Note

Reduced interhemispheric coherence in dyslexic adults

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A R T I C L E   I N F O

A B S T R A C T

Introduction: Developmental dyslexia has been associated with reduced interhemispheric neural connectivity in children. The present study investigated functional interhemispheric connectivity in male dyslexic adults.
Methods: A group of 19 dyslexic men were compared to a group of 15 controls on interhemispheric coherence of the dominant frequency in the power spectrum during a visuo-spatial attention task. The coherence between a left hemisphere central–parietal electrode and the respective right hemisphere electrode and surrounding sites was analysed.
Results: Compared to controls, the dyslexic group demonstrated reduced, and more diffuse, interhemispheric coherence of alpha activity in the central–parietal cortex. No group differences in interhemispheric coherence were found on frontal, temporal or central sites.
Conclusions: The deviant pattern of functional connectivity in dyslexics is suggestive of an altered development of neural circuitry that may lead to deficits in magnocellular processing.

1.   Introduction

Developmental dyslexia is a neurologically-based, disorder in learning to read. Besides phonological deficits, visual-perceptual problems have been found in psychophysiological and neuroimaging experiments that are consistent with functional deviances in the magnocellular stream of the visual system, such as decreased sensitivity to low spatial and high temporal frequencies, visuo-spatial attention difficulties, and decreased activation of motion area V5/MT (Eden et al., 1996; Facoetti et al., 2006; Lovegrove, 1996).

Genetic studies of monozygotic twins have estimated hereditability of developmental dyslexia at 50–70% (DeFries et al., 1987). The biological basis of the disorder has been further supported by post-mortem research, which led to the discovery of (cyto)architectural deviances in dyslexic brains (Galaburda et al., 1985; Humphreys et al., 1990), such as microscopic disruptions in cortical organisation, i.e., micro-gyria (cortex with only four layers), and ectopias, which are neurons that have shifted from their original layer to form clusters. These abnormalities are suggestive of a disturbance in the migration of neurons, which in turn could lead to an altered pattern of cortical connectivity.

In animal studies, anatomical and functional anomalies of the dyslexic brain have been mimicked by inducing freezing injuries to the parietal cortex of neonatal rats. This not only

causes microgyria to form at the location of the injury, but is also responsible for widespread changes throughout the rodent's brain. In the normally developing brain, axons in one hemisphere form connections, through the corpus callosum, with corresponding areas in the opposite hemisphere. However, in treated rats, the number of connections was found to be decreased, and the connections that were made showed a more diffuse projection. Moreover, there were fewer thalamico-cortical connections with the microgyria, though the surrounding areas had an increased amount of connections with the thalamus. In addition, malformations were found in the size and distribution of magnocellular layers of lateral geniculate nuclei, involved in transient visual perception, and in medial geniculate nuclei necessary for transient auditory perception (Galaburda et al., 1994; Livingstone et al., 1991). Besides architectural abnormalities, the freezing injuries led to reduced discrimination of rapidly presented auditory stimuli in rats with cortical lesions, characteristically seen in developmental dyslexics (Clark et al., 2000). Female rats that had received cortical injuries did not show the thalamic or behavioural deficits seen in males (Herman et al., 1997), suggesting gender-specific divergent effects of early damage. Altered medial geniculate cells and afflicted auditory discrimination was observed in female offspring of rats that had received testosterone, suggesting that testosterone mediates a reorganisation (Rosen et al., 1999).

Brain imaging studies of functional connectivity in dyslexia have focussed mainly on reading and phonological processing. In a PET study by Horwitz et al. (1998), diminished functional connections within the left hemisphere between the angular gyrus and parietal and temporal areas, involved in grapheme-to-phoneme conversion, were found in dyslexic men. Subsequent fMRI studies demonstrated decreased functionality in left posterior areas in dyslexic adults (Pugh et al., 2000a, 2000b) as well as abnormal connectivity between left and right hemisphere (Shaywitz et al., 2003).

In our previous study, visual information processing was investigated in adults with dyslexia (Dhar et al., 2008) using Event-Related Potentials (ERPs). The behavioural results of this study are reported elsewhere. In short, compared to controls, longer reaction times and variability of reaction times were found in dyslexics, accompanied by reduced parietal brain potentials in response to exogenous cues presented in a visuo-spatial attention task. These results indicated deficient processing of cues in the parietal cortex, part of the dorsal stream where magnocellular pathways terminate.

The present study aimed to investigate the hypothesis of altered neural connectivity in dyslexic adults. To investigate whether adult men with dyslexia demonstrate lowered and more diffuse connectivity between hemispheres, the present study used electroencephalographic (EEG) coherence analyses. This technique provides a measure of functional connectivity between brain regions through the pairwise correlation of spectral energy in various frequency bands of the EEG, measured at distinct electrode sites. As left hemisphere functioning has repeatedly been found to be inferior in dyslexics (Pugh et al., 2000a, 2000b), we studied the left hemisphere response to a visual stimulus presented in the right visual field during a visuo-spatial attention task. Based on the results of our previous study, neuroimaging studies,

and animal model, as well as the nature of the (visual orienting) task, differences were expected to be found parietally. A left hemisphere electrode was selected for coherence with the corresponding right hemisphere electrode and surrounding electrodes. We expected dyslexics to demonstrate reduced coherence with the corresponding right hemisphere electrode, and to show a more diffuse pattern of interhemispheric coherence. Earlier EEG coherence studies, including studies on dyslexic children, may have been unreliable due to methodological flaws such as the use of a biased reference and disregard of electrode distance effects (French and Beaumont, 1984). Nevertheless, a later study (Leisman, 2002) found evidence for lower interhemispheric coherence in dyslexic children in the parieto-occipital cortex during performance of a visual sustained attention task. The present study is the first to investigate interhemispheric coherence in dyslexic adults, while taking the abovementioned methodological considerations into account. In this study, electrode distance and reference effects were controlled for by performing a Laplacian transformation on the data (Nunez, 2000). Furthermore, the study incorporated only male participants, considering that the effects of cortical dysfunction were reported to be dependent on gender (Rosen et al., 1999), and that gender differences were previously found in interhemispheric EEG coherence in normal children (Hanlon et al., 1999; Marosi et al., 1993), thus prohibiting an equal comparison of men and women.

2. Materials and methods

2.1. Participants

Nineteen male participants with dyslexia (mean age = 34.6 years, SD = 8.9), and 15 male controls (mean age = 34.2 years, SD = 9.0) took part in the study. The age range of participants was 19–49 years. Participants were matched for age and handedness (Van Strien, 1992). Exclusion criteria for all participants were: history of brain-related illness, diagnosed neurological disorder, and estimated IQ below 85. Intelligence was assessed with an abbreviated version of the Groninger Intelligentie Test (GIT) (Luteijn and Van der Ploeg, 1983). Mean IQ for dyslexia was 111.2 (SD 11.4), and for controls this was 116.4 (SD 9.3). Groups did not differ significantly for IQ. The Adult Self-Report (ASR) (Achenbach and Rescorla, 2003), which was used to screen for potential behavioural problems, was completed by all participants. All participants had normal or corrected-to-normal vision.

All participants were screened for the presence of dyslexia. To this end, two standardised Dutch reading tests were used: the EMT (Eén Minuut Test: One Minute Test), which is a single word reading test (Brus and Voeten, 1973) and the KLEPEL, a pseudoword reading test (Van den Bos et al., 1994). For inclusion in the dyslexic group one of three criteria had to be met. (1) EMT or KLEPEL reading score had to be below the 11th percentile. (2) Both had to fall within the lowest quartile. (3) Percentile score of the verbal comprehension minus percentile score for pseudoword reading had to be greater or equal to 60. This criterion is based on a discrepancy between reading achievement and IQ which is important for discerning readers

who are average on the reading tests but poorer than would be expected based on intelligence (Scarborough, 1989; APA, 2000). Verbal comprehension was measured using a subtest of the Wechsler Adults Intelligence Scale-III (WAIS-III) and had to be above the 15th percentile.

Adults were included in the control group, provided there were no reading problems on the dyslexia screening tests or behavioural problems, as determined by the ASR.

The study protocol was approved by the medical ethics committee of the University Medical Center Groningen. All participants were required to give informed consent before taking part in experiment.

2.2. Tasks and stimuli

Participants were seated approximately 60 cm from a computer screen. Each task trial consisted of a centrally located fixation dot presented for 1000 msec followed by a peripheral cue and subsequently a target letter, each appearing at 1° either to the left or the right of fixation, which remained visible during the task. Both cue and target duration were 50 msec with a stimulus onset asynchrony of 200 msec. The cue could be valid, i.e., predicted target location correctly, or invalid; the target appeared in the opposite visual field. However, the target was cued on only two thirds of the 300 presented trials. Participants were required to respond to targets with a button press. (A more detailed description of the task can be found in Dhar et al., 2008).

2.3. Electrophysiological recording and analysis

Continuous EEG was sampled at 500 Hz using a SynAmps model 5083 amplifier (Neuroscan) with an input impedance of 10 MΩ, from 72 Ag/AgCl-sintered ring electrodes embedded in an EEG recording cap made by EASYCAP GmbH. Reference electrodes were attached to the mastoids. A ground electrode was placed on the right cheekbone. Electrodes were arranged according to the international 10/20 system (Jasper, 1958). Horizontal electro-oculogram (EOG) was recorded from the outer canthus of each eye. Vertical EOG was recorded from infraorbital and supraorbital electrodes placed in line with the pupil of the left eye. Electrodes were filled with conductive gel using a syringe without a needle. Cotton buds were used to ensure that the impedance was maintained below 15 kΩ. With an input impedance of the amplifier as high as 10 MΩ, there was no need to reduce electrode impedance any further at the risk of skin abrasion, which may cause infection (Ferree et al., 2001).

A high cut-off filter of 70 Hz with a time constant of .3 and notch filter (50 Hz) were applied to the raw data. The Gratton and Coles algorithm (Gratton et al., 1983) was used to correct for ocular artefacts. The filtered EEG was segmented from −200 to 800 msec from cue onset. After baseline correction (−200 to 0 msec), segments containing activity above 75 µV or below −75 µV rejected as artefacts and subsequently averages were computed. The current source density (CSD) was calculated from the unaveraged data to control for artificially high coherence due to dense electrode arrays (Nunez, 2000). An interval was segmented from 120 to 250 msec from cue onset, encompassing frequency information of only right cue

processing. The results were based on 100 trials. A fast Fourier transform (FFT) was performed on the CSD. Subsequently, cross-spectrum coherences were calculated between electrode CP3 in the left hemisphere and its mirror electrode (CP4) as well as surrounding electrodes in the right hemisphere: CP3–CP2, CP3–CP4, CP3–CP6, CP3–C2, CP3–C4, CP3–C6, CP3–P2, CP3–P4, and CP3–P6. Fig. 1 illustrates the positioning of the electrodes used for calculation of coherence. The right hemisphere electrodes were divided into 3 groups according to their proximity to the central mirror electrode CP4. The central group consisted only of the electrode CP4. The proximate group consisted of C4, CP2, CP6, and P4. The less proximate group comprised C2, C6, P2, and P6. The coherences were averaged for the proximate and less proximate group. The resulting mean coherences were submitted to repeated measures analyses of variance with between-subjects factor group, with 2 levels (control and dyslexic), and within-subjects factor proximity, with 3 levels (central, proximate and less proximate).

3. Results

The dominant frequency in the cue-evoked power spectrum, as was determined through visual inspection of the FFT was 8.5 Hz. The groups did not differ for this frequency ($p = .79$). Consequently, all statistical coherence analyses were conducted for this frequency. Box's test indicated that the assumption of homogeneity of variance was met ($p = .95$). A main effect was found for group [$F(1,32) = 8.61$, $p = .006$], signifying reduced 8.5 Hz coherence for dyslexics between CP3 and predefined right hemisphere electrodes. Furthermore, a group × proximity interaction was found [$F(2,31) = 4.34$, $p = .017$], suggesting that the groups differed as a function of proximity level. Fig. 2 depicts the average coherence between CP3 and the right hemisphere electrode groups: central (CP4), proximate, and less proximate. The figure illustrates that controls show a decrease in coherence from central to proximal electrodes, whereas dyslexics demonstrate a reversed pattern, with reduced coherence at the more proximal electrodes.

In light of the presumed altered topographical distribution of coherence in dyslexia, an additional analysis was performed. Taking potential topographical shifts in coherence
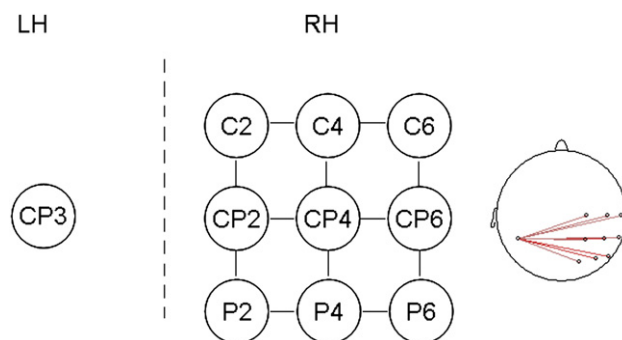

Fig. 1 – Electrode positions in left hemisphere (LH) and right hemisphere (RH) used for coherence.
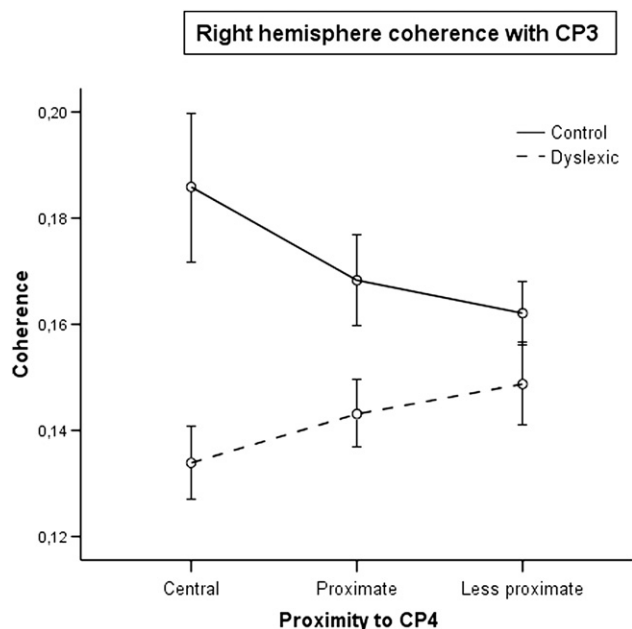
Fig. 2 – The coherence between CP3 and right hemisphere central, proximate, and less proximate electrodes is shown for the control and the dyslexic group.

into account, the maximal coherence values per participant were obtained from the aforementioned positions. Subsequently, maximum coherence was compared between groups, without taking cortical location into consideration. As expected, there was no significant group difference in maximal coherence values between groups [$F(1,32) = 1.86$, $p =$ n.s.], suggesting that coherence may have dislocated to another region.

In order to examine the specificity of the findings to the parietal cortex, an auxiliary analysis was performed and the groups were compared on interhemispheric coherence in frontal, temporal and central regions. Specifically, coherence between twelve homologous left and right hemisphere electrode pairs was analysed: T7–T8, TP7–TP8, FT7–FT8, F1–F2, F3–F4, F5–F6, FC1–FC2, FC3–FC4, FC5–FC6, C1–C2, C3–C4, C5–C6. The groups did not differ in level of coherence for any of the individual electrode pairs, confirming the hypothesis that the findings are specific to the parietal cortex. Mean (SD) coherence for grouped frontal, temporal, and central leads per group is depicted in Table 1.

Table 1 – Mean coherence values at frontal, temporal and central areas.

	Frontal mean (SD)	Temporal mean (SD)	Central mean (SD)
Group			
Control	.18 (.03)	.19 (.04)	.18 (.04)
Dyslexia	.18 (.03)	.17 (.17)	.16 (.16)

4. Discussion

The aim of the present study was to investigate whether qualitative differences in neural processing may be present in dyslexic adults. Our findings clearly demonstrated decreased interhemispheric coherence of 8.5 Hz (α) for dyslexics compared to controls in the central–parietal cortex during the performance of a visuo-spatial attention task. In addition, coherence was found to be more diffuse in dyslexics, providing further support for less efficient collaboration between hemispheres in dyslexics. Furthermore, no group difference was found in the maximum coherence level, suggesting that other areas may have been receiving input in order to take over functionality in a compensatory manner. The group difference in coherence was found to be specific to the parietal cortex, considering that no group differences were found on frontal, temporal and central leads.

Our results are in accordance with the finding of lower interhemispheric coherence in dyslexic children during a visual attention task (Leisman, 2002), and are suggestive of an altered functional hemispheric organisation in dyslexia, compatible with the neuroanatomical changes in post-mortem (Galaburda et al., 1985; Humphreys et al., 1990) and (f)MRI studies (Pugh et al., 2000a, 2000b; Von Plessen et al., 2002). The altered functional organisation may ultimately lead to deficits in magnocellular visual processing, resulting in the observed differences in the parietal cortex where this pathway terminates.

In the present study, the dyslexics demonstrated a deviating pattern of coherence. Hence, the evidence so far clearly points towards qualitative differences in addition to quantitative differences in neural processing (e.g., slower reading and reduced ERP amplitudes) in dyslexia. Consequently, differences in functional connectivity need to be acknowledged as a significant direction for further research. Moreover, as functional disconnection has been related to a variety of disorders such as autism spectrum disorder (Coben et al., 2008) and schizophrenia (e.g., Higashima et al., 2007), future studies will need to address the specificity of the present findings to dyslexia.

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