fast SPGR Sequence with 188 sagittal slices of 1 mm thickness, and an in-plane voxel size of 1.02×1.02 mm. For the fMRI BOLD data we collected 320 EPI-volumes (80 per run). We used the following parameters: TR=3.0 s, TE=30 ms, 1.72×1.72 mm in-plane voxels, 128×128 matrix, slice thickness 3.5 mm, 0.5 mm gap, and 35 axial slices. Eight full scans were acquired per ON-block, and the same per OFF-block. Signal saturation of the cerebrospinal fluid, and hence steady state signal intensity, was assured by the acquisition of eight dummy scans before each run.

2.5. Behavioural data

We assessed reading performance in the MR scanner by measuring average response-time per condition, as well as registering the number of correct and incorrect responses. Due to a technical problem, behavioural data were not recorded for one participant at age 8 (typical) and six participants (one with dyslexia, five typical) at the last fMRI data acquisitions session at age 12.

2.6. Experimental design

Since the research question required sorting the participants into groups of at-risk/control and dyslexia/typical groups, randomization at this stage was not possible. However, the MR-technicians performing the MR-scanning and instructing the participants of the task requirements were blind as to group status. Also, as specified above, randomization was in effect when assigning the participants to response categories, based on a set sequence of categories being assigned as the participants came in for their appointments.

2.7. Statistical analyses

fMRI data were analysed with the SPM12 software (Wellcome Department of Cognitive Neurology, http://www.fil.ion.ucl.ac.uk) run in MATLAB (www.mathworks.com). Images were first pre-processed using realignment and unwarping procedures available in SPM12. Before normalizing, the images were inspected for excessive movement (> 2 mm and 2°). Prior to the normalization, a new study-specific brain anatomy template was generated out of the structural MRI scans and across the age span, using the TOM8 toolbox (Wilke et al., 2008), which resulted in a new brain anatomy template consisting of six tissue-probability maps. The fMRI data of all participants were subsequently normalized to this new template, resampled with a cubic voxel size of 2 mm, and smoothed using a 6 mm Gaussian kernel.

In order to simplify the specification of DCM models, a new first-level data analysis was conducted for each participant. The new model contained only the two reading conditions, i.e. the alphabetic and orthographic conditions. These were treated as one condition (Reading) with two levels of difficulty (Alphabetic/Orthographic), defined as parametric modulation. In addition, the realignment parameters were included as covariates of no interest. Thus, the DCM models could be specified as a single condition model with one varying experimental parameter.

The next step was to define the regions to go into the DCM analyses. We wanted to investigate the model presented by Richlan (2012, 2014). Hence, we consulted the most recent meta-analysis from the same group (Richlan et al., 2011) to identify appropriate regions for our analyses. The final regions were the IFG (MNI (−50, 14, 14)), the STG (MNI (−60, −32, 6)), the OT (MNI (−40, −42, −20)), the Pre-G (MNI (−52, −4, 16)) and the IPL (MNI (−40, −48, 42)). In order to extract the time courses, an F-contrast was specified and a liberal threshold of $p < 0.05$ was applied. Data were extracted from the most significant voxel within 8 mm around the target coordinate. Exact coordinates used in the analyses are presented in Table 2. Due to distinct functional organisation of the inferior frontal gyrus (Heim et al., 2009; Mechelli et al., 2005), the precise localisation was evaluated for each participant, using the neuroanatomical atlas as implemented in SPM12. This revealed that time courses were predominantly extracted from the IFG pars opercularis, corresponding to Brodmann's area (BA) 44, and only in 5 cases from an area closer to the pars triangularis (BA45).

In total, 18 DCM models were specified. We sub-divided the model space into three families of models that varied with respect to their connectivity matrix (A-matrix). We used (1) a fully connected model, (2) a model where Pre-G was only connected to IFG and where no connection was assumed between OT and IFG, and, finally (3), where, in addition to (2), OT was not connected to IPL. For the effective connectivity (B-matrix), the effect of the orthographic condition was assumed to modulate the connection from (1) OT to STG, (2) OT to IPL, (3) STG to IPL, (4) STG to IPL and STG to IFG, (5) STG to IFG and IPL to IFG, and (6) STG to Pre-G. The area OT served as input area for all models (C-matrix). Bayesian model selection (BMS) was used to select the most probable family of models and the most probable model within this family (Penny et al., 2010). Bayesian model averaging was applied for estimating the averaged connection strength.

The individual posterior connectivity estimates extracted from the winning DCM model were subsequently subjected to fixed-effects factorial ANOVAs (2 Groups: Dyslexia/Typical by 3 Literacy stages: 6 years/8 years/12 years), one for each connection in the model. The significant effects from the ANOVAs were analysed post-hoc with Fisher's Least Significant Difference (LSD) test in order to further examine the details of the effects. Eta squared (η^2) was used as a measure of effect size.

Behavioural data were analysed in an ANOVA analysis with the factors group and age, and posthoc t-tests have been performed for each age group separately using two-tailed t-tests in order to identify any significant differences between the groups.

3. Results

3.1. DCM analyses

The effective connectivity model resulting from our analyses is presented in Fig. 2.

There were no main-effects of Group, but there were main effects of Literacy stage in the triangle OT – IFG – Pre-G. Furthermore there were five connections showing an interaction effect between Literacy stage and Group. Three of these went from OT, two went from IFG. Interestingly, the three OT-connections display a similar pattern over time, as do the two IFG-connections. Further details on the significant connections in the model are given in Table 3. Also, for the sake of clarity, the five connected regions displaying interaction-effects are visualized in Fig. 3. Remaining connections did not show any significant variation after Bonferroni correction, as analysed with a series of paired t-tests. The orthographic condition did not exert significant modulation upon any of the connections we investigated.

Table 2
Regions for DCM analyses.

Region	x	y	z
1. IPL	−44.5 ± 4.2	−44.5 ± 4.8	41.5 ± 5.2
2. STG	−60.0 ± 4.8	−33.2 ± 4.8	0.6 ± 3.9
3. OT	−25.5 ± 4.1	−90.9 ± 3.5	−18.1 ± 3.8
4. IFG	−46.9 ± 4.7	18.0 ± 5.0	16.6 ± 5.1
5. Pre-G	−40.0 ± 4.2	−1.4 ± 4.5	34.4 ± 4.0

3.2. Behavioural analyses

An overview of behavioural data, correct responses and response times, is given in Table 4. In total, four ANOVA analyses have been carried out, with either number of correct responses or response times, and for the alphabetic or orthographic condition, respectively. All ANOVA analyses showed significant main effects of age but no main effects of group (see Table 4, Fig. 4). In addition, the analysis on the correct responses for the orthographic condition as well as the analysis on the response times for the alphabetic condition demonstrated a significant interaction effect (see Table 4). Post hoc analyses revealed significant group differences at Age 8, only (see Fig. 4). However, after Bonferroni correction these values would no longer reach significance.

4. Discussion

In this study we found that effective connectivity during reading tasks changes over the course of reading development. These changes were especially related to the inferior frontal gyrus and the occipito-temporal cortex, and the course of development was different for readers with dyslexia and readers with typical literacy development. Specifically, the dyslexia group seems to show a delay in the transition into the Pre-literacy and Emergent literacy stages.

In line with our first hypothesis, connections from the OT to the IFG and the Pre-G (bi-directionally) did change with age and development. Contrary to what we anticipated, the connections to the STG and the IPL did not show any effects of literacy stage. The changes we observed were, however, not entirely compatible with the idea of an occipito-temporal skill zone (Sandak et al., 2004), predicting general increase in connections from and to the OT over time. Rather, the three connections showed three different patterns of development: (1) OT to IFG: showed an increase from 6 to 8, and a corresponding decrease from 8 to 12 for the dyslexia group and a constant decreased connectivity from 6 to 8 to 12 for the typical group (Fig. 3, top-right). (2) OT to Pre-G: showed a steep decreased connectivity from 6 to 8 and a moderate decreased connectivity from 8 to 12 years for the typical group, while the dyslexia showed again an increase from 6 to 8 and a decreased connectivity from 8 to 12 years (Fig. 3, top-left). (3) Pre-G to OT: showed increased connectivity from six to eight to 12 for both groups (Fig. 3, bottom-right). However, both (1) and (2), together with the connection from OT to STG showed interaction-effects, indicating that the course of development was different for the two groups, hence these effects need to be explored in more detail.

First, all three interactions showed a similar pattern of connectivity: the typical group actually seemed to downregulate or stabilize connection strength over time, whereas the dyslexia group started out at a level well below the typical group, followed by an increase in connectivity from 6 to 8 years and then a downregulation from 8 to 12 years. One could speculate that for the typical group the general downregulation of connectivity could reflect that they require and recruit these connections to establish reading skill, but that once

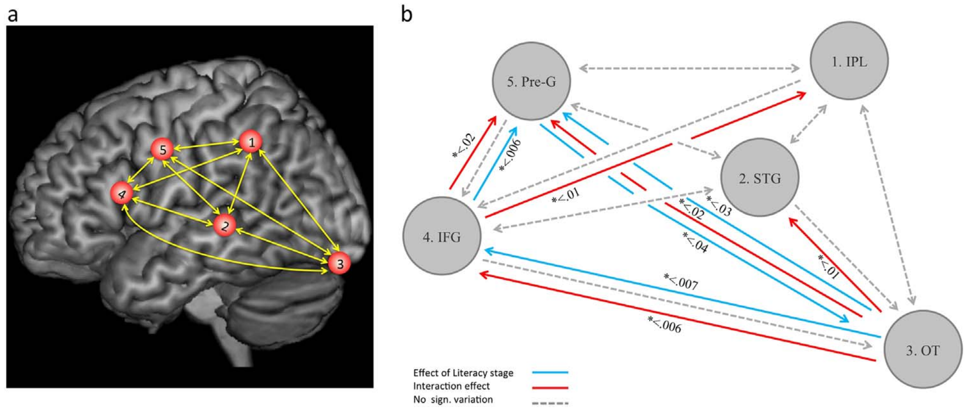

Fig. 2. Effective connectivity model. (A) Anatomical localisation of the five areas, centred on the coordinates, as reported in Table 2. (B) DCM result with all connections. Asterisks mark significant effects with *p*-values (≤.05).

Table 3
Details for the significant connections in the effective connectivity model.

Connection	Effect	p	F	v	η^2	Post-hoc (p-value)
OT→STG	Group×age	.01	4.486	2,70	.11	D6 < All *(.02)*
OT (intrinsic)	Age	.02	3.962	2,70	.09	6 < All *(.007)*
OT→IFG	Age	.007	5.300	2,70	.11	8 > 12 *(.006)*
	Group×age	.006	5.495	2,70	.12	D6 < T6, T8, D8 *(.006)* D8 > T12, D6, D12 *(.02)* T6 > T12, D6, D12 *(.04)*
OT→Pre-G	Age	.03	3.821	2,70	.09	6 > 12 *(.002)*
	Group×age	.04	3.327	2,70	.08	T6 > T8, T12, D12 *(.01)* D8 > T8, T12 *(.03)*
Pre-G→OT	Age	.02	4.223	2,70	.11	6 < All
IFG→IPL	Group×age	.04	3.451	2,70	.08	D8 < T6, T8, D12 *(.02)* T6 > T12, D8 *(.04)*
IFG→Pre-G	Age	.006	5.582	2,70	.12	8 < All *(.04)*
	Group×age	.02	4.284	2,70	.10	D8 < All *(.02)*

Notes: v=Degrees of freedom, Post-hoc tests: D=Dyslexia, T=Typical, Number=Age (e.g. D6=Dyslexia group 6 years old).

automaticity is reached, the connections are no longer needed, and hence taper off. This is along the same lines as the findings of Bitan et al. (2007). The dyslexia group, then, show late development of these OT connections (Fig. 3, top row). However, they seem to show overcompensation around age 8, followed by normalization before age 12. Interestingly, all connectivity measures at age 12 showed no difference between the groups. This is further corroborated by a lack of correlation between connectivity strength and the literacy skill parameters we used for the dyslexia diagnosis. Furthermore, this is consistent with the observation that the participants with dyslexia had also, by age 12, reached an acceptable level of reading skill. However, the results could potentially indicate that there is a delay in the transition into the Pre-literacy and Emergent literacy stages for the dyslexia group. It remains to be clarified, however, whether such a delay causes or is caused by the deviant connectivity patterns.

As seen in Fig. 2, the hub of these connections is the OT, a region that has been claimed to be specialized for decoding printed text (Cohen and Dehaene, 2004; Dehaene, 2009; Dehaene and Cohen, 2011). As such, it is no great surprise that this region plays a central role in the reading network. The IFG has been associated with grapheme-phoneme conversion and lexical access. More specifically, there is a functional distinction between different IFG areas. Relevant for the present study is the anatomical and functional distinction between the IFG pars triangularis, mostly corresponding to BA45, and the more dorsal IFG pars opercularis, mostly corresponding to BA44. In reading tasks, BA44 and BA45 are likely to process different aspects (Heim et al., 2009; Mechelli et al., 2005). BA44 is assumed to be mainly involved in sub-lexical and phonological processing, while BA45 is more related to lexical retrieval processes. As can be seen from Table 2, the averaged coordinate of the IFG region is within BA44 (see also Fig. 2). As previously mentioned, IFG is thought to be especially important in beginning reading (Sandak et al., 2004). In Sandak et al.'s (2004) model, the Pre-G was subsumed under the frontal network. Richlan (2012, 2014), on the other hand, suggested that the frontal network should be divided into two regions, namely the IFG and the Pre-G. The latter has been shown to be involved in compensatory sub-articulatory processes in speech processing (Wilson et al., 2004), sub-lexical phonological decoding (Joubert et al., 2004) and phonological assembly (Twomey et al., 2015). These are processes that are likely to be more prominent in beginning reading than in skilled and automatized reading. Finally, the STG has been associated with phonological processing (Hugdahl et al., 1998; Simos et al., 2011; Specht, 2013, 2014), again a process that is likely to be more important for less proficient readers. This may be especially true in a relatively regular orthography, like Norwegian. Landerl et al. (2013) investigated 8–12 year-olds in six different European orthographies of varying complexity. They found variance in reading skills, and hence in phonological skills, to be reduced in more regular orthographies compared to more complex orthographies. This held even for participants with dyslexia. This all supports the notion that these connections are more important for the early stages of literacy development, and hence, that the normal development over time should be a down-regulation of connectivity, whereas the dyslexia group shows late recruitment of the necessary networks (Fig. 3, top-middle).

Our second hypothesis stated that the connections with frontal regions should be steady in typical readers, and weaker in readers with dyslexia. This hypothesis was partly supported. The only main effect of literacy stage was seen from the IFG to the Pre-G (Fig. 3, bottom-left), showing for the dyslexia group a downregulation from six to eight followed by an upregulation from eight to 12 years, while the typical group demonstrated only a small decrease. This connection did, however, also show an interaction between literacy stage and group, indicating that the literacy stage effect is complex. The connection from IFG to IPL showed a similar interaction pattern to the connection from IFG to Pre-G (Fig. 3, bottom-middle): the typical group again showed a slight downregulation over time. This is contrary to the results reported by Bitan et al. (2007, 2009) who found increased connectivity to and from the dorsal part of the IFG. However, their model did not consist of the same regions as ours, and the results are therefore not directly comparable. The dyslexia group, on the other hand, showed a connectivity pattern that was rather different from the patterns going to and from OT. Here, connectivity was rather strongly downregulated from 6 to 8 followed by upregulation from 8 to 12. Once again, they end up relatively similar to the typical group.

Parietal regions, including the IPL, are usually associated with attentional mechanisms (Bush, 2011; Tamm et al., 2006), which should

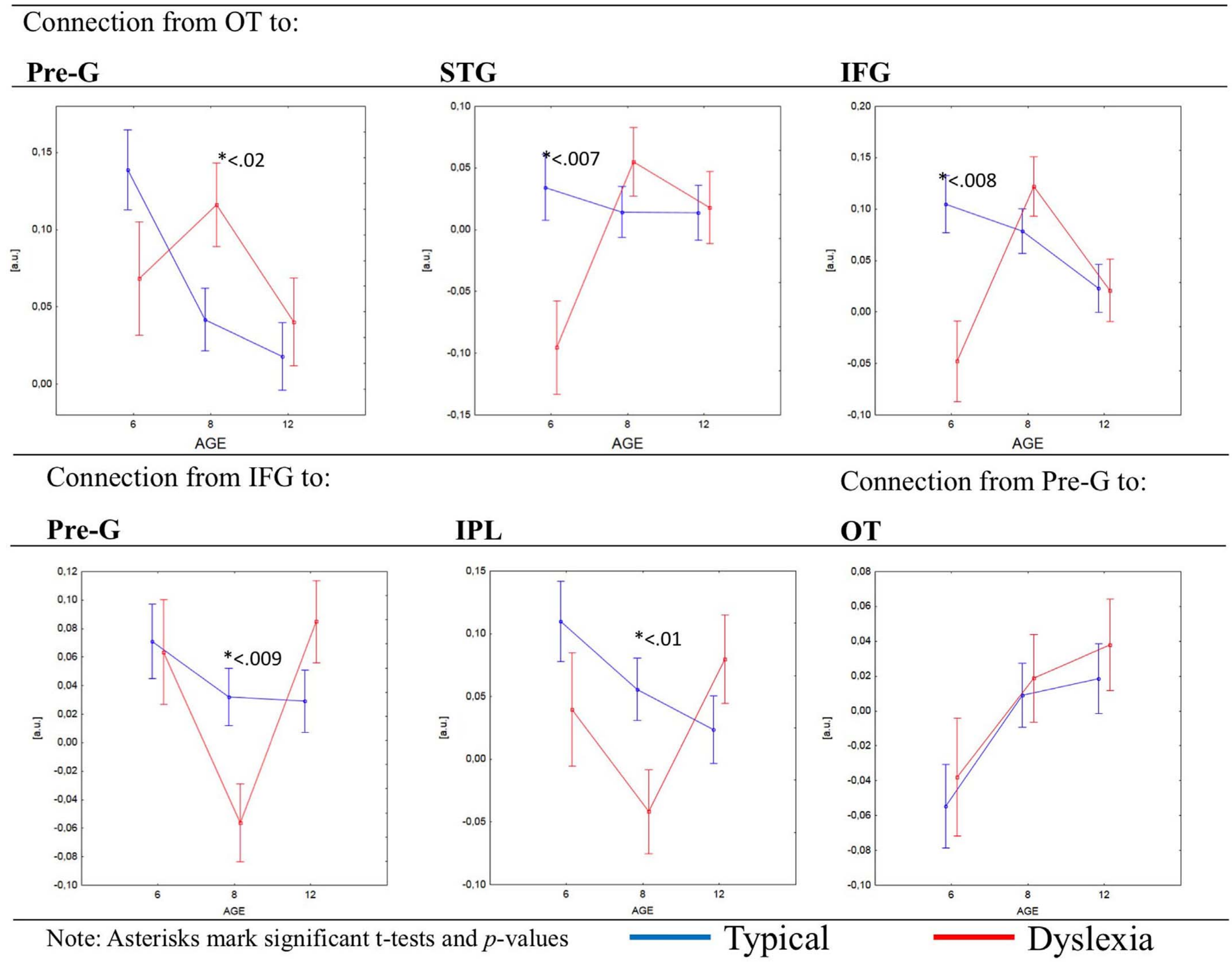

Fig. 3. Connection strength in arbitrary units (a.u.) for six connections that showed significant changes with literacy or significant group by age interactions. Asterisks mark significant interaction effects between group and age, as estimated with posthoc tests.

Table 4
Behavioural data. Results from the ANOVA analyses on correct responses (CR) and response times (RT) for each condition. Only the significant main effects and interactions are listed (p < 0.05).

	Effect	p	F	*v*
CR alphabetic	Age	< 0.001	31.185	2, 62
CR orthographic	Age	< 0.001	53.098	2, 62
	Group×age	0,004	6.010	2, 62
RT alphabetic	Age	< 0.001	25.391	2, 62
	Group×age	0,023	4.051	2, 62
RT orthographic	Age	< 0.001	15.785	2, 62

υ=Degrees of freedom.

be more essential in the early stages of reading acquisition. Skilled and automatized readers do not rely strongly upon attentional mechanisms in order to read at the (familiar) word level (Shaywitz and Shaywitz, 2008). The relatively moderate effects in connectivity with the IPL in this study are in accordance with the findings of the DCM-study by Booth et al. (2008), who reported no developmental effects in the IPL regions in their data.

A pattern seems to emerge around the age of eight years where the Emergent literacy stage is critical. At this age the dyslexia group was clearly lagging behind in the development of the networks that are considered necessary for skilled reading. As described above, the different connection strengths for participants with dyslexia converge with those from the typical group by age 12 as evidenced by Fig. 3 plots. A similar trend is also observable in the behavioural data from the fMRI task (see Fig. 4). This could be seen as a kind of normalization – at least in terms of functional connectivity and reading of single words. But even so, they do not necessarily catch up with their reading skill level. Hence, these delays in the early phases of literacy development may be detrimental to the outcome of literacy acquisition. This is also in line with the findings of our previous study (Helland and Morken, 2015), showing that even though related cognitive skills normalize by age 12, reading skills continue to lag behind, and the gap between children with and without dyslexia tends to increase further. Also, in this particular age group, the participants with dyslexia, as previously indicated, had reached functional, albeit poor, reading skill. This could, of course, be reflected in the relative normalization of effective connectivity we observed in data, where group differences were no longer present at age 12. However, between the ages of six and eight there seem to be rather great changes in connectivity in the dyslexia group, that was not present in the typical group, and we suggest that this reflects delayed entering into the Pre-literacy and Emergent literacy stages for the participants with dyslexia. The causal mechanisms of this delay are not clear, but a previous study from our group (Clark et al., 2014) suggested that structural abnormalities in lower-

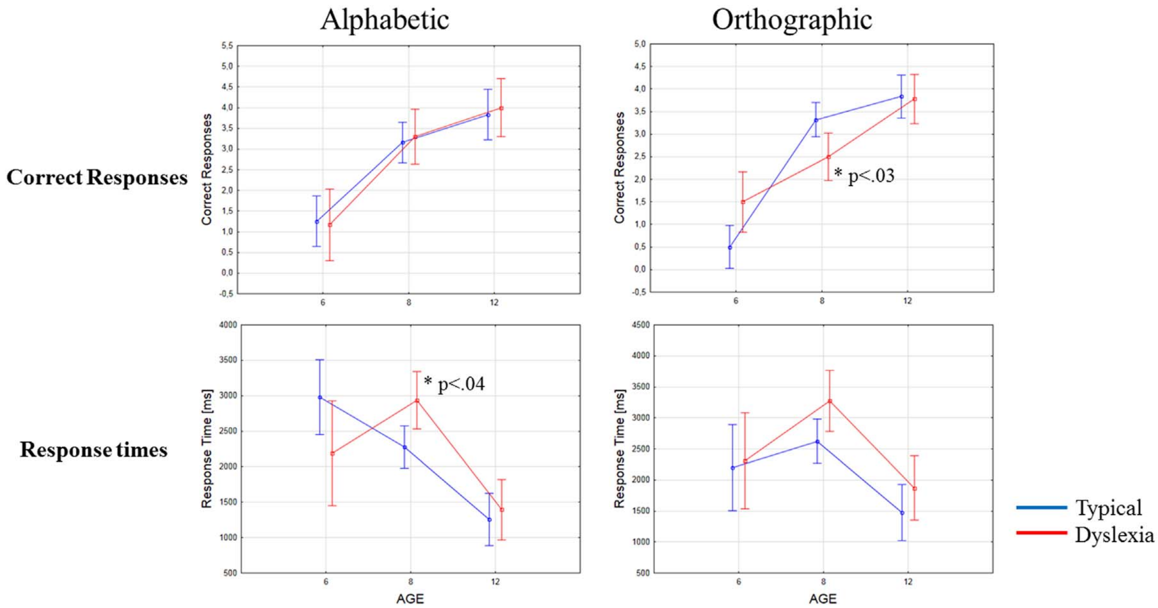

Fig. 4. Results from the analysis of the behavioural data for number of correct responses (top row) and response times (bottom row), for both the alphabetic condition (left column) and the orthographic condition (right column). Asterisks mark significant interaction effects, as estimated with posthoc *t*-tests.

level areas of processing and executive function precede dysfunction of the actual reading network. These mechanisms should be further explored, preferably with larger groups of participants.

Our final hypothesis was that the observed effects would be reinforced by increased processing demands. We did not find support for this hypothesis in our results, as the orthographic condition did not add any further modulation to the model. However, especially for the 12-year-olds the literacy processing demands were in general rather low, thus, for them the task was not difficult. The stimuli were single words, and even though some of them were relatively complex, they were all within a familiar sphere. With more complex stimuli, like sentences, it is possible that the hypothesized effect would have been observed. This is a possible topic for future studies.

4.1. Concluding remarks

This study is rather unique in its kind, reporting longitudinal fMRI analyses of children across three literacy stages, and including children as young as six years old. Though the study had relatively few participants, especially at the youngest age, and conclusions can therefore only be indicative, it is still an important window into the developmental aspects of dyslexia. The indications that development of network connectivity for reading may be delayed in children with dyslexia should be further investigated.

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