Chapter 7
The Magnocellular Theory of Developmental Dyslexia

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Abstract The late 19th neurological concept of dyslexia had 3 crucial elements: selectively poor reading, with unaffected other cognitive skills and a genetic background. The contemporary 'phonological theory' has undermined the selectivity criterion because all poor readers, dyslexic or otherwise, have phonological problems. Here I argue that the phonological theory is pitched at too high a cognitive level so that it does not illuminate the mechanisms that cause reading problems in dyslexia. Recent genetic and imaging studies have confirmed their biological basis. In children with visual reading problems there is strong evidence that they suffer impaired development of the visual magnocellular (M-) system which is vital for tracking shifts of the focus of visual attention and of eye movements. This can often be ameliorated by viewing text through deep yellow or blue filters because they can facilitate the M- system. Likewise children with phonological problems seem to suffer an analogous impairment of sound sequencing, which can be ameliorated by musical training, particularly in rhythm; whilst those with impaired motor sequencing can often be helped by motor training. Thus in dyslexics the neural sub system which is required for rapid and accurate temporal processing and is distributed throughout the brain, appears to be compromised. This system's 'M-' neurones express a specific surface marker that renders them susceptible to autoimmune attack, and the rapidity with which they have to respond, makes them particularly vulnerable to lack of omega 3 long chain polyunsaturated fatty acids in the diet. But its weaknesses for temporal processing may be balanced by exceptional talents for other kinds of cognitive task.

Keywords Temporal processing · Vision · Magnocellular · Colored filters · Audition · Embodied cognition · Genetics · Handedness · Omega 3s · Dyslexia talents

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7.1 Introduction

In 1896 W. Pringle Morgan described the first case of developmental, as opposed to acquired, "word blindness" in a young boy. "Percy F had not yet learned to read by the age of 14, even though he knew his letters well. In spite of laborious and persistent training, he can only with difficulty spell out words of one syllable; yet the schoolmaster who taught him for some years says that he would be the smartest lad in the school if the instruction were entirely oral." Pringle Morgan also speculated that his inability to read was so remarkably selective and so profound, that he had no doubt that it was due to "some congenital defect". These three crucial elements described by Morgan in Percy, namely inability to read all but the simplest words, yet reasonable intelligence in other respects, and a probable genetic cause, have set the scene for arguments about developmental dyslexia, its definition and causes, that still continue 120 years later.

7.2 The Phonological Theory

Until the 1950s most of those interested in why some children find it so difficult to learn to read, believed that it was due to a failure of visual processing; Kerr, Hinshelwood and Orton called it "word blindness". After all, blind people cannot read ordinary text – reading obviously requires vision. But in 1957 Noam Chomsky published his seminal book, "syntactic structures", which revolutionised linguistics and ushered in their scientific study (Chomsky 1957). This book suggested that humans alone are genetically endowed with an "encapsulated linguistic processor" which mediates a "Universal Grammar" that underlies all languages.

These ideas quickly transformed the study of language and with it, reading. Some children's reading problems were already thought to be hereditary, and christened "dyslexic". So they speedily became attributed to a fault in Chomsky's linguistic processor, and any role for visual processing was abandoned. This meant that the "medical" neurological explanation for dyslexia became less attractive than a linguistic one, and its study passed into the hands of linguistic and educational psychologists. Dyslexia became a linguistic, phonological, problem, not a visual one (Liberman & Shankweiler 1977).

However more recently it has become clear that there is no "special" linguistic processor; human language has developed out of pre-existing gestural and auditory specializations found in our primate ancestors and even in lower mammals and birds. This means that the basis of language comprehension may be found in auditory processing functions far deeper than phonology, in the sound analysis that underlies phonology. Hence today many researchers are trying to identify the faulty auditory processing that causes the phonological problems from which most dyslexic suffer (Goswami, Power, Lallier, & Facoetti 2014; McAnally & Stein 1996).

Indeed we can now view the phonological theory of dyslexia as almost a tautology – merely restating the fact that dyslexics cannot translate visual symbols into the sounds they stand for, rapidly and accurately. The phonological theory does not provide a helpful explanation for dyslexic reading problems because it is set at too high a cognitive level. A more useful explanation would trace the genetic mechanisms that set up the neural processes whose failure leads to the phonological deficits we see; this would explain why children have problems hearing the sounds in a word in their right order and seeing the letters properly.

7.3 Arguments Against the Concept of Dyslexia

This enterprise should carry with it the additional advantage of providing biomarkers of true dyslexia, so that it could be distinguished from other causes of reading failure, such as bad teaching, lack of home support or very low general ability. Unfortunately at present we do not have such identifiers; hence we cannot make this distinction reliably. This has even led some people to want to completely abandon the whole concept of dyslexia as a distinct neurological syndrome (Elliott & Grigorenko 2014).

Here I argue the opposite, that true dyslexia is a genetically based neurological syndrome which leads via aberrant brain development to a spectrum of symptoms characterized by impaired temporal sequencing. These include not only impaired ability to sequence sound streams accurately which underlies the inability to acquire phonological skills, but it also leads to inaccurate sequencing in general: of visual symbols reliably in the right order, hence poor orthography together with wider ramifications: slow learning of the order of letters in the alphabet, misordering the days of the week, months of the year, slow learning to tell left from right, poor sequencing of the actions required for tying shoelaces, poor time keeping etc. (Miles 1993). Elucidating the neural basis of these temporal sequencing problems will enable us to design principled and effective treatments for each child's individual difficulties. It would have the additional advantage of enabling us to establish diagnostic biomarkers to distinguish the neurological syndrome, dyslexia, from other causes of reading failure. In so doing I hope also to re-establish the importance of visual processing in reading.

The basic hypothesis outlined here is that genetic vulnerability early in the growth of the brain in utero in dyslexics impairs development of a system of magnocellular neurones throughout the brain (Stein & Walsh 1997). These cells appear to be a specialized lineage since they all express a common surface signature recognized by selective antibodies such as CAT 301 (Hockfield & Sur 1990). They are adapted for the rapid temporal processing that is required for accurate sequencing in all domains: auditory, visual, proprioceptive and motor.

7.4 Dyslexia Genetics

Paradoxically the one feature for which Pringle Morgan had the least evidence is nowadays the least controversial; this is his conjecture that developmental dyslexia is hereditary. The evidence is now overwhelming. Twin studies have established a heritability of at least 60% (Kirkpatrick, Legrand, Iacono, & McGue 2011; Olson et al. 2013). But note that these estimates leave 40% of reading variance in the hands of environmental factors. Hence immune attack, poor nutrition, family poverty and stress, deficient education, may all contribute to convert a vulnerable genotype into overt dyslexia. Conversely reading problems may not occur if such environmental factors can be avoided. Thus studying populations with high educational standards may actually increase our chances of identifying the real genetic contributions to dyslexia because adverse environmental factors may then be absent (Asbury & Plomin 2013).

Recent advances in molecular genetics have now become so powerful that more than a dozen gene variants (alleles) have now been identified that confer vulnerability to dyslexia. As techniques develop even more genes will undoubtedly emerge, but it is notable that the number discovered so far is very much smaller than those suggested for much more highly hereditary conditions such as schizophrenia, for which nearly 200 gene variants have been fingered (Schizophrenia Working Group of the Psychiatric Genomics Consortium 2014). Perhaps this difference is partly because reading skills can be measured so much more accurately in the phenotype, than can the symptoms of schizophrenia.

7.5 Genes and Brain Development

Normally, during the early development of the brain in utero, the neurones destined to form the surface of the cerebral hemispheres, are born around the ventricles in the center of each hemisphere and then migrate outwards to form its six surface layers. But when Galaburda and colleagues examined histologically the brains of severe dyslexics from the Orton brain bank, now at Harvard University, they found that they were characterized by significant malformations, in particular periventricular heterotopias and surface ectopias, caused either by the neurones failing to migrate at all or migrating to the wrong places (Galaburda, Sherman, Rosen, Aboitiz, & Geschwind 1985).

What has been most exciting in relation to these observations is the discovery that five of the genes which now have the strongest evidence of association with dyslexia (DYX1C1, DCDC2, KIAA0319, KIAA0319L and ROBO1) all affect the development of the brain very early in utero, by helping to control this migration. For example in the rat, if the expression of DCDC2 is prevented in embryonic brain by local electroporation of an inhibitory RNA specific to this gene, many neurones do not migrate at all, but remain stuck around the ventricles where they

were born, forming "periventricular heterotopias" (Rosen et al. 2007). Knockdown of KIAA0319 or KIAA0319L in this way causes less dramatic changes, but local electroporation of the RNAi still impairs successful migration; and this emerges in the rats when they mature being less accurate at discriminating rapid sequences of sounds (Centanni et al. 2014). The same 5 genes are also involved in the formation of the connections between these cortical neurones once they reach their final destination (axon and dendrite outgrowth, guidance and the formation of the synapses between them). Probably they control the expression of neuronal membrane surface proteins, such as those recognized by CAT 301, that direct both their migration and their interconnections.

Another set of genes which has been shown to be associated with dyslexia include FOXP2 and its partner, CNTNAP2. These are particularly important in setting up the frontal cortex language areas and they were already known to be also associated with developmental dysphasia, which often causes dyslexic problems later (Newbury et al. 2011). A further set includes C20ORF3 and MCR5 both of which play important roles in fatty acid metabolism and neuronal membrane structure (Fisher et al. 2002). This relationship with essential fatty acids will be developed later in this paper.

7.6 Comorbidities

One tricky problem with the definition and diagnosis of dyslexia is that there are very few "pure" dyslexics. Clinically there are very large overlaps between the symptoms of dyslexia with most other neurodevelopmental conditions. Indeed it is often largely a matter of chance according to which professional a child sees first, as to whether s/he is diagnosed as having dyslexia, dyspraxia, dysphasia (also known as specific language impairment – SLI), dyscalculia, ADHD, Tourette's syndrome, obsessive/compulsive or autism spectrum disorders, because there is so much overlap in their symptoms. Accordingly, all these conditions tend to be found in the same families and it seems as if it might be better to talk of a spectrum of neurodevelopmental conditions; their overlap is so great that the points at which we categorize one way or another are highly arbitrary. For example up to 50% of children diagnosed with dyslexia would also meet the criteria for ADHD, SLI or dyspraxia (Rice, Smith, & Gayan 2009). These overlaps can probably be explained by shared genetic components. Increasing evidence shows that the same genetic factors may underlie different traits as in the case of the CNTNAP2 which is implicated in SLI as well as many other neurodevelopmental disorders (Graham & Fisher 2013). Equally, genes originally identified for either dyslexia (e.g. KIAA0319) or SLI (e.g., *CMIP*) have been found to contribute to both reading and language measures (Scerri et al. 2011).

None of the alleles so far discovered, or likely to be discovered, contributes individually a substantial component to the total genetic background to dyslexia – dyslexia is usually caused by the interaction of many genes with individually

small effects. Therefore they could not be used for diagnosis as some people have suggested. In fact the main reason for studying the molecular genetics of dyslexia is not for diagnosis, but to attempt to understand more about the mechanisms whereby the gene variants contributing to dyslexia, may do so. This should give us insights about how to help these children's problems.

7.7 Brain Differences in Dyslexia

The ectopias seen by Galaburda et al. in the Harvard Orton brain bank are too small to be seen reliably even with the most powerful current imaging techniques. But magnetic resonance imaging has shown that there are clear anatomical and functional differences between the brains of dyslexics and those of good readers. There is widespread agreement that in the cerebral cortex the left occipitotemporal, occipitoparietal and superior temporal areas have less neuropil in dyslexics compared with good readers whilst the left arcuate fasciculus projecting to the left inferior frontal gyrus (Broca's area) is also less developed. Conversely the right inferior frontal gyrus may be thicker in dyslexics (Richlan, Kronbichler, & Wimmer 2013). However the largest differences are seen in the cerebellum (Rae et al. 2002; Stoodley 2014). Here the right neocerebellum, which projects to the left cortical language areas is smaller in dyslexics and its size predicts how well they perform in both phonological and irregular word tests. It has been argued that most of the anatomical differences in both cortex and cerebellum could in fact be the result of low reading experience rather than its cause. However even though reading experience must play a part, there is now abundant evidence that some of these differences can be detected soon after birth, long before any reading exposure (Hoeft et al. 2011).

7.8 Visual Sequencing and Dyslexia

What we really want to know is how these genetically based brain differences cause the symptoms we see in dyslexic children, so that we can design scientifically based treatments to alleviate them. Here I commence with their problems with visual sequencing because visual processing is obviously the starting point for reading and because many children complain of visual symptoms when attempting to read.

How do we build up representations of the sequence of letters in a word in our visual, orthographic, lexicon? The first step in reading is to learn to recognise individual letters. Actually, dyslexics are initially just as good as good readers at recognizing single letters (Lachmann & van Leeuwen 2007). As this basic process is the same for visual recognition of any object, this shows that dyslexics do not have significant problems with the very earliest stages of visual processing. However, letters do not come singly, but in groups, and their order matters. When children are first learning to read they inspect each letter individually moving their eyes from

letter to letter. They need to know where their eyes were pointing when they fixate on each letter in order to determine its order in the word. Therefore, to remember the letter sequence, they have to learn to associate the visual form of each letter being fixated with signals about where the eyes were pointing at the time.

Many dyslexics fail to achieve this process accurately. Each time we move our eyes, images stream across the retina. Although this is happening physically, we are not usually consciously aware of this motion, because the neural command to move the eyes which is generated in the frontal eye fields in the dorsomedial part of the prefrontal cortex is also sent to the conscious vision centers in the brain, and this is used to blank out the apparent movement. At the same time, the letter seen at the new position of the eyes is automatically associated with that position, using the eye movement signal just before it, together with the image motion signal. Even though we do not see the image motion consciously it enables us to ascertain that the letter now being inspected comes just after the previous one. Thus we are able to keep an account not only of its identity but also of its position in a word. When described and dissected in this clumsy way, the process sounds very complicated and effortful. But most of us learn to sequence not only letters, but also numbers, objects and lists, fast, effortlessly and accurately.

7.9 Magnocellular Neurones

The special image motion and eye movement signals required for these associations are provided by the set of large nerve cells mentioned earlier; they are called visual magnocellular neurones (from the Latin “magnus”, meaning large). The distinctive properties of magnocellular neurones have been most studied in the visual system. The ganglion cells in the retina receive information from the light receptors at the back of the eye and project it via the optic nerves to the lateral geniculate nucleus (LGN) of the thalamus, thence to the visual cortex which is situated on the back of the occipital cortex at the very back of the brain. 10% of these ganglion cells are much larger than the others; these are the magnocellular (M-) ones. They capture information over a very large retinal area – as much as a square millimetre; this is up to 50 x larger than that of the much more numerous parvocellular (P-) ganglion cells. These are much smaller but 10 times more numerous. Being smaller they respond more slowly but they can define the fine detail and colour of objects. Therefore for reading, it is actually the P-system that provides the main input to the brain’s “visual word form area” (VWFA) where letters are identified, and a word’s orthography stored.

The magnocellular neurones cannot define such fine detail and they do not discriminate colors; but because they are larger, they respond and conduct signals much more rapidly than the parvo cells (Schmolesky et al. 1998). This means that they are much more sensitive to temporal changes in the outside world such as flicker and movement. Thus they can rapidly signal changes in the environment and capture attention.

Both the M- and P-ganglion cells project to the lateral geniculate nucleus en route to the primary visual (striate-V1) cortex. But the M- cells project to the ventral magnocellular layers of the LGN whereas the P-cells project to the more dorsal parvocellular layers. This separation is preserved in the onwards projection from the LGN via the optic radiations to layer 4 of the striate cortex. Here magnocells project to layer 4C alpha and parvo cells project to layer 4C beta. But thereafter M and P inputs converge greatly.

7.10 Dorsal and Ventral Visual Pathways

Nevertheless the magnocellular system provides the main input to the "dorsal stream" (see Fig. 7.1) which is one of the two major forward projections from the primary visual cortex in the occipital lobe to the rest of the brain: the dorsal and ventral pathways (Goodale & Milner 1992). The dorsal stream is responsible for the visual guidance of attention and of eye and limb movements. Accordingly the dorsal stream passes to the visual motion sensitive area (MT/V5) which is situated in the middle temporal gyrus at the occipitotemporal junction, and thence to the posterior parietal cortex. But we are unaware of most of what the dorsal stream does, because, serving the visual control of movement, most of its actions are automatic and do not enter consciousness.

The slower ventral pathway passes forward ventrally underneath the occipital and temporal cortex; its main function is to detect the form and color of objects in order to identify them; hence it is the system that is able to identify individual letters and it dominates our conscious visual perception.

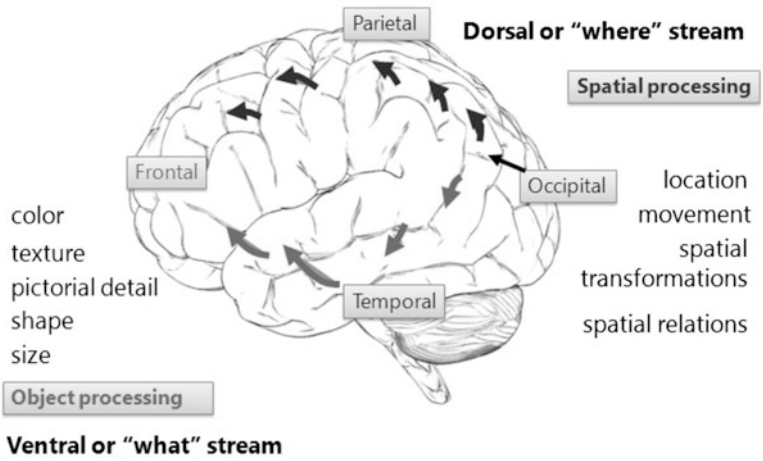

Fig. 7.1 The dorsal and ventral pathways

In the left hemisphere the dorsal stream angular and supramarginal parietal areas are particularly important for reading. They are responsible for associating the visual form of a word with its sound and meaning. An area known as the VWFA situated in the ventral, P-dominated, form analyzing, pathway, receives from and projects back to the supramarginal gyrus. It responds to the visual form of the word (Dehaene et al. 2010). The job of the angular and supramarginal gyri is now thought to be very rapidly to focus visual attention on the letters and their order in words to be read and to associate this visual word form with its pronunciation. The ventral route and VWFA system can recognize individual letters, but they cannot code their precise location, i.e. their order in a word, which is of course vitally important for reading. So the rapid dorsal route sends back to V1 and to the VWFA a signal about where to attend in order to identify letters and thereby to specify their order in a word (Cheng, Eysel, & Vidyasagar 2004). Then if this word is already in the reader's visual lexicon, it can be linked to the sound of the word which is stored in Wernicke's area situated at the back of the superior temporal gyrus. Its meaning can then be grasped by connection via the arcuate fasciculus with Broca's speech area in the inferior frontal gyrus, even if the word is not actually spoken. Thus when learning to read, the angular and supramarginal gyri focus V1 and VWFA attention on individual letters and their order; then these areas link the visual word form with the word sounds stored in Wernicke's area.

7.11 Magnocellular Impairment in Dyslexia

Thus the visual magnocellular input to the dorsal attentional stream appears to play a crucial role in reading; so the accumulating evidence that it is poorly developed in many dyslexics has especial significance. Although the theory that a visual M- cell deficit underlies visual problems in reading is still highly controversial, over 90% of the studies made over the last 10 years that have sought evidence for M- impairment in dyslexics have found it in at least some.

7.12 Subcortical M- system

Strictly speaking, visual M- cells can only be distinguished from P- cells with complete certainty in the subcortical visual system because only in the LGN are they anatomically separated from the P- system. Thereafter magno and parvo systems converge and interact strongly. Hence the only way to be sure that deficits in dyslexics are confined to the M- system is to use stimuli that are selectively processed by the subcortical M- neurones in the retina and LGN. Skottun (2015) has made this point repeatedly. But even if we confine ourselves to the M- system in the retina and LGN the evidence for M- impairment in dyslexics is strong.

7.13 Contrast Sensitivity

Perception of low contrasts in the environment is set by the properties of M-ganglion cells in the retina. The simplest way of assessing their variability in individuals is to measure subjects' sensitivity to the contrast of coarse gratings (spatial frequency <1 cycle per degree) flickered at high temporal frequencies >10 Hz, since M- cells respond much more sensitively to this combination. Since Lovegrove, Heddle, and Slaghuis (1980)'s first report, there have been many studies that have confirmed that the contrast sensitivity (CS) of many dyslexics is lower than that of controls', particularly at the low spatial and high temporal frequencies mediated by the M- system (Bednarek & Grabowska 2002; Cornelissen, Richardson, Mason, Fowler, & Stein 1995).

Interestingly, at the M- cell threshold such gratings appear perceptually twice as fine; this is known as the spatial frequency doubling illusion. It is thought to depend on the non-linear properties of the M- cells (Maddess, James, Goldberg, Wine, & Dobinson 2000). Although the details of this dependence have been contested (White, Sun, Swanson, & Lee 2002), nevertheless, whether or not the grating appears twice as fine, it is accepted that as the contrast of such a grating is decreased, the point at which observers first see the pattern is determined by their retinal M-cells. Dyslexics have been consistently shown to require more contrast to see the gratings, confirming their M- cell weakness (Pammer & Wheatley 2001).

M- cells are responsible for timing visual events, so their sensitivity in individuals can also be assessed by various timing tests. For example Lovegrove et al. (1980) tested people's ability to detect a discontinuity (a temporal "gap") in the display of a low contrast, low spatial frequency grating; they found that dyslexics needed a much longer gap to perceive it than the controls. When the frequency at which a light is flickered is increased, above around 30× per second the M- system can no longer respond fast enough and the light appears to cease flickering. This is the "critical flicker fusion frequency". Chase and Jenner (1993), Mason, Cornelissen, Fowler, and Stein (1993), Felmingham and Jakobson (1995) all showed that this frequency tends to be lower in many dyslexics.

7.14 Lateral Geniculate Nucleus

Further strong support for the idea of M- cell impairment in dyslexics came from further post mortem histological studies of dyslexic brains from the Orton dyslexia brain bank at Harvard University (Livingstone, Rosen, Drislane, & Galaburda 1991). They found that the M- layers in the LGN in the dyslexic brains were selectively impaired. Not only were the cells 25% smaller in the dyslexic as compared to control brains, but also the M- cells were not confined to their proper M- layers; many had mismigrated into the adjacent konio and parvo layers of the LGN. As we have seen this theme of mismigration relates to at least 5 of the genes that have been associated with dyslexia.

Recently the spatial resolution of MR imaging has been improved considerably with the introduction of stronger 7 Tesla magnets, so that the structure of the LGN can now be visualized in more detail (Denison, Vu, Yacoub, Feinberg, & Silver 2014). Galaburda's observations were made in only 5 dyslexic brains post mortem, but 7 Tesla MRI has confirmed in 13 young dyslexics that their left LGN, was significantly smaller in volume than controls'. This difference was confined to the magnocellular layers in the 13 dyslexics, so that their LGNs also differed in shape (Giraldo-Chica et al. 2015).

7.15 The Cortical Dorsal "Where" Pathway

The dorsal stream (see Fig. 7.1) is dominated by visual M- input as we have seen. Abnormalities have been found in dyslexics at every level in this stream from the prestriate visual motion area (MT/V5), via the posterior parietal cortex to the ultimate goal of both M- and P-systems, the prefrontal cortex (Rao, Rainer, & Miller 1997).

90% of the visual input to the motion sensitive neurons in the middle temporal visual motion area (V5/MT) is provided by the M- system and only 10% comes from other sources. One way of assessing the sensitivity of these MT neurons in individuals is to measure their responses to visual motion in "random dot kinematograms" (RDKs). Clouds of dots moving in the same direction, "coherently", are progressively diluted with noise dots moving in random directions until the subject can no longer detect any coherent motion in the display. This threshold therefore defines that individual's motion (visual dorsal stream) sensitivity. Several researchers have shown that this is reduced in many dyslexic individuals (Cornelissen et al. 1995; Downie, Jakobson, Frisk, & Ushycky 2003; Hill & Raymond 2002; Samar & Parasnis 2007; Talcott, Hansen, Assoku, & Stein 2000). Other work has similarly shown reduced velocity discrimination (Demb, Boynton, Best, & Heeger 1998; Eden et al. 1996) and elevated speed thresholds for motion-defined form (Felmingham & Jakobson 1995) in dyslexics.

People with low motion sensitivity can still be adequate readers however (Skoyles & Skottun 2004), so that weak M- function by no means predestines a child to reading failure. Other vulnerabilities must contribute to dyslexia as well. Nevertheless, individual differences in motion sensitivity explain over 25% of the variance in reading ability (Witton et al. 1998). In other words, individuals' dorsal stream performance, which is dominated by M- cell input, plays an important part in determining how well visual reading skills develop, and this is true of everybody, not just those diagnosed with dyslexia.

The posterior parietal cortex (PPC) receives its main visual input from V5/MT; this input plays a crucial role in guiding visual attention, eye and limb movements (Cheng et al. 2004). Dyslexics have been found to be worse than good readers at cueing visual attention (Kinsey, Rose, Hansen, Richardson, & Stein 2004), visual

search (Iles, Walsh, & Richardson 2000), visual short term "retain and compare" memory (Ben-Yehudah, Sackett, Malchi-Ginzberg, & Ahissar 2001) and attentional grouping in the Ternus test (Cestnick & Coltheart 1999). These findings confirm that dorsal stream function is often impaired in dyslexia. Many of the studies mentioned above incorporated control tests for parvo function, such as visual acuity or color discrimination; and dyslexic populations usually proved to be as good or better at these. This confirms that the tests assess dorsal stream function specifically, rather than the subjects' attending to the stimulus or the difficulty of the task.

7.16 Cross Modal Attention

Dyslexics show not only slow deployment of visual attention but they also show difficulty shifting their attention between sensory modalities, for instance between vision and hearing. But it seems that such "sluggish attention shifting" (Hari & Renvall 2001) is worst when dyslexics shift their attention from the visual to the auditory modality, rather than vice versa (Harrar et al. 2014). Thus dyslexics are not only slower, but particularly slow when they have to attend to a visual stimulus and shift to an auditory one, as when reading.

Taken together all this evidence suggests that dyslexics' poor dorsal stream performance can be mainly attributed to M- system weakness even in the presence of robust parvocellular function.

7.17 Eye Movement Control by the Dorsal Stream

Normally the dorsal stream not only directs visual attention to a target but also subsequently redirects the eyes towards it. Hence numerous studies have found not only that the direction of visual attention is disturbed in dyslexics (Facoetti et al. 2010; Vidyasagar 2004), but also that their eye control during reading is poor (Eden, Stein, Wood, & Wood 1994; Kirkby, Webster, Blythe, & Liversedge 2008). However it is strongly argued that these abnormalities are not a cause of reading problems but rather that they are the result of not understanding the text; hence the person has to make longer fixations and more reinspections of previous letters to try to decode words (Rayner 1985). But poor eye control in dyslexics has also been demonstrated in several non-reading situations, using tests of fixation stability (Fischer & Hartnegg 2000) and of smooth pursuit and saccadic control (Crawford & Higham 2001), implying that poor eye control comes first and may be a significant cause of reading problems.

7.18 Event Related Potentials

Recording averaged electroencephalographic (EEG) potentials in response to a moving, low contrast visual target provides a more objective measure of cortical dorsal stream processing than psychophysical techniques. Of recent visual event-related potential (ERP) studies in dyslexics the great majority have either confirmed the original observation by Livingstone et al. (1991) that dyslexics have weaker responses to moving, low contrast, targets than good readers (e.g., Kuba, Szanyi, Gayer, Kremlacek, & Kubova 2001), or they have found that dyslexics show slower, smaller and spatially abnormal visual attentional ERP responses. These observations are in line with a multitude of psychophysical results showing deficient allocation of visual attention (Hari & Renvall 2001; Lallier et al. 2011).

7.19 Criticism of Magnocellular Theory

Nevertheless even though the vast majority of new research that has looked for visual magnocellular deficits in dyslexics has confirmed that at least some dyslexics demonstrate them, the idea has not gained full acceptance. Skottun, while not ruling out that dyslexics may have some kind of visual deficit, has written over 30 critiques of the idea that these involve the M- system (Skottun 2016). But the only one of these which reports new research findings (Gross-Glenn et al. 1995) actually partially supports the magnocellular theory! Skottun's main point is that standard tests of visual magnocellular function do not entirely distinguish M- from P-inputs to the dorsal stream. Nevertheless, since the M- system provides 90% of the input this probably not a substantial problem.

In summary so far, there is now overwhelming evidence that many dyslexics have impaired development of the visual magnocellular system, so that their visual temporal processing is impaired. Because this hinders their ability to associate each letter they inspect with its position in a word, their sequencing of the letters in a word is slow and inaccurate. The degree of this deficiency predicts the severity of their visual reading difficulties. What this means in practice is that we can in principle distinguish visual dyslexia from other causes of reading problems simply by looking for symptoms of visual magnocellular impairment.

7.20 Visual Difficulties in the Classroom

Teachers should therefore always ask children with reading difficulties whether they have any visual symptoms when attempting to read. Do letters appear to blur, or split into two, or move around when you try to read? Does reading make your eyes or your head ache? Further investigations for research, such as measuring

eye fixation, convergence and accommodation, recording brain waves evoked by moving or flickering stimuli or functional MRI investigations, may then confirm their visual temporal processing problems, but these are not essential. Asking the right questions about any visual problems is.

7.21 Yellow Filters

The idea that viewing text through colored filters may help some children to overcome their visual problems and learn to read is highly controversial and sullied by commercial interest and wild claims. Part of the problem is that not all reading problems are due to visual deficits, so that the contention that all children can be helped by the right color is easy to refute. However the magnocellular theory leads to a rationale for supposing that particular colored filters may help some children.

Visual magnocells receive most of their input from the red (long wavelength) and green (medium wavelength) color receptors (cones) in the retina. Yellow light combines both those wave lengths. So magnocells are best stimulated by yellow light. Looking at text through yellow filters reduces the amount of blue light entering the eye, and causes the pupils to dilate. So the amount of yellow light falling on the retina increases and retinal magnocells are selectively activated. If the main visual problems that the child has are that letters look blurry and out of focus and they tend to split into two, which symptoms are often associated with a reduced vergence range, viewing text through yellow filters often boosts their magno input sufficiently to help them overcome these problems; hence their reading improves rapidly. Ray, Fowler, and Stein (2005) found that giving yellow filters to children with these symptoms improved their accommodation and convergence, and their reading progress tripled thereafter.

7.22 Blue Filters

However, yellow filters only appear to help about half of dyslexic children with visual reading symptoms. Another subset who complain mainly of eye and head aches and of letters moving around and over each other are more likely to be helped by viewing text though deep blue filters. These cut out most of the long wavelengths that directly stimulate magno cells. Nevertheless their reading may improve even more than in those who benefit from yellow (Clisby et al. 2000). They probably work in a very different way.

7.23 The Hypothalamic Clock

The blue filters optimally excite a newly discovered set of ganglion cells in the retina which do not contribute directly to conscious vision (Hankins, Peirson, & Foster 2008). Instead, they feed into the hypothalamic suprachiasmatic nucleus; this is where the body's internal "clock" which times out our daily rhythms is situated. The blue input is required to entrain the clock to seasonal changes in day length, so that we wake up earlier in summer and later in winter. On arousal by blue light the first neural system that is woken up is the dorsal attentional and visuomotor stream, in order to prepare us for rapid responding. Hence blue filters probably help these children by enhancing their arousal and this helps them to focus their attention more accurately, in particular by helping them to keep proper track of their eye movements, so that letters cease to appear to move around.

Not surprisingly therefore, we found that the blue filters not only improve arousal, concentration and reading, but they also reduce difficulties with getting to sleep at night because they help to improve synchronization of the body clock. What we didn't expect as well however, was that they also had a dramatic effect on these children's headaches. Even more surprising was that a mother with recurrent migraines, on noting that her son's headaches had greatly improved, began wearing blue filters herself; and her migraines disappeared. We have since found that if blue filters improve sleep patterns, they will often also improve headaches.

To summarize so far, the visual magnocellular system is crucial for reading. It is responsible for signaling the moments in time when visual events occur. Each time the eyes move, visual magnocells signal the command to move and also the resultant movements of the letters across the retina, so that these can be discounted, and the letters kept stationary. Thus, if the magnocell responses are weak, as in many dyslexics, letters may appear to blur or move around, making reading very difficult. But now we know that using either yellow or blue filters we can often help these children make the letters keep still.

With such a strong case, it may seem odd that the magnocellular theory is not yet generally accepted. However because phonology lies at the heart of reading, phonological impairments are fairly easy to show in most dyslexics, whereas the visual magnocellular impairment may be mild and not detectable at all in some. This may either be because it is absent and auditory problems predominate or too mild to be demonstrated using current techniques.

Nevertheless visual M- weakness probably contributes also to phonological problems. Morais and colleagues found that not until children, and also illiterate adults, learn that words can be represented as a sequence of separate letters, do they learn that they can also be broken down and heard as separate sounds (Morais, Cary, Alegria, & Bertelson 1979). Hence successful acquisition of phonological skill at the phonemic level probably depends to a large extent on first learning how a word can be visually represented orthographically. Indeed Chinese who have learned only to read Chinese characters, not alphabetic scripts, are not able to parse words down to the phonemic level until they learn an alphabetic script

(Read, Yun-Fei, Hong-Yin, & Bao-Qing 1986). In alphabetic scripts therefore, if orthographic analysis is compromised by weak visual magnocellular function, then acquiring good phonemic skills will naturally be secondarily affected also. This may help to explain the apparently paradoxical result of some studies; namely that the visual impairment in dyslexics correlate not only with measures of their visual/orthographic ability, but also with their phonological performance (e.g., Cestnick & Coltheart 1999).

7.24 Auditory Problems

However it is clear that some dyslexics have no visual reading difficulties at all. Particularly in dyslexics who have a background of speech and language delay, auditory analysis rather than visual sequencing inefficiency, may be their main problem (Bradley & Bryant 1978; Hornickel & Kraus 2013; Manis et al. 1997).

In order to break down a word into a sequence of phonemes, the auditory system needs to perform a series of operations analogous to those for visual sequencing. First the continuous speech sound needs to be broken down into words, then syllables and then phonemes. This is accomplished mainly by tracking changes in the amplitude and frequency of the sounds, also known as amplitude and frequency modulation (AM & FM). Words and syllables are marked by "stresses", mainly amplitude peaks. In English often the first syllable is the primary stress. Speaking rate is about two words per second, syllable rate is about five per sec and the spoken phoneme rate is about ten per sec. Within each phoneme the amplitude and frequency changes that enable us to distinguish them occur at up to 50 times per sec.

There is a system of large neurones in the auditory system, analogous to the visual magnocells, which is specialized for tracking these sound modulations in real time. They can follow AM and FM frequencies from less than 1 to 100 Hz. Tallal was the first to suggest that developmental dysphasics may be poor at the rapid auditory temporal processing that is required for such discrimination of speech sounds (Tallal & Piercy 1973) and she subsequently showed that many dyslexics show a similar impairment. In the last few years there have been many more studies testing such basic auditory processing capabilities in dyslexics. Almost all have shown abnormalities in at least some dyslexics that could help to explain their phonological weaknesses (Hämäläinen, Salminen, & Leppänen 2013; McAnally & Stein 1996). Indeed auditory sensitivity to frequency and amplitude modulations has been shown to account for nearly 50% of individual differences in phonological skill (Witton, Stein, Stoodley, Rosner, & Talcott 2002).

Unlike in the visual system, the auditory system does not have an anatomically separate magnocellular pathway. Nevertheless it does contain large cells that seem to be specialized for temporal processing. These large neurones could be termed magnocells because, like visual magnocells, they may be recognised by M- specific antibodies, such as CAT 301 (Lurie, Pasic, Hockfield, & Rubel 1997). The detection of the frequency and amplitude changes in real time that underlies phonological

processing, seems to be mediated by these auditory magnocells. The development of auditory M- like cells may also be impaired in dyslexics. For example in dyslexic brains, like those in the dyslexic LGN, the magnocellular division of the auditory medial geniculate nucleus was found to contain fewer large cells on the left (Galaburda, Menard, & Rosen 1994). Impaired development of large M- like cells in the auditory system might therefore also underlie dyslexics' problems with acquiring good phonological skills. Interestingly deficient auditory temporal processing mediated by the auditory M- system is often accompanied by poor visual magnocellular function, suggesting a common aetiological causation, maybe involving immune recognition of the CAT 301 M- specific antigen (Talcott et al. 2000).

However not all dyslexics who show phonological problems can be shown to have either auditory or visual weaknesses; thus these are neither necessary nor sufficient to cause dyslexia. Some have argued from this that they cannot be considered causal at all (Ramus, Pidgeon, & Frith 2003). But this is like saying that because smoking is neither necessary nor sufficient to cause lung cancer it can never cause it – patently false. The probability is that impaired auditory and visual temporal processing are important, but not the only, causes of impaired phonological processing.

7.25 The Cerebellum

Impaired motor control is another potential cause of some dyslexic and dyspraxic problems. The cerebellum is the brain's autopilot responsible for automatizing motor skills. Since accurate timing of sensory feedback and motor outflow is an essential requirement for this function, the cerebellum receives a rich input from visual, auditory, proprioceptive and motor magnocellular systems (Stein 1986). The cerebellum plays an essential role in maintaining balance. Hence many people have studied balance stability in dyslexics. Almost all have confirmed that they show deficits (Fawcett, Nicolson, & Dean 1996; Gouleme, Gerard, & Bucci 2015; Stoodley, Fawcett, Nicolson, & Stein 2005). More direct evidence has come from measuring cerebellar morphology by magnetic resonance imaging (MRI) (Rae et al. 2002; Stoodley 2016). In fact differences between dyslexics and controls are seen in the cerebellum more consistently than any other part of the brain (Eckert et al. 2005).

Another way of strongly activating the cerebellum is by mean of visual tracking tasks (Miall, Weir, Wolpert, & Stein 1993). Nicolson et al. (1999) showed that cerebellar activation during learning to track a novel trajectory is greatly reduced in dyslexics. Thus in summary, there is now a great deal of evidence that cerebellar function is impaired in dyslexics, and this provides yet further indirect evidence for magnocellular involvement in dyslexic problems (Stoodley & Stein 2011).

7.26 Embodied Cognition

When reading, brain activity occurs not only in the classic "language areas" such as Wernicke's and Broca's areas, but also in areas which control movement. Evolutionarily our cognitive skills, particularly language, seem to have developed from neural representations of gestural movements (Corballis 2003). Hence cognitive reasoning probably engages subliminal activation of the motor neural systems that would participate in such gestures if they were actually produced. Thus cognition is "embodied". Hence it is reasonable to postulate that training children's awareness, "mindfulness", of how they control their own movements might improve their cognitive skills.

We have therefore helped to develop a new classroom physical training program, called Move4words, based on embodied cognition, and administered it to pupils aged 7–13 years in 10 mainstream UK schools. We showed significant improvements in reading, writing and maths performance in those given the program compared with pupils receiving normal teaching. Struggling pupils performing in the lowest 20 percentile did particularly well (Hedges' g = 0.86). Their performance gains were maintained for at least 1 year after the end of the intervention (McClelland, Pitt, & Stein 2014).

7.27 A General Magnocellular System for Temporal Processing?

Magnocells with rapid temporal processing, "transient" sensitivity and expressing M- cell surface antigens such as that recognized by CAT 301, are found throughout the whole nervous system (McGuire, Hockfield, & Goldman-Rakic 1989; Mueller, Davis, Sovich, Carlson, & Robinson 2016). As we have seen, when visual and auditory transient (M- cell) sensitivity are measured in the same individuals they tend to correlate with each other, suggesting that both might be under the same genetic neurodevelopmental control (Talcott et al. 2000). Therefore one can speculate that perhaps all the visual, auditory, memory and motor temporal processing impairments that are seen in dyslexics may be due to underlying weak development of this generalized, CNS wide, pansensory, transient processing, magnocellular system (Hari & Renvall 2001; Stein 2001). This impairment might affect different individuals more in one system than another, idiosyncratically, so that one dyslexic might suffer mainly visual problems, another mainly auditory, and a third mainly motor symptoms; he might be termed "dyspraxic".

One can take this idea a stage further. Ramus showed in a small group of well compensated undergraduate dyslexics that only a few of them had demonstrable auditory, visual or motor problems, whereas despite their compensation most could still be shown to have residual phonological difficulties (Ramus et al. 2003). So he attributed the latter to a higher level developmental abnormality, perhaps in the

angular gyrus (Ramus 2004). Since the angular gyrus is an important node in the M- cell dominated dorsal visuomotor stream; clearly this higher level impairment might also be caused by impaired magnocellular connectivity.

7.28 The Immune System

Carla Shatz and her colleagues have shown that the development of magnocells, at least in the visual system and in the hippocampus, is regulated by the Major Histocompatibility Complex (MHC) cell recognition system which is the main controller of the immune system (Corriveau, Huh, & Shatz 1998). Most of the genes controlling the MHC system reside on the short arm of chromosome 6. It is unlikely to be a coincidence that among genetic studies of dyslexic families the most widely replicated linkage to reading problems is to just such sites on the short arm of chromosome 6 (Francks et al. 2004). Close to the MHC system genes are located the KIAA0319, DCDC2 and NRSN1 genes which are not only associated with dyslexia but also, as we have seen, involved in cell/cell signaling, helping to control the developmental migration of neurones and their interconnections (Paracchini et al. 2006).

Thus the immune system probably plays an important role in the development of "magnocellular" timing systems all over the brain. It has been known for some time that dyslexia and related neurodevelopmental conditions are associated with an increased incidence of immunological abnormalities, in the children or their families (Bashir & Al-Ayadhi 2015; Galaburda 1993; Jariabkova, Hugdahl, & Glos 1995; Lahita 1988; Warren et al. 1990).

The developmental disorder, arthrogryposis multiplex congenita is caused by maternal antibodies attacking the fetal isoform of the acetylcholine receptor (Riemersma et al. 1996). Jacobson, Polizzi, Morriss-Kay, and Vincent (1999) showed that this condition could be reproduced in mice by maternal-to-fetal transfer of the human maternal IgG antibodies. We therefore postulated that maternal antibodies might likewise contribute to the impaired brain development seen in dyslexia and other neurodevelopmental disorders. To test this hypothesis, we obtained sera from mothers of children with dyslexia and injected them into pregnant mice to see if the sera would affect the development of their pups. As we have seen, both functional and structural changes have been described in the cerebellum in dyslexia (Fawcett et al. 1996; Nicolson et al. 1999; Rae et al. 1998), so we particularly focused on alterations in cerebellar function. The pups exposed in utero to the serum of the women who had two or more dyslexic or autistic children, showed deficits in motor tests which correlated with lower cerebellar neuronal choline and creatine levels. Thus it seems that maternal antibodies can contribute to dyslexic deficits, and possibly to other neurodevelopmental disorders.

7.29 Handedness

From the very first descriptions of either acquired or developmental dyslexia, the idea that it might be related to abnormal lateralization of the cerebral hemispheres became widely accepted, mainly because it was already known that speech and language skills were centered in the left hemisphere, which was thought to be the explanation why the majority of people wrote with their right hands. Hence it was natural to conclude that among individuals with dyslexia left handedness might be more frequent than expected. The truth has turned out to be rather more complex than this, but the basic association between anomalous laterality and dyslexia still stands. Imaging has shown that handedness and hemispheric lateralization for speech are not directly related however. In most left handers speech is still controlled mainly by the left hemisphere, and most dyslexics are still right handed (Herve, Zago, Petit, Mazoyer, & Tzourio-Mazoyer 2013). Nevertheless dyslexics tend to be less skilled with either hand, therefore they are less strongly either left or right handed than typically developing children, but overall they are no more likely to be left handed for writing.

Nevertheless magnetic resonance imaging experiments have proved unequivocally that atypical brain hemispheric specialization is indeed associated with dyslexia. The left planum temporale is a structure at the back of the temporal lobe which is known to be important for the comprehension of speech. In typically developing children it is larger on the left than in the right hemisphere; but in dyslexics the right side is larger than normal, so that their hemispheric asymmetry is reduced (Leonard & Eckert 2008).

In typically developing children a network of left sided structures is activated when reading. These include the left anterior fusiform gyrus underneath the occipital lobe, the angular and supramarginal parts of the left posterior parietal cortex and the left inferior frontal gyrus, but in dyslexic children these areas activate much less during reading, whereas homologous areas in the right hemisphere activate more, again leading to reduced asymmetry (Zhao, Thiebaut de Schotten, Altarelli, Dubois, & Ramus 2016). Of course these experiments cannot by themselves tell us whether the reduced asymmetry is a cause or consequence of their impaired reading, but recent studies in young infants before reading onset show similar reduced asymmetries (Lyytinen, Erskine, Hämäläinen, Torppa, & Ronimus 2015). This suggests strongly that the anatomical differences precede reading failure and therefore probably contribute to their causation.

It used to be thought that hemispheric asymmetry is uniquely human. But it is now known that left/right asymmetries are found throughout the animal kingdom. For example marine mammals show stronger left hemisphere controlled right turning biases than even man's right handedness; and left sided dominance for vocalizations is found in frogs, birds, rats and mice. Two thirds of our closest relatives, chimpanzees are right handed. Conversely a right hemisphere/ left visual field dominance for detection and expression of emotions, visuospatial skills and attention is present in all primates so far investigated, suggesting an evolutionary

provenance extending back at least 50 million years. Thus the origin of hemispheric specialization greatly predates speech. It probably relates to early specialization of the left hemisphere for correctly sequencing actions, hence gestures which evolved into speech, whilst the right hemisphere became specialized for the holistic allocation of attention (Corballis 2009).

However the molecular basis of these asymmetries is almost unknown. We have carried out a genome-wide association study meta-analysis for a quantitative measure of relative hand skill in individuals with reading disability (Brandler et al. 2013). In dyslexics the strongest association was found with the PCSK6 gene. But this locus is not associated with relative hand skill in the general population. As PCSK6 is known to regulate NODAL in the development of left/right (LR) asymmetry in mice, we developed a novel approach to GWAS pathway analysis, using gene- set enrichment to test for an over-representation of highly associated variants within the orthologs of genes whose disruption in mice yields LR asymmetry phenotypes. Four out of 15 LR asymmetry phenotypes showed an over- representation. We replicated three of these phenotypes; situs inversus, heterotaxia, and double outlet right ventricle, in the general population. Thus it seems that handedness is a polygenic complex trait controlled in part by the molecular mechanisms that establish LR body asymmetry early in development, but particularly in dyslexics.

7.30 Omega 3 Long Chain Polyunsaturated Fatty Acids

One gene, not implicated in neuronal migration early in development, but strongly linked to dyslexia, is the MCR5 gene situated on Chromosome 18 (Scerri et al. 2011). This gene is of great interest because it is known to be involved in stress, production of sebum and pheromones, obesity, immunity and inflammation. What links all these functions is probably its role in the metabolism of fatty acids. It encodes one of the huge family of seven-pass transmembrane G protein-coupled receptors that stimulate cAMP signal transduction. The encoded protein is a receptor for melanocyte-stimulating and adrenocorticotropic hormones and it is one of the few of these MSH receptors that is expressed in the brain; it is particularly strongly expressed in the retina and in the hypothalamus which explains its role in fatty acid and metabolic control and obesity. Although this has not been directly demonstrated, its functions in fatty acid metabolism, the retina, and immunity together with its association with dyslexia suggests that it may be particularly important in magnocellular function.

A crucial component of all excitable cell membranes, particularly magnocells because of their very large surface area, is a unique long chain omega 3 polyunsaturated fatty acid (LCPUFA), docosahexaenoic acid (DHA). This has exactly the right physical and electrostatic properties in the membrane lipid bilayer to maintain the separation of charges underlying the neuronal resting membrane potential. More importantly, due to its flexibility, it facilitates rapid reorganization of the membrane

when ionic channels open and close to allow the ionic currents that cause action and synaptic potentials to occur. Thus if it is replaced in artificial membranes by saturated fats of the same physical length, channel opening and closing times can be prolonged by up to ten times. The main source of DHA comes from eating oily fish because humans cannot synthesize LCPUFAs from scratch. But the modern Western diet contains very little fish and 75% of teenagers in the UK eat no fish at all. Our brains contain 5 g of DHA but we lose about 5 mg per day. So this has to be replaced if magnocellular membranes are going to function optimally. Yet the majority of the population has dangerously low levels of DHA together with another important omega 3 LCPUFA, eicosapentaenoic acid (EPA). In recent studies of children from disadvantaged backgrounds, discussed later, we found that their red blood corpuscle levels of DHA & EPA were less than 1/2 that regarded as optimal.

These considerations encouraged us to investigate whether giving children with reading problems omega 3 DHA & EPA supplements might help them to improve their magnocellular function and with it their reading. In double blind randomized control trials my colleagues have shown that this is indeed the case (Montgomery, Burton, Sewell, Spreckelsen, & Richardson 2013; Parletta, Niyonsenga, & Duff 2016; Richardson, Burton, Sewell, Spreckelsen, & Montgomery 2012; Richardson & Montgomery 2005). After 3 months of supplementation and without any extra reading help, children with initially low reading ability and very poor diets given extra DHA improved their reading by 9 months on average.

7.31 Antisocial Behavior

Another change we observed after improving the diet of these poor readers, noticed also by their teachers, was that they were much less prone to fight each other in the playground. This was probably not just because they were learning to read more easily, but because they were more sociable and less easily angered. In 1942, Hugh Sinclair, a pioneer in human nutrition, helped to persuade the wartime British government to supplement the diet of all pregnant mothers and their infants with cod-liver oil; along with Vitamins A & D, this contains omega 3 LCPUFAs. He had speculated that among other ills, poor diets could lead to antisocial behavior (Sinclair 1956). Since that time, ample evidence has accrued that he was right; and improving diet can reduce such antisocial behavior (Corrigan et al. 1994; Gesch, Hammond, Hampson, Eves, & Crowder 2002; Hamazaki et al. 1996; Hibbeln et al. 1998; Rutter, Giller, & Hagell 1998).

I have postulated that the link between deficient omega 3 LCPUFA levels and antisocial behavior is that the temporal processing mediated by magnocellular neurones is crucially important not only for reading but also for social communication-tracking facial expressions, anger, pleasure etc. Hence I was not at all surprised to find that our poorly reading children's behavior improved with the omega 3s they were receiving. We have therefore carried out a more formal trial in which we showed that supplements of omega 3s, minerals and fatty acids not only raised

the omega 3 levels in the blood of poorly fed teenagers, from initially dangerously low values, but it also did improve their sociability (Tammam, Steinsaltz, Bester, Semb-Andenaes, & Stein 2015). We have also carried out a large trial giving 750 prisoners in 3 jails in the UK capsules containing either fish oils, vitamins and minerals or placebo for 4 months; this also confirmed that this improvement in their diet improved their behavior significantly.

7.32 Dyslexia Talents

Dyslexia is extremely common; estimates of its prevalence range from 5 to as high as 17%. The precise figure depends on exactly how it is diagnosed. Such high numbers in a strongly hereditary condition suggests the operation of a "balanced polymorphism". This is when an apparently deleterious version of a gene is retained in the gene pool at relatively high rates because as well as its disadvantage, it confers a selective advantage. In the case of reading this selective advantage might have been overwhelming, until recently when inability to learn to read became a general disadvantage. What might that advantage have been?

More artists than you'd expect by chance (Everatt, Steffert, & Smythe 1999; Wolff & Lundberg 2002), and architects, engineers and entrepreneurs (Logan 2009) are dyslexic. But this doesn't prove that dyslexics are inherently more artistic or entrepreneurial. Maybe art, architecture and risky business attract dyslexics simply because there's less reading involved in these pursuits. However this argument is not very convincing. Art and architectural courses include art history which requires a great deal of reading. Engineering and business also need a fair amount of reading.

Unfortunately scientific research on the talents of people with dyslexia is rare, even though its possible advantages are widely discussed. Because it is widely known that the left hemisphere is specialized for speech and language, it is often argued that dyslexics have "stronger right hemispheres" and that this may compensate for their poor reading skills. It may endow them with exceptional artistic and creative talents, and this may be what keeps the "dyslexia genes" in the human gene pool. However such conjectures are very difficult to substantiate scientifically. Artistic talent is difficult to measure; creativity, whether in the Arts, engineering or business, is very subjective. For every study that claims talents in dyslexics there is another that disputes them. This may result from an overly simplistic and crude conceptualization of right hemispheric function.

To settle whether dyslexics have inherently superior right hemisphere skills for art etc., first we would need to agree what general skill a right hemisphere advantage would provide them with and then agree a test or selection of tests which will reliably measure that skill. We would then need to administer them to a large group of dyslexics compared to matched controls. Despite the importance of answering this question, it has proved impossible to raise funds to do such a study. In the meantime however there have been a few small studies that point to dyslexics indeed showing superiority in some tasks likely to involve the right hemisphere. These are

tasks that do not depend on sequential local temporal processing (bit by bit), but do call on static global holistic skills. Thus dyslexics tend to show superior ability in tasks calling on the visual parvocellular system, suggesting that magnocellular weakness in dyslexics may be compensated by parvocellular strength, during the competition for connectivity that occurs during the early development of the brain. These P- strengths include higher sensitivity to stationary high spatial frequency gratings (Bednarek & Grabowska 2002), better blue/yellow color discrimination (Dain, Floyd, & Elliot 2008), quicker identification of "impossible figures" (von Károlyi, Winner, Gray, & Sherman 2003). The latter requires ability to distribute current attention over a wider area, a skill characteristic of dyslexics (Geiger & Lettvin 1987) which may be mediated by greater long range connectivity of the p-system, particularly in the right hemisphere. This aspect of dyslexics" attention, often treated as a disadvantage, may explain their superiority in virtual reality visuospatial localization (Attree, Turner, & Cowell 2009).

In summary, although there is much dispute it seems likely that dyslexics do demonstrate superior skills in certain kinds of visuospatial tasks, in particular those that depend on wide ranging, holistic appreciation of a scene rather than moment to moment sequential processing.

7.33 Conclusion

Since Livingstone et al. (1991) first showed a selective visual magnocellular deficit in dyslexic people, the great majority of the neuroanatomical, electrophysiological and psychophysical evidence has supported the hypothesis that a significant proportion exhibit a visual magnocellular weakness. Analogous neural systems have been demonstrated in the auditory, somatosensory, motor systems, indeed throughout the whole brain, which are characterized by their expression of particular surface signature molecules. Many of these magnocellular temporal processing systems have also been shown to be impaired in some dyslexics. This suggests that a fundamental disorder of temporal processing mediated by magnocellular systems throughout the brain may underlie all the manifold and variable symptoms of dyslexia. The particular areas of the brain most affected as a result of genetic inheritance, random play of immune attack, poor nutrition make each individual completely unique, but may also endow exceptional talents.

References

Asbury, K., & Plomin, R. (2013). *G is for genes: The impact of genetics on education and achievement (understanding children's worlds)*. Hoboken, USA: Wiley.

Attree, E. A., Turner, M. J., & Cowell, N. (2009). A virtual reality test identifies the visuospatial strengths of adolescents with dyslexia. *Cyberpsychology & Behavior, 12*(2), 163–168. https://doi.org10.1089/cpb.2008.0204

Bashir, S., & Al-Ayadhi, L. (2015). Endothelial antibody levels in the sera of children with autism spectrum disorders. *Journal of the Chinese Medical Association, 78*(7), 414–417. https://doi.org10.1016/j.jcma.2015.01.008

Bednarek, D. B., & Grabowska, A. (2002). Luminance and chromatic contrast sensitivity in dyslexia: The magnocellular deficit hypothesis revisited. *Neuroreport, 13*(18), 2521–2525. https://doi.org10.1097/01.wnr.0000048921.00321.35

Ben-Yehudah, G., Sackett, E., Malchi-Ginzberg, L., & Ahissar, M. (2001). Impaired temporal contrast sensitivity in dyslexics is specific to retain-and-compare paradigms. *Brain, 124*(7), 1381–1395. https://doi.org10.1093/brain/124.7.1381

Bradley, L., & Bryant, P. E. (1978). Difficulties in auditory organisation as a possible cause of reading backwardness. *Nature, 271*(5647), 746–747. https://doi.org10.1038/271746a0

Brandler, W. M., Morris, A. P., Evans, D. M., Scerri, T. S., Kemp, J. P., Timpson, N. J., … Paracchini, S. (2013). Common variants in left/right asymmetry genes and pathways are associated with relative hand skill. *PLoS genetics, 9*(9), e1003751. https://doi.org10.1371/journal.pgen.1003751

Centanni, T. M., Booker, A. B., Sloan, A. M., Chen, F., Maher, B. J., Carraway, R. S., … Kilgard, M. P. (2014). Knockdown of the dyslexia-associated gene KIAA0319 impairs temporal responses to speech stimuli in rat primary auditory cortex. *Cerebral Cortex, 24*(7), 1753–1766. https://doi.org10.1093/cercor/bht028

Cestnick, L., & Coltheart, M. (1999). The relationship between language-processing and visual-processing deficits in developmental dyslexia. *Cognition, 71*(3), 231–255. https://doi.org10.1016/S0010-0277(99)00023-2

Chase, C., & Jenner, A. R. (1993). Magnocellular visual deficits affect temporal processing of dyslexics. *Annals of the New York Academy of Sciences, 682*(1), 326–329. https://doi.org10.1111/j.1749-6632.1993.tb22983.x

Cheng, A., Eysel, U. T., & Vidyasagar, T. R. (2004). The role of the magnocellular pathway in serial deployment of visual attention. *The European Journal of Neuroscience, 20*(8), 2188–2192. https://doi.org10.1111/j.1460-9568.2004.03675.x

Chomsky, N. (1957). *Syntactic structures*. Paris: Mouton.

Clisby, C., Fowler, M. S., Hebb, G. S., Walters, J., Southcott, P., & Stein, J. F. (2000). Outcome of treatment of visual problems of children with reading difficulties. *Professional Association of Teachers in Special Situations (PATOSS)*.

Corballis, M. C. (2003). From mouth to hand: Gesture, speech, and the evolution of right-handedness. *The Behavioral and Brain Sciences, 26*(2), 199–208. https://doi.org10.1017/S0140525X03000062

Corballis, M. C. (2009). The evolution and genetics of cerebral asymmetry. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences, 364*(1519), 867–879. https://doi.org10.1098/rstb.2008.0232

Cornelissen, P., Richardson, A., Mason, A., Fowler, S., & Stein, J. F. (1995). Contrast sensitivity and coherent motion detection measured at photopic luminance levels in dyslexics and controls. *Vision Research, 35*(10), 1483–1494. https://doi.org10.1016/0042-6989(95)98728-R

Corrigan, F., Gray, R., Strathdee, A., Skinner, R., van Rhijn, A., & Horrobin, D. (1994). Fatty acid analysis of blood from violent offenders. *The Journal of Forensic Psychiatry, 5*(1), 83–92. https://doi.org10.1080/09585189408410899

Corriveau, R. A., Huh, G. S., & Shatz, C. J. (1998). Regulation of class I MHC gene expression in the developing and mature CNS by neural activity. *Neuron, 21*(3), 505–520. https://doi.org10.1016/S0896-6273(00)80562-0

Crawford, T. J., & Higham, S. (2001). Dyslexia and the centre-of-gravity effect. *Experimental Brain Research, 137*(1), 122–126. https://doi.org10.1007/s002210000659

Dain, S. J., Floyd, R. A., & Elliot, R. T. (2008). Color and luminance increment thresholds in poor readers. *Visual Neuroscience, 25*(3), 481–486. https://doi.org10.1017/S0952523808080565

Dehaene, S., Pegado, F., Braga, L. W., Ventura, P., Nunes Filho, G., Jobert, A., … Cohen, L. (2010). How learning to read changes the cortical networks for vision and language. *Science, 330*(6009), 1359–1364. https://doi.org10.1126/science.1194140

Demb, J. B., Boynton, G. M., Best, M., & Heeger, D. J. (1998). Psychophysical evidence for a magnocellular pathway deficit in dyslexia. *Vision Research, 38*(11), 1555–1559. https://doi.org10.1016/S0042-6989(98)00075-3

Denison, R. N., Vu, A. T., Yacoub, E., Feinberg, D. A., & Silver, M. A. (2014). Functional mapping of the magnocellular and parvocellular subdivisions of human LGN. *NeuroImage, 102*(2), 358–369. https://doi.org10.1016/j.neuroimage.2014.07.019

Downie, A. L. S., Jakobson, L. S., Frisk, V., & Ushycky, I. (2003). Periventricular brain injury, visual motion processing, and reading and spelling abilities in children who were extremely low birthweight. *Journal of the International Neuropsychological Society, 9*(3), 440–449. https://doi.org10.1017/S1355617703930098

Eckert, M. A., Leonard, C. M., Wilke, M., Eckert, M., Richards, T., Richards, A., & Berninger, V. (2005). Anatomical signatures of dyslexia in children: Unique information from manual and voxel based morphometry brain measures. *Cortex, 41*(3), 304–315. https://doi.org10.1016/S0010-9452(08)70268-5

Eden, G. F., Stein, J. F., Wood, H. M., & Wood, F. B. (1994). Differences in eye movements and reading problems in dyslexic and normal children. *Vision Research, 34*(10), 1345–1358. https://doi.org10.1016/0042-6989(94)90209-7

Eden, G. F., VanMeter, J. W., Rumsey, J. M., Maisog, J. M., Woods, R. P., & Zeffiro, T. A. (1996). Abnormal processing of visual motion in dyslexia revealed by functional brain imaging. *Nature, 382*(6586), 66–69. https://doi.org10.1038/382066a0

Elliott, J., & Grigorenko, E. L. (2014). *The dyslexia debate* (Vol. 14). New York, NY: Cambridge University Press.

Everatt, J., Steffert, B., & Smythe, I. (1999). An eye for the unusual: Creative thinking in dyslexics. *Dyslexia, 5*(1), 28–46. https://doi.org10.1002/(sici)1099-0909(199903)5:1\T1\textless28::aid-dys126\T1\textgreater3.0.co;2-k

Facoetti, A., Ruffino, M., Gori, S., Bigoni, A., Benassi, M., Bolzani, R., … Cecchini, P. (2010). On the relationship between magnocellular pathway and automatic attentional orienting: Evidences from developmental dyslexia. *Journal of Vision, 10*(7), 281. https://doi.org10.1167/10.7.281

Fawcett, A. J., Nicolson, R. I., & Dean, P. (1996). Impaired performance of children with dyslexia on a range of cerebellar tasks. *Annals of Dyslexia, 46*(1), 259–283. https://doi.org10.1007/BF02648179

Felmingham, K. L., & Jakobson, L. S. (1995). Visual and visuomotor performance in dyslexic children. *Experimental Brain Research, 106*(3), 467–474. https://doi.org10.1007/BF00231069

Fischer, B., & Hartnegg, K. (2000). Stability of gaze control in dyslexia. *Strabismus, 8*(2), 119–122. https://doi.org10.1076/0927-3972(200006)821-2FT119

Fisher, S. E., Francks, C., Marlow, A. J., MacPhie, I. L., Newbury, D. F., Cardon, L. R., … Monaco, A. P. (2002). Independent genome-wide scans identify a chromosome 18 quantitative-trait locus influencing dyslexia. *Nature Genetics, 30*(1), 86–91. https://doi.org10.1038/ng792

Francks, C., Paracchini, S., Smith, S. D., Richardson, A. J., Scerri, T. S., Cardon, L. R., … Monaco, A. P. (2004). A 77-kilobase region of chromosome 6p22.2 is associated with dyslexia in families from the united kingdom and from the united states. *American Journal of Human Genetics, 75*(6), 1046–1058. https://doi.org10.1086/426404

Galaburda, A. M. (1993). *Dyslexia and development: Neurobiological aspects of extra-ordinary brains*. Cambridge, MA: Harvard University Press.

Galaburda, A. M., Menard, M. T., & Rosen, G. D. (1994). Evidence for aberrant auditory anatomy in developmental dyslexia. *Proceedings of the National Academy of Sciences of the United States of America, 91*(17), 8010–8013. https://doi.org10.1073/pnas.91.17.8010

Galaburda, A. M., Sherman, G. F., Rosen, G. D., Aboitiz, F., & Geschwind, N. (1985). Developmental dyslexia: Four consecutive patients with cortical anomalies. *Annals of Neurology, 18*(2), 222–233. https://doi.org10.1002/ana.410180210

Geiger, G., & Lettvin, J. Y. (1987). Peripheral vision in persons with dyslexia. *The New England Journal of Medicine, 316*(20), 1238–1243. https://doi.org10.1056/NEJM198705143162003

Gesch, C. B., Hammond, S. M., Hampson, S. E., Eves, A., & Crowder, M. J. (2002). Influence of supplementary vitamins, minerals and essential fatty acids on the antisocial behaviour of

young adult prisoners. randomised, placebo-controlled trial. *The British Journal of Psychiatry, 181*, 22–28. https://doi.org10.1192/bjp.181.1.22

Giraldo-Chica, M., Hegarty, J. P., & Schneider, K. A., (2015). Morphological differences in the lateral geniculate nucleus associated with dyslexia. NeuroImage: Clin. http://dx.doi.org/10.1016/j.nicl.2015.03.011

Goodale, M. A., & Milner, A. (1992). Separate visual pathways for perception and action. *Trends in Neurosciences, 15*(1), 20–25. https://doi.org10.1016/0166-2236(92)90344-8

Goswami, U., Power, A. J., Lallier, M., & Facoetti, A. (2014). Oscillatory "temporal sampling" and developmental dyslexia: Toward an over-arching theoretical framework. *Frontiers in Human Neuroscience, 8*, 904. https://doi.org10.3389/fnhum.2014.00904

Gouleme, N., Gerard, C.-L., & Bucci, M. P. (2015). The effect of training on postural control in dyslexic children. *PloS One, 10*(7), e0130196. https://doi.org10.1371/journal.pone.0130196

Graham, S. A., & Fisher, S. E. (2013). Decoding the genetics of speech and language. *Current Opinion in Neurobiology, 23*(1), 43–51. https://doi.org10.1016/j.conb.2012.11.006

Gross-Glenn, K., Skottun, B. C., Glenn, W., Kushch, A., Lingua, R., Dunbar, M., … Duara, R. (1995). Contrast sensitivity in dyslexia. *Visual Neuroscience, 12*(01), 153–163. https://doi.org10.1017/S0952523800007380

Hämäläinen, J. A., Salminen, H. K., & Leppänen, P. H. T. (2013). Basic auditory processing deficits in dyslexia: Systematic review of the behavioral and event-related potential/field evidence. *Journal of Learning Disabilities, 46*(5), 413–427. https://doi.org10.1177/0022219411436213

Hamazaki, T., Sawazaki, S., Itomura, M., Asaoka, E., Nagao, Y., Nishimura, N., … Kobayashi, M. (1996). The effect of docosahexaenoic acid on aggression in young adults: A placebo-controlled double-blind study. *The Journal of Clinical Investigation, 97*(4), 1129–1133. https://doi.org10.1172/JCI118507

Hankins, M. W., Peirson, S. N., & Foster, R. G. (2008). Melanopsin: An exciting photopigment. *Trends in Neurosciences, 31*(1), 27–36. https://doi.org10.1016/j.tins.2007.11.002

Hari, R., & Renvall, H. (2001). Impaired processing of rapid stimulus sequences in dyslexia. *Trends in Cognitive Sciences, 5*(12), 525–532. https://doi.org10.1016/S1364-6613(00)01801-5

Harrar, V., Tammam, J., Perez-Bellido, A., Pitt, A., Stein, J. F., & Spence, C. (2014). Multisensory integration and attention in developmental dyslexia. *Current Biology, 24*(5), 531–535. https://doi.org10.1016/j.cub.2014.01.029

Herve, P.-Y., Zago, L., Petit, L., Mazoyer, B., & Tzourio-Mazoyer, N. (2013). Revisiting human hemispheric specialization with neuroimaging. *Trends in Cognitive Sciences, 17*(2), 69–80. https://doi.org10.1016/j.tics.2012.12.004

Hibbeln, J. R., Umhau, J. C., Linnoila, M., George, D. T., Ragan, P. W., Shoaf, S. E., … Salem, N. (1998). A replication study of violent and nonviolent subjects: Cerebrospinal fluid metabolites of serotonin and dopamine are predicted by plasma essential fatty acids. *Biological Psychiatry, 44*(4), 243–249. https://doi.org10.1016/S0006-3223(98)00143-7

Hill, G. T., & Raymond, J. E. (2002). Deficits of motion transparency perception in adult developmental dyslexics with normal unidirectional motion sensitivity. *Vision Research*, *42*(9), 1195–1203. https://doi.org10.1016/S0042-6989(02)00042-1

Hockfield, S., & Sur, M. (1990). Monoclonal antibody Cat-301 identifies Y-cells in the dorsal lateral geniculate nucleus of the cat. *The Journal of Comparative Neurology*, *300*(3), 320–330. https://doi.org10.1002/cne.903000305

Hoeft, F., McCandliss, B. D., Black, J. M., Gantman, A., Zakerani, N., Hulme, C., … Gabrieli, J. D. E. (2011). Neural systems predicting long-term outcome in dyslexia. *Proceedings of the National Academy of Sciences of the United States of America, 108*(1), 361–366. https://doi.org10.1073/pnas.1008950108

Hornickel, J., & Kraus, N. (2013). Unstable representation of sound: A biological marker of dyslexia. *The Journal of Neuroscience, 33*(8), 3500–3504. https://doi.org10.1523/jneurosci.4205-12.2013

Iles, J., Walsh, V., & Richardson, A. (2000). Visual search performance in dyslexia. *Dyslexia, 6*(3), 163–177. https://doi.org10.1002/1099-0909(200007/09)6:3\T1\textless163::AID-DYS150\T1\textgreater3.0.CO;2-U

Jacobson, L., Polizzi, A., Morriss-Kay, G., & Vincent, A. (1999). Plasma from human mothers of fetuses with severe arthrogryposis multiplex congenita causes deformities in mice. *The Journal of Clinical Investigation, 103*(7), 1031–1038. https://doi.org10.1172/JCI5943

Jariabkova, K., Hugdahl, K., & Glos, J. (1995). Immune disorders and handedness in dyslexic boys and their relatives. *Scandinavian Journal of Psychology, 36*(4), 355–362. https://doi.org10.1111/j.1467-9450.1995.tb00993.x

von Károlyi, C., Winner, E., Gray, W., & Sherman, G. F. (2003). Dyslexia linked to talent: Global visual-spatial ability. *Brain and Language, 85*(3), 427–431. https://doi.org10.1016/S0093-934X(03)00052-X

Kinsey, K., Rose, M., Hansen, P., Richardson, A., & Stein, J. F. (2004). Magnocellular mediated visual-spatial attention and reading ability. *Neuroreport*, *15*(14), 2215–2218. https://doi.org10.1097/00001756-200410050-00014

Kirkby, J. A., Webster, L. A. D., Blythe, H. I., & Liversedge, S. P. (2008). Binocular coordination during reading and non-reading tasks. *Psychological Bulletin, 134*(5), 742–763. https://doi.org10.1037/a0012979

Kirkpatrick, R. M., Legrand, L. N., Iacono, W. G., & McGue, M. (2011). A twin and adoption study of reading achievement: Exploration of shared-environmental and gene-evironment-interaction effects. *Learning and Individual Differences, 21*(4), 368–375. https://doi.org10.1016/j.lindif.2011.04.008

Kuba, M., Szanyi, J., Gayer, D., Kremlacek, J., & Kubova, Z. (2001). Electrophysiological testing of dyslexia. *Acta Medica, 44*(4), 131–134.

Lachmann, T., & van Leeuwen, C. (2007). Paradoxical enhancement of letter recognition in developmental dyslexia. *Developmental Neuropsychology, 31*(1), 61–77. https://doi.org10.1080/87565640709336887

Lahita, R. G. (1988). Systemic lupus erythematosus: Learning disability in the male offspring of female patients and relationship to laterality. *Psychoneuroendocrinology, 13*(5), 385–396. https://doi.org10.1016/0306-4530(88)90045-5

Lallier, M., Tainturier, M.-J., Dering, B., Donnadieu, S., Valdois, S., & Thierry, G. (2011). Behavioral and ERP evidence for amodal sluggish attentional shifting in developmental dyslexia. *Neuropsychologia, 48*(14), 4125–4135. https://doi.org10.1016/j.neuropsychologia.2010.09.027

Leonard, C. M., & Eckert, M. A. (2008). Asymmetry and dyslexia. *Developmental Neuropsychology, 33*(6), 663–681. https://doi.org10.1080/87565640802418597

Liberman, I. Y., & Shankweiler, D. (1977). Phonetic segmentation in the beginning reader. In A. S. Reber & D. L. Scarborough (Eds.), *Toward a psychology of reading.* Hillsdale, NJ: Lawrence Erlbaum Associates

Livingstone, M. S., Rosen, G. D., Drislane, F. W., & Galaburda, A. M. (1991). Physiological and anatomical evidence for a magnocellular defect in developmental dyslexia. *Proceedings of the National Academy of Sciences of the United States of America, 88*(18), 7943–7947. https://doi.org10.1073/pnas.88.18.7943

Logan, J. (2009). Dyslexic entrepreneurs: The incidence: Their coping strategies and their business skills. *Dyslexia, 15*(4), 328–346. https://doi.org10.1002/dys.388

Lovegrove, W. J., Heddle, M., & Slaghuis, W. (1980). Reading disability: Spatial frequency specific deficits in visual information store. *Neuropsychologia, 18*(1), 111–115. https://doi.org10.1016/0028-3932(80)90093-7

Lurie, D. I., Pasic, T. R., Hockfield, S. J., & Rubel, E. W. (1997). Development of CAT-301 immunoreactivity in auditory brainstem nuclei of the gerbil. *The Journal of Comparative Neurology, 380*(3), 319–334. https://doi.org10.1002/(SICI)1096-9861(19970414)380:3\T1\textless319::AID-CNE3\T1\textgreater3.0.CO;2-5

Lyytinen, H., Erskine, J., Hämäläinen, J., Torppa, M., & Ronimus, M. (2015). Dyslexia-early identification and prevention: Highlights from the Jyvaskyla longitudinal study of dyslexia. *Current Developmental Disorders Reports, 2*(4), 330–338. https://doi.org10.1007/s40474-015-0067-1

Maddess, T., James, A. C., Goldberg, I., Wine, S., & Dobinson, J. (2000). A spatial frequency-doubling illusion-based pattern electroretinogram for glaucoma. *Investigative Ophthalmology & Visual Science, 41*(12), 3818–3826.

Manis, F. R., Mcbride-Chang, C., Seidenberg, M. S., Keating, P., Doi, L. M., Munson, B., & Petersen, A. (1997). Are speech perception deficits associated with developmental dyslexia? *Journal of Experimental Child Psychology, 66*(2), 211–235. https://doi.org10.1006/jecp.1997.2383

Mason, A., Cornelissen, P., Fowler, S., & Stein, J. F. (1993). Contrast sensitivity, ocular dominance and specific reading disability. *Clinical Vision, 8*(4), 345–353.

McAnally, K. I., & Stein, J. F. (1996). Auditory temporal coding in dyslexia. *Proceedings. Biological Sciences, 263*(1373), 961–965. https://doi.org10.1098/rspb.1996.0142

McClelland, E., Pitt, A., & Stein, J. F. (2014). Enhanced academic performance using a novel classroom physical activity intervention to increase awareness, attention and self-control: Putting embodied cognition into practice. *Improving Schools, 18*(1), 83–100. https://doi.org10.1177/1365480214562125

McGuire, P. K., Hockfield, S., & Goldman-Rakic, P. S. (1989). Distribution of CAT-301 immunoreactivity in the frontal and parietal lobes of the macaque monkey. *The Journal of Comparative Neurology, 288*(2), 280–296. https://doi.org10.1002/cne.902880207

Miall, R. C., Weir, D. J., Wolpert, D. M., & Stein, J. F. (1993). Is the cerebellum a smith predictor? *Journal of Motor Behavior, 25*(3), 203–216. https://doi.org10.1080/00222895.1993.9942050

Miles, T. R. (1993). *Dyslexia: The pattern of difficulties*. London: Whurr Wyke.

Montgomery, P., Burton, J. R., Sewell, R. P., Spreckelsen, T. F., & Richardson, A. J. (2013). Low blood long chain omega-3 fatty acids in UK children are associated with poor cognitive performance and behavior: A cross-sectional analysis from the DOLAB study. *PloS One, 8*(6), e66697. https://doi.org10.1371/journal.pone.0066697

Morais, J., Cary, L., Alegria, J., & Bertelson, P. (1979). Does awareness of speech as a sequence of phones arise spontaneously? *Cognition, 7*(4), 323–331. https://doi.org10.1016/0010-0277(79)90020-9

Mueller, A. L., Davis, A., Sovich, S., Carlson, S. S., & Robinson, F. R. (2016). Distribution of N-acetylgalactosamine-positive perineuronal nets in the macaque brain: Anatomy and implications. *Neural Plasticity*, 6021428. https://doi.org10.1155/2016/6021428

Newbury, D. F., Paracchini, S., Scerri, T. S., Winchester, L., Addis, L., Richardson, A. J., … Monaco, A. P. (2011). Investigation of dyslexia and SLI risk variants in reading- and language-impaired subjects. *Behavior Genetics, 41*(1), 90–104. https://doi.org10.1007/s10519-010-9424-3

Nicolson, R. I., Fawcett, A. J., Berry, E. L., Jenkins, I. H., Dean, P., & Brooks, D. J. (1999). Association of abnormal cerebellar activation with motor learning difficulties in dyslexic adults. *The Lancet, 353*(9165), 1662–1667. https://doi.org10.1016/S0140-6736(98)09165-X

Olson, R. K., Hulslander, J., Christopher, M., Keenan, J. M., Wadsworth, S. J., Willcutt, E. G., … DeFries, J. C. (2013). Genetic and environmental influences on writing and their relations to language and reading. *Annals of Dyslexia, 63*(1), 25–43. https://doi.org10.1007/s11881-011-0055-z

Pammer, K., & Wheatley, C. (2001). Isolating the M(y)-cell response in dyslexia using the spatial frequency doubling illusion. *Vision Research, 41*(16), 2139–2147. https://doi.org10.1016/S0042-6989(01)00092-X

Paracchini, S., Thomas, A., Castro, S., Lai, C., Paramasivam, M., Wang, Y., … Monaco, A. P. (2006). The chromosome 6p22 haplotype associated with dyslexia reduces the expression of KIAA0319: A novel gene involved in neuronal migration. *Human Molecular Genetics, 15*(10), 1659–1666. https://doi.org10.1093/hmg/ddl089

Parletta, N., Niyonsenga, T., & Duff, J. (2016). Omega-3 and Omega-6 polyunsaturated fatty acid levels and correlations with symptoms in children with attention deficit hyperactivity disorder, autistic spectrum disorder and typically developing controls. *PloS One, 11*(5), e0156432. https://doi.org10.1371/journal.pone.0156432

Rae, C., Harasty, J. A., Dzendrowskyj, T. E., Talcott, J. B., Simpson, J. M., Blamire, A. M., … Stein, J. F. (2002). Cerebellar morphology in developmental dyslexia. *Neuropsychologia, 40*(8), 1285–1292. https://doi.org10.1016/S0028-3932(01)00216-0

Rae, C., Lee, M. A., Dixon, R. M., Blamire, A. M., Thompson, C. H., Styles, P., … Stein, J. F. (1998). Metabolic abnormalities in developmental dyslexia detected by 1H magnetic resonance spectroscopy. *The Lancet, 351*(9119), 1849–1852. https://doi.org10.1016/S0140-6736(97)99001-2

Ramus, F. (2004). Neurobiology of dyslexia: A reinterpretation of the data. *Trends in Neurosciences, 27*(12), 720–726. https://doi.org10.1016/j.tins.2004.10.004

Ramus, F., Pidgeon, E., & Frith, U. (2003). The relationship between motor control and phonology in dyslexic children. *Journal of Child Psychology and Psychiatry, 44*(5), 712–722. https://doi.org10.1111/1469-7610.00157

Rao, S. C., Rainer, G., & Miller, E. K. (1997). Integration of what and where in the primate prefrontal cortex. *Science, 276*(5313), 821–824. https://doi.org10.1126/science.276.5313.821

Ray, N. J., Fowler, S., & Stein, J. F. (2005). Yellow filters can improve magnocellular function: Motion sensitivity, convergence, accommodation, and reading. *Annals of the New York Academy of Sciences, 1039*, 283–293. https://doi.org10.1196/annals.1325.027

Rayner, K. (1985). Do faulty eye movements cause dyslexia? *Developmental Neuropsychology, 1*(1), 3–15. https://doi.org10.1080/87565648509540294

Read, C., Yun-Fei, Z., Hong-Yin, N., & Bao-Qing, D. (1986). The ability to manipulate speech sounds depends on knowing alphabetic writing. *Cognition, 24*(1–2), 31–44. https://doi.org10.1016/0010-0277(86)90003-X

Rice, M. L., Smith, S. D., & Gayan, J. (2009). Convergent genetic linkage and associations to language, speech and reading measures in families of probands with specific language impairment. *Journal of Neurodevelopmental Disorders, 1*(4), 264–282. https://doi.org10.1007/s11689-009-9031-x

Richardson, A. J., Burton, J. R., Sewell, R. P., Spreckelsen, T. F., & Montgomery, P. (2012). Docosahexaenoic acid for reading, cognition and behavior in children aged 7–9 years: A randomized, controlled trial (the DOLAB study). *PloS one, 7*(9), e43909. https://doi.org10.1371/journal.pone.0043909

Richardson, A. J., & Montgomery, P. (2005). The Oxford-Durham study: A randomized, controlled trial of dietary supplementation with fatty acids in children with developmental coordination disorder. *Pediatrics, 115*(5), 1360–1366. https://doi.org10.1542/peds.2004-2164

Richlan, F., Kronbichler, M., & Wimmer, H. (2013). Structural abnormalities in the dyslexic brain: A meta-analysis of voxel-based morphometry studies. *Human Brain Mapping, 34*(11), 3055–3065. https://doi.org10.1002/hbm.22127

Riemersma, S., Vincent, A., Beeson, D., Newland, C., Hawke, S., Vernet-der Garabedian, B., … Newsom-Davis, J. (1996). Association of arthrogryposis multiplex congenita with maternal antibodies inhibiting fetal acetylcholine receptor function. *The Journal of Clinical Investigation, 98*(10), 2358–2363. https://doi.org10.1172/JCI119048

Rosen, G. D., Bai, J., Wang, Y., Fiondella, C. G., Threlkeld, S. W., LoTurco, J. J., & Galaburda, A. M. (2007). Disruption of neuronal migration by RNAi of Dyx1c1 results in neocortical and hippocampal malformations. *Cerebral Cortex, 17*(11), 2562–2572. https://doi.org10.1093/cercor/bhl162

Rutter, M., Giller, H., & Hagell, A. (1998). *Antisocial behavior by young people*. Cambridge, NY: Cambridge University Press.

Samar, V. J., & Parasnis, I. (2007). Cortical locus of coherent motion deficits in deaf poor readers. *Brain and Cognition, 63*(3), 226–239. https://doi.org10.1016/j.bandc.2006.08.004

Scerri, T. S., Paracchini, S., Morris, A., MacPhie, I. L., Talcott, J., Stein, J. F., … Richardson, A. J. (2011). Identification of candidate genes for dyslexia susceptibility on chromosome 18. *PloS One, 5*(10), e13712. https://doi.org10.1371/journal.pone.0013712

Schizophrenia Working Group of the Psychiatric Genomics Consortium. (2014). Biological insights from 108 schizophrenia-associated genetic loci. *Nature, 511*(7510), 421–427. https://doi.org10.1038/nature13595

Schmolesky, M. T., Wang, Y., Hanes, D. P., Thompson, K. G., Leutgeb, S., Schall, J. D., & Leventhal, A. G. (1998). Signal timing across the macaque visual system. *Journal of Neurophysiology, 79*(6), 3272–3278.

Sinclair, H. (1956). Deficiency of essential fatty acids and atherosclerosis. *The Lancet, 267*(6919), 381–383. https://doi.org10.1016/S0140-6736(56)90126-X

Skottun, B. C. (2015). The need to differentiate the magnocellular system from the dorsal stream in connection with dyslexia. *Brain and Cognition, 95*, 62–66. https://doi.org10.1016/j.bandc.2015.01.001

Skottun, B. C. (2016). A few remarks on the utility of visual motion perception to assess the integrity of the magnocellular system or the dorsal stream. *Cortex, 79*, 155–158. https://doi.org10.1016/j.cortex.2016.03.006

Skoyles, J., & Skottun, B. C. (2004). On the prevalence of magnocellular deficits in the visual system of non-dyslexic individuals. *Brain and Language, 88*(1), 79–82. https://doi.org10.1016/S0093-934X(03)00162-7

Stein, J. F. (1986). Role of the cerebellum in the visual guidance of movement. *Nature, 323*(6085), 217–221. https://doi.org10.1038/323217a0

Stein, J. F. (2001). The magnocellular theory of developmental dyslexia. *Dyslexia, 7*(1), 12–36. https://doi.org10.1002/dys.186

Stein, J. F., & Walsh, V. (1997). To see but not to read: The magnocellular theory of dyslexia. *Trends in Neurosciences, 20*(4), 147–152. https://doi.org10.1016/S0042-6989(99)00170-4

Stoodley, C. J. (2014). Distinct regions of the cerebellum show gray matter decreases in autism, ADHD, and developmental dyslexia. *Frontiers in Systems Neuroscience, 8*, 92. https://doi.org10.3389/fnsys.2014.00092

Stoodley, C. J. (2016). The cerebellum and neurodevelopmental disorders. *Cerebellum, 15*(1), 34–37. https://doi.org10.1007/s12311-015-0715-3

Stoodley, C. J., Fawcett, A. J., Nicolson, R. I., & Stein, J. F. (2005). Impaired balancing ability in dyslexic children. *Experimental Brain Research, 167*(3), 370–380. https://doi.org10.1007/s00221-005-0042-x

Stoodley, C. J., & Stein, J. F. (2011). The cerebellum and dyslexia. *Cortex, 47*(1), 101–116. https://doi.org10.1016/j.cortex.2009.10.005

Talcott, J. B., Hansen, P. C., Assoku, E. L., & Stein, J. F. (2000). Visual motion sensitivity in dyslexia: Evidence for temporal and energy integration deficits. *Neuropsychologia, 38*(7), 935–943. https://doi.org10.1016/S0028-3932(00)00020-8

Tallal, P., & Piercy, M. (1973). Defects of non-verbal auditory perception in children with developmental aphasia. *Nature, 241*(5390), 468–469. https://doi.org10.1038/241468a0

Tammam, J. D., Steinsaltz, D., Bester, D. W., Semb-Andenaes, T., & Stein, J. F. (2015). A randomised double-blind placebo-controlled trial investigating the behavioural effects of vitamin, mineral and n-3 fatty acid supplementation in typically developing adolescent schoolchildren. *The British Journal of Nutrition, 115*(2), 361–373. https://doi.org10.1017/S0007114515004390

Vidyasagar, T. R. (2004). Neural underpinnings of dyslexia as a disorder of visuo-spatial attention. *Clinical & Experimental Optometry*, *87*(1), 4–10. https://doi.org10.1111/j.1444-0938.2004.tb03138.x

Warren, R. P., Cole, P., Odell, J. D., Pingree, C. B., Warren, W. L., White, E., … Singh, V. K. (1990). Detection of maternal antibodies in infantile autism. *Journal of the American Academy of Child and Adolescent Psychiatry, 29*(6), 873–877. https://doi.org10.1097/00004583-199011000-00005

White, A. J. R., Sun, H., Swanson, W. H., & Lee, B. B. (2002). An examination of physiological mechanisms underlying the frequency-doubling illusion. *Investigative Ophthalmology & Visual Science, 43*(11), 3590–3599.

Witton, C., Stein, J. F., Stoodley, C. J., Rosner, B. S., & Talcott, J. B. (2002). Separate influences of acoustic AM and FM sensitivity on the phonological decoding skills of impaired and normal readers. *Journal of Cognitive Neuroscience, 14*(6), 866–874. https://doi.org10.1162/089892902760191090

Witton, C., Talcott, J. B., Hansen, P. C., Richardson, A. J., Griffiths, T. D., Rees, A., … Green, G. G. (1998). Sensitivity to dynamic auditory and visual stimuli predicts nonword reading ability in both dyslexic and normal readers. *Current Biology, 8*(14), 791–797. https://doi.org10.1016/S0960-9822(98)70320-3

Wolff, U., & Lundberg, I. (2002). The prevalence of dyslexia among art students. *Dyslexia, 8*(1), 34–42. https://doi.org10.1002/dys.211

Zhao, J., Thiebaut de Schotten, M., Altarelli, I., Dubois, J., & Ramus, F. (2016). Altered hemispheric lateralization of white matter pathways in developmental dyslexia: Evidence from spherical deconvolution tractography. *Cortex, 76*, 51–62. https://doi.org10.1016/j.cortex.2015.12.004