Brain Imaging Findings in Dyslexia

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Dyslexia is a brain-based disorder that has been intensively studied in the Western world for more than a century because of its social burden. However, affected individuals in Chinese communities are neither recognized nor formally diagnosed. Previous studies have concentrated on the disadvantages of reading deficits, and few have addressed non-linguistic skills, which are included in the symptoms. In addition, certain dyslexics possess visual spatial talents that have usually been ignored. In this review, we discuss the available information regarding brain imaging studies of dyslexia based on studies in Caucasian subjects. Gray matter deficits have been demonstrated in dyslexics using structural magnetic resonance imaging. Reduced neural activities in the left temporal and left parietal cortices, and diffuse widespread activation patterns in the cerebellum could be detected using functional magnetic resonance imaging. Changes in lactate levels, N-acetylaspartate/choline-containing compounds and N-acetylaspartate/creatine ratios, and phosphomonoester peak area were detected in magnetic resonance spectroscopy studies. Lower fractional anisotropy values in bilateral white matter tracts have been demonstrated by diffusion tensor imaging. Abnormal Broca’s area activation was found using positron emission tomography imaging. Increased activities in the right frontal and temporal brain regions were detected using electroencephalography. Reduced hemispheric asymmetry and increased left inferior frontal activation were reported following magnetoencephalography. Although these imaging modalities are not currently diagnostic or prognostic, they are able to provide information on the causes of dyslexia beyond what was previously provided by behavioral or cognition studies.

1. Introduction

Dyslexia is a common childhood learning disorder. It has been recognized by the World Health Organization (ICD-10 code R48.0) and is listed in the tenth edition of The International Statistical Classification of Diseases and Related Health. The definition of dyslexia differs between research groups. However, the International Dyslexia Association has defined dyslexia as a disorder “characterized by difficulties with accurate and/or fluent word recognition and by poor spelling.” Affected individuals are intellectually, emotionally and medically normal. The main deficits include an inability to process sensory input (i.e., acoustic information) that comes into the nervous system rapidly, and an
impaired reading ability.\textsuperscript{4} It is associated with linguistic and non-linguistic skills (e.g., balance).\textsuperscript{5,6} Moreover, dyslexics are notorious for lacking any sense of time.\textsuperscript{7} Grigorenko et al\textsuperscript{8} suggested that it represented one of the most important public health problems as the symptoms are incurable, and the impact is lifelong. Despite these disadvantages, some dyslexics display good visual spatial talents.\textsuperscript{9} The etiology of dyslexia is not clear, but 10 susceptibility genes have been identified.\textsuperscript{10} The estimation of prevalence varies considerably, but has been estimated to be 15\% in Western countries.\textsuperscript{11} There is a consensus opinion that dyslexia occurs with all languages\textsuperscript{12} and shares a similar biological origin.\textsuperscript{13,14} The incidence and prevalence in the Chinese population, however, remain unknown.

Ramus\textsuperscript{15} stated that dyslexia could be approached from three domains: the behavioral, the cognitive, and the biological. The advent of imaging tools such as magnetic resonance imaging (MRI), functional MRI (fMRI), magnetic resonance spectroscopy (MRS), diffusion tensor imaging (DTI), positron emission tomography (PET), electroencephalography (EEG), and magnetoencephalography (MEG) has allowed us to investigate brain function in dyslexics, and study in vivo the biological nature of this complex disorder. Driven by the statement, “current confusion and lack of progress is attributable to the fact that dyslexics were formally diagnosed by behavioral symptoms (i.e., poor reading)”,\textsuperscript{5} we aimed to consider the outcomes of neuroimaging studies. In this review, we analyzed alterations in brain structure, function and chemical metabolites in dyslexics based on information from MRI, fMRI, MRS, DTI, PET, EEG and MEG studies. These neurobiological observations should improve our understanding of the causes of the disease and aid in its clinical diagnosis. The information could be useful for investigating the problem of dyslexia in communities that use a logographic system for communication, such as the Chinese language.

2. Findings From Imaging Tools

2.1. Findings from MRI studies

2.1.1. Gray matter reduction

Gray matter volume was found to be reduced in German adult dyslexics.\textsuperscript{16} This affected the bilateral superior temporal gyrus and was detected using voxel-based morphometry (VBM).\textsuperscript{17} A reduced gray matter volume was also found in the bilateral fusiform gyrus, the bilateral anterior cerebellum, and the right supramarginal gyrus in adolescent dyslexics (aged 14–16 years) from Austria, using optimized VBM.\textsuperscript{17} Structural irregularities were observed in Norwegian adolescents with dyslexia using combined gray and white matter volume measurements and fractal dimension of the gray-white matter border, specifically the altered ratio of gray/white matter in the left hemisphere.\textsuperscript{18} Smaller gray matter volumes were found in the right posterior superior parietal lobe, the precuneus, and the right supplementary motor area of subjects with developmental dyslexia from Italy.\textsuperscript{19}

Both the VBM method and manual measurement have identified gray and white matter differences in the right cerebeller anterior lobe, and the right and left pars triangularis in male dyslexic children (aged 121–152 months) from the United States.\textsuperscript{20} Reduced gray matter volumes of the left and right temporal lobes, and a reduced gray matter density in the middle and inferior left temporal gyri have also been detected in male dyslexics.\textsuperscript{21} Gray matter volume was reduced bilaterally in the planum temporale (PT), inferior temporal cortex, and cerebellar nuclei of familial dyslexics from Italy.\textsuperscript{22} Decreased gray matter within the left temporal lobe and significant differences in the frontal area were observed in right-handed male dyslexics (aged 18–40 years) from France.\textsuperscript{23} Evidence of decreased gray matter has been found in dyslexic subjects, most notably in the left temporal lobe and bilaterally in the tempoparietococcipital juncture, but also in the frontal lobe, the caudate, the thalamus, and the cerebellum.\textsuperscript{24}

Most previous studies have found a reduced volume of gray matter in dyslexic brains; however, an increased density of gray matter has been found in the bilateral precentral gyri in male dyslexics.\textsuperscript{21} One study found no changes in the ratio of gray to white matter in dyslexics.\textsuperscript{25} Overall, these results suggest that alterations in gray matter are present in the brain cortex, sub-cortical regions, and cerebellum in dyslexic children, adolescents and adults.

2.1.2. Planum temporale (PT)

In normal subjects, the size of the left PT on the superior temporal plane and part of the Wernicke’s area, is usually larger than that in the right hemisphere.\textsuperscript{26} The results of imaging studies of this asymmetry in dyslexics have been inconsistent, due to diagnostic uncertainties and differences in diagnosis, measurement criteria, handedness, and cognitive ability.\textsuperscript{27} However, research has consistently demonstrated that 60–70\% of the population have leftward asymmetry of the PT and that dyslexic individuals tend to have either rightward asymmetry or symmetrical plana.\textsuperscript{28} In an MRI study, planum symmetry among grade 8 dyslexics in Norway was
Dyslexia and human brain imaging

70%, whereas symmetry was observed in only 30% of the controls. In contrast, normal PT asymmetry was found in some Norwegian right-handed male dyslexics, i.e., there was no significant difference in the degree of PT asymmetry between the groups. Another study found that the right PT area was similar in dyslexic and control groups, but that the left PT was significantly smaller in the dyslexic group (10–12-year-old Norwegian students). Individuals with a moderate brain size and asymmetry typically demonstrated the best overall performance. Some subgroups of dyslexic individuals show unusual symmetry or reversed asymmetry of the PT. An extreme leftward asymmetry of the PT and a rare form of Sylvian fissure morphology (Steinmetz type 4) were found in a compensated dyslexic from the United States; this specific brain organization might thus be related to behavioral compensation.

The inconsistent outcomes of the literature might be due to the heterogeneous nature of the various groups of dyslexics. Fiber-track studies using DTI might provide further evidence to confirm the size of the PT. If the size of PT is related to compensation, remedial strategies might be expected to have an impact on its volume.

2.1.3. Corpus callosum

It has been reported that phonological dyslexia involves deficits in the transfer of information across the corpus callosum. Studies on the size of the corpus callosum in dyslexics have produced conflicting findings. One study found no changes in the cross-sectional area of the corpus callosum in dyslexics. An MRI study in Norway using shape model analysis found that right-handed dyslexic boys (mean age 11 years) had a shorter corpus callosum than control subjects, localized in the posterior midbody/isthmus region. Defective callosal transfer was detected in dyslexic subtypes in a study of Italian children aged 7–15 years. Another study in the United States indicated that the anterior region of the corpus callosum (the genu) was significantly smaller in dyslexic children (mean age 9.7 years). The area of the posterior third of the corpus callosum, roughly equivalent to the isthmus and splenium, was found to be larger in dyslexic men (mean age 27 years) from the United States.

2.1.4. Combined alterations of anatomical structures

Imaging studies in vivo have linked dyslexia to abnormalities in the structures associated with the parietal operculum (e.g., PT, supramarginal gyrus and angular gyrus). With regard to the anatomical measures that differentiated the phonological dyslexics from the remainder of the subjects, including normal control and non-phonological dyslexics, Leonard et al listed the following: (1) marked rightward cerebral asymmetry, (2) marked leftward asymmetry of the anterior lobe of the cerebellum, (3) combined leftward asymmetry of the planum and posterior ascending ramus of the Sylvian fissure, and (4) a large duplication of Heschl’s gyrus, the primary auditory area on the left. Leonard et al summarized that, “When these four measures were normalized and summed, the resulting variable predicted short- and long-term phonological memory.”

A smaller cerebral volume is related to the comprehension of oral and written skills. Dyslexic patients seem to have a significantly smaller total cerebral volume and a reduced gyrification index; however, no changes were noted in cortical thickness, which has an impact on information processing capacity.

2.1.5. Cerebellum

The degree of cerebellar symmetry has been correlated with the severity of dyslexics’ phonological decoding deficit. Those with more symmetric cerebella made more errors on a nonsense word-reading measure of phonological decoding ability. “The cerebellum is one of the most consistent locations for structural differences between dyslexic and control participants in imaging studies. The anomalies in a cerebellar-frontal circuit are associated with rapid automatic naming and the
double-deficit subtype of dyslexia." Smaller right anterior lobes of the cerebellum (Figure 2), bilateral pars triangularis, and brain volume were recorded among children in grades 4–6 from the United States. Gray matter volume was reduced in the cerebellar nuclei in familial dyslexics from Italy.

Children without dyslexia demonstrated greater rightward cerebellar hemisphere asymmetry than children with dyslexia; the only statistically significant correlation was between rapid naming errors and left hemisphere volume.

2.2. Findings from functional MRI studies

Reduced activation in the left posterior temporoparietal cortex and abnormal activation in the perisylvian and extrasylvian temporal cortex during an auditory rhyming task in dyslexics were found using fMRI. Functional imaging studies of developmental dyslexia have reported reduced task-related neural activity in the temporal and inferior parietal cortices. Activation likelihood estimate meta-analyses showed that the left side of the brain was activated in normal readers, but that right brain activation occurred in dyslexics. There was no evidence to support dysfunction of the cerebellum. An fMRI study showed disruption of the two left hemisphere posterior brain systems: one within the parietal-temporal area, the other within the occipital-temporal region. The compensatory engagement of the anterior system around the inferior frontal gyrus and the posterior (right occipital-temporal) system were found.

In a study of 18 children with dyslexia from the United States, a significant difference in fMRI connectivity in the left inferior frontal gyrus was found between children with dyslexia and normal reading controls. This correlated with the right and left middle frontal gyrus, right and left supplemental motor area, left precentral gyrus, and right superior frontal gyrus. Using a noun-verb semantic association paradigm, Baillieux et al demonstrated that the activation patterns within the cerebellum of 15 dyslexic children were widespread and diffuse, in contrast with the controls, who showed bilaterally well-defined and focal activation.

2.3. Findings from MRS studies

Biochemical differences (lower ratio of choline-containing compounds to N-acetylaspartate) were
Dyslexia and human brain imaging found in the left temporo-parietal lobe and the right cerebellum between dyslexic men and controls using proton-MRS. Dyslexic boys showed a greater area of elevated brain lactate ($2.33 \pm 0.84$ voxels) in the left anterior quadrant (Figure 3) compared with the control group ($0.57 \pm 0.30$ voxels) during a phonological task. A group of adult male dyslexics had a lower N-acetylaspartate/choline ratio in the right cerebellar hemisphere, together with a higher choline/creatine ratio in the left cerebellar hemisphere. These findings, however, conflicted with those of the Rae et al study. A pilot study of a potential female dyslexic proband, who is a native Chinese speaker, showed that the N-acetylaspartate/choline ratio of the right cerebellar hemisphere (1.27) is smaller than that of the left (1.26) (unpublished data, Figure 4).

Phosphorus-MRS also showed that the phosphomonoester peak area was significantly elevated in a dyslexic group, as evidenced by higher phosphomonoester/total phosphorus ratio. These findings are consistent with the hypothesis of abnormal membrane phospholipid metabolism in dyslexics.

2.4. Findings from DTI studies

Significant correlations were found between white matter anisotropy and speed of pseudoword reading. The fractional anisotropy values within the bilateral frontotemporal and left temporoparietal white matter (inferior and superior longitudinal fasciculus) regions were decreased in adult German dyslexics compared to controls. A lower fractional anisotropy value was detected in bilateral white matter tracts within the frontal, temporal, occipital and parietal lobes in adult, right-handed native English dyslexics using tract-based spatial statistics DTI. The results of both studies suggest that dyslexia is a syndrome involving disconnections within the brain structure and function, which reflects the biological, rather than the behavioral or cognitive domains.

2.5. Findings from PET studies

In a PET study, the left temporoparietal brain region failed to activate in dyslexic men compared with controls during auditory phonological tasks such as rhyme detection (not during testing or intentional tasks). Another PET study using compensated adult dyslexic subjects found the activation...
of both Broca’s area (during rhyming tasks) and the temporoparietal area (during short-term memory tasks); however, concerted activation of these areas did not occur in the control subjects. In addition, the left insula (the anatomic bridge of Broca’s region, superior temporal and the inferior parietal cortex) was never activated in dyslexics. The defective left insula might contribute to the weak connectivity between the anterior and posterior language areas, so causing the phonological processing deficits in dyslexics in the study. Eight dyslexic participants, scanned by PET, showed reduced activation in a left occipitotemporal area during both word reading and picture naming, compared with the controls. PET detected reduced activation within frontal and parietal left hemisphere regions during a discrimination task in dyslexics but not controls. Further, the regions activated in the right frontal cortex were larger than those of the controls.

These PET studies seem to confirm the fact that dyslexic brains are activated differently to those of non-dyslexics during phonological tasks.

2.6. Findings from EEG studies

Quantitative EEG and neuropsychological tests were used to investigate the underlying neural processes in dyslexia. Dyslexic children showed increased slow activity (delta and theta) in the frontal and right temporal regions of the brain. These results support the double-deficit theory of dyslexia, and demonstrate that the differences between dyslexics and controls might reflect compensatory mechanisms. Another EEG study demonstrated that a delay in behavioral responses of dyslexic children, which was paralleled by sustained peak theta EEG activity. In addition, controls showed greater theta and beta activation at left frontal sites specifically during the phonological task, whereas dyslexics showed a dysfunctional pattern, and were right-lateralized at these sites in all tasks. At posterior locations, however, in contrast to normal subjects, dyslexics showed greater left lateralization during both phonological and orthographic tasks. This result indicates an altered and difficult phonological transcoding process during verbal working-memory phases of word processing and suggests a deficit in subjects with phonological dyslexia.

2.7. Findings from MEG studies

The left inferior temporoparietal region failed to activate at 200 ms in Finnish-speaking developmental dyslexics compared with controls when silently reading words and pseudowords. During the 400–700 ms post-stimulus onset, the activation in the dyslexics was less than that of the controls; however, the left inferior frontal region was activated, which was not detected in the controls.

Sixty-four dyslexic and 22 normal children from Germany were examined by MEG. The cortical activity during a passive auditory oddball-paradigm was conducted. An event-related magnetic field source evoked by the standard stimulus/ba/ was localized. Reduced hemispheric asymmetry in the localization of the auditory N260m was revealed in dyslexics. There was also a lack of PT asymmetry, and the cortical auditory (language) processing is organized differently in dyslexic subjects than in controls. It was concluded that localization of event-related magnetic field components is a tool that can be applied when investigating cortical variation in dyslexia.

3. Summary and Future Work

All the above studies in dyslexics were based on research in Western countries, using Caucasian subjects. In this context, imaging tools have allowed dyslexia to be examined from a biological point of view using an in vivo approach. This investigates the fundamental nature of this complex disorder more effectively than behavioral and cognitive approaches. Due to differences in MRI scanning techniques, analytical methods and inclusion criteria for dyslexic subjects, however, findings from imaging studies of dyslexics are not always consistent. For example, a meta-analysis failed to detect any cerebellar dysfunction, even though recent imaging studies have identified the cerebellum as the brain region that seems to contain the greatest number of alterations in structure, function and brain biochemical metabolites. Another example of MRS studies also showed inconsistent N-acetylaspartate/choline ratios in cerebellum regions. However, functional studies using fMRI and PET have all pointed to a reduction in activated left brain regions in dyslexics compared with controls, with a compensatory system in the left anterior inferior frontal area; this is in accord with MEG findings. The boundary of specific anatomic structures revealed by MRI could probably be refined by identifying activated regions in functional studies. The combined use of different imaging tools might thus help to clarify the inconsistencies.

Since dyslexia is thought to occur in all languages, it is likely that native Chinese-speaking dyslexics who use a logographic system of reading and writing do exist, and that these individuals will have some, if not all, of the above biological phenotypes. A preliminary investigation is therefore needed to identify whether or not dyslexia, as found in Western
countries, is present in a Chinese population in biological phenotypes.

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