Deficits in the magnocellular pathway of people with reading difficulties

[1,2,3]Tsz-wing Leung, Ph.D., [1,2,3]Allen Ming-yan Cheong, Ph.D., [1,2,3]Henry Ho-lung Chan

[1]School of Optometry, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong SAR

[2]Research Centre for SHARP Vision (RCSV), The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong

[3]Centre for Eye and Vision Research (CEVR), 17W Hong Kong Science Park, Hong Kong

Correspondence: Tsz-wing Leung.

Address: HJ528, School of Optometry, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong SAR.

Email: jeffrey.TW.leung@polyu.edu.hk

Voice: (852) 2766-4268

Co-authors' email addresses:

Allen Ming-yan Cheong: allen.my.cheong@polyu.edu.hk

Henry Ho-lung Chan*: henryhl.chan@polyu.edu.hk

* *Henry Ho-lung Chan is the co-corresponding author.*

Keywords: Developmental dyslexia; Magnocellular deficits; Reading difficulties; Magnocellular-dorsal system

Abstract

Purpose of review: The magnocellular theory is one of the well-accepted neurobiological theories to explain developmental dyslexia. However, criticism remains on whether the weaker magnocellular-dorsal system in dyslexics is a consequence of insufficient practice in reading skills. This mini-review summarizes recent publications investigating the causal relationship of magnocellular theory in developmental dyslexia.

Recent findings: Emerging evidence highlights visual magnocellular-dorsal deficits as a cause, not a consequence, of reading difficulties. Recent studies have indicated that cognitive impairment of magnocellular-dorsal functions is a biomarker of developmental dyslexia and does not relate to the reading experience. However, training magnocellular-dorsal functions can also improve the reading skills in dyslexic children.

Summary: Magnocellular-dorsal functions should be included in the battery of tests to identify children at risk of developmental dyslexia. However, other factors discussed in this review, including the involvement of the parvocellular system and noise cancellation deficit, should also be considered.

Introduction

Reading is an essential survival skill, but not all people can learn and master this skill well. About 5% to 17.5% of the population worldwide have developmental dyslexia (DD),[1] a neurodevelopmental disorder characterized by persistent impairment in reading skills, including reading accuracy, fluency, and comprehension, even after receiving formal education.[2] People with DD have ordinary intellectual levels and mental health, and are free from neurological and sensory diseases, but still read less well than their peers of similar age.[2]

The hardships borne by dyslexics are far more than just simple reading difficulties. In the current competitive education system, dyslexic children and youths are often labelled as 'lazy' or 'stupid,' even though they are as intelligent as (or sometimes even more intelligent than) their peers. They have to endure anxiety, emotional stress, and depression due to failure to achieve expectations from family, school, or themselves.[3-6] Some dyslexic youths may decide or are compelled to quit school early, leading to the school dropout rate in dyslexics being six times higher than for typical readers.[7] Those who can no longer withstand the tremendous academic pressure may consider or even attempt suicide, the rate of which is three times higher than that of their peers.[7] Given that DD creates substantial impacts on individual and society, various disciplines have investigated the neurobiological roots of DD and attempted to develop genuine solutions to improve dyslexics' reading performance.

Various theories have been proposed to explain the reading difficulties of DD, including phonological theory, rapid auditory processing theory, visual theory, cerebellar theory, and magnocellular theory.[8] Among these, the magnocellular theory is the one that attempts to unify other theories by attributing the reading difficulties to dysfunction of the magnocellular-dorsal system. It attracts researchers' attention because it provides a neurobiological explanation of DD and opens a new direction to train dyslexics' reading skills. However, the theory is not without criticism, and the underlying causes of DD are still a widely debated topic. This mini-review aims to summarize recent relevant research findings to support the magnocellular theory of DD. The literature search was conducted between January 2017 and March 2022 using PubMed, Scopus, and PsycInfo digital bibliographic databases. The following keywords were included in the literature search: ("Dyslexia" OR "Developmental dyslexia" OR "Reading disorder") AND ("Magnocellular" OR "Dorsal"). In general, emerging evidence affirms the magnocellular deficit, particularly the visual magnocellular-dorsal system, as a root cause of DD. However, other factors discussed in this review should also be considered when further investigating the neurobiological basis of DD and applying this theory in clinical practice.

Magnocellular theory

Before discussing the recent research, the magnocellular theory will be briefly reviewed. For more details, reference may be made to earlier comprehensive review articles.[9-14] The magnocellular theory describes inaccurate timing of the magnocellular networks in processing visual temporal information when reading. The visual magnocellular pathway originates from the retina, where the parasol retinal ganglion cells project visual signals to the inner two layers of the lateral geniculate nucleus (LGN), which then travel primarily to the layer 4Cα of the primary visual cortex.[15, 16] Because the magnocellular cells are sizable, with extended dendritic arborization and myelinated axons, the magnocellular system is more sensitive to visual stimulations characterized by rapid motion (high temporal frequency) and coarse details (low spatial frequency).[17-19] About 90% of visual inputs from the magnocellular pathway are then projected to the dorsal (or parietal) stream, also called the "where pathway", which travels from the visual cortex via V5/MT (the motion-sensitive area) to the parietal lobe. The dorsal stream

mediates visual motion perception and is responsible for guiding visual action and recognizing spatial location with respect to the viewer.[19-22] When reading a book, the magnocellular-dorsal system deploys visual attention to the letter strings of interest,[21, 22] controls corresponding eye movements,[21, 22] recognizes letter sequences,[9, 13, 14] and integrates the rapid coarse visual signals.[9, 13, 14] Once this rapid temporal processing skill is disturbed, it leads to errors in sequencing the letter orders and sounding out the words.[9-14]

The magnocellular theory was mainly developed based on the observation that dyslexics often exhibit impairments in cognitive and neurophysiological functions mediated by the magnocellular-dorsal stream. Figure 1 summarizes the reported magnocellular deficits in dyslexia. Basically, dyslexics underperform in visual tasks that involve low spatial and high temporal frequency,[23-28] motion discrimination,[24, 29-33] and heavy attention load[34-36]. In addition to cognitive impairment, post-mortem histological examination has also revealed more disorganized magnocellular layers and smaller cell bodies in the LGN of dyslexic than age-matched non-dyslexic brains.[37] Data from magnetic resonance imaging supports the histological evidence, showing a reduced volume of left LGN and impaired brain areas over the magnocellular-dorsal pathway in dyslexic children and adults.[38-41]

One major criticism of the magnocellular theory is the causal link between magnocellular-dorsal deficits and DD. While dyslexics often perform visual motion and attention tasks less well than typical readers, it does not mean that these impairments are the causes of DD. It has been argued that dyslexics have a weaker magnocellular-dorsal system because of the lack of practice in reading-associated visual skills.[42, 43] In other words, the magnocellular deficit is a consequence, not a cause, of dyslexia. However, recent studies refute this argument and provide further evidence to confirm the causal role of the magnocellular-dorsal system in DD.

Visual motion perception is an endophenotype of dyslexia

Endophenotype (EP) is a measurable biomarker correlated genetically to an illness and can be used to identify those at high risk of a disorder. Only cognitive phenotypes that fulfil the six restrictive criteria can be classified as an EP (see references[44, 45] for details). Mascheretti et al.[46]•• recently investigated which previously reported cognitive phenotypes of DD met the criteria of EP. The cognitive phenotypes included rapid auditory processing (RAP), rapid automatized naming, multisensory nonspatial attention, and visual motion processing (rotating-tilted-line illusion). These phenotypes were measured in a total of 100 nuclear families with DD (229 offspring) and 83 unrelated typical readers. Their results indicated that visual motion and RAP were the only two cognitive phenotypes fulfilling all testable criteria (except for the criterion that required a longitudinal study design) and could be considered potential EPs of DD. Given that visual motion perception is mediated via the dorsal stream, their results support the magnocellular-dorsal deficit as a cause of DD.

Magnocellular deficits are not related to reading experience

Because dyslexics struggle with reading, it has been argued that they read less than typical readers.[42] The magnocellular-dorsal functions are less practiced or developed, thus, making it less efficient.[42, 43] To test whether the impaired magnocellular-dorsal system is related to reading experience, Flint and Pammer[47]• compared coherent motion and frequency-doubling illusion sensitivities among dyslexics, illiterate, semi-illiterate, and typical readers. If magnocellular-dorsal deficits result from lack of practice in reading-related visual skills, illiterate and semi-literate persons, who have received little or no education, should underperform in these rapid visual motion tasks. They found that dyslexics were, as expected, less sensitive to coherent motion and frequency-doubling illusion. However, illiterate and

semi-illiterate subjects performed similarly to typical readers. Their findings refute the argument that magnocellular-dorsal deficit is secondary to inadequate reading experience.

Retina is involved in DD

Recent and earlier studies show that dyslexics usually exhibit lower sensitivity to frequency doubling (FD) illusion than typical readers.[25-27, 48, 49] This drop in FD sensitivity is believed to reflect a deficit of the retinal ganglion cells (RGC). In clinical practice, FD technology has been applied to detect patients with glaucoma,[50, 51] an eye disease resulting from damaged RGC. The reduced FD indices correlate significantly with the loss in retinal nerve fibre layer thickness in glaucomatous eyes.[52, 53] However, FD technology, using a psychophysical approach, does not determine the retinal function directly. To confirm the involvement of retinal function in DD, the steady-state pattern electroretinogram (PERG) response between dyslexics and typical readers has been compared.[48] By presenting visual stimulation with low spatial (0.3 c/deg) and high temporal frequency (15 Hz), PERG selectively measures the electrophysiological response of the RGC that mainly activate the magnocellular system. In agreement with the FD illusion findings, the reduced PERG response in dyslexics suggests an impaired retinal function for ganglion cells diverging to the magnocellular pathway. Because reading experience is not likely to alter retinal function, it is improbable that the reduced retinal ganglion cell response is a consequence of DD. However, this study was limited by small sample size (dyslexics, n = 10; typical readers, n = 10), reducing generalization. In addition to retinal function, further studies, including retinal imaging measurements, are required to confirm retinal involvement in terms of the RGC layer thickness in DD, to explore the relationship between structural and functional deficits related to the magnocellular pathway.

Reading performance in dyslexics can be improved by magnocellular-dorsal training

If DD does indeed result from a magnocellular-dorsal deficit, the reading performance of dyslexics should improve once magnocellular-dorsal function is recovered. Training on the magnocellular-dorsal system refers to repetitive practising tasks that demand rapid visual signal processing or heavy visual attention. The aim is to enhance the magnocellular-dorsal function through accumulating experience with relevant visual stimulation. Table 1 summarizes five recent publications investigating direct or indirect (i.e., by action video games) magnocellular-dorsal training on the reading performance of dyslexics. All revealed that reading skills in dyslexic children can be improved after alleviating magnocellular-dorsal deficits, further supporting the magnocellular theory.

Ebrahimi et al.[54, 55]• investigated how training a series of magnocellular-dorsal functions affected dyslexic children's reading performance. The training included visual tasks targeting saccadic eye movement, coherent motion, and digital and dot counting skills. They found that the training improved magnocellular-dorsal functions, and importantly, these improvements were transferred to the reading performance. To understand training sustainability, they repeated the reading tests one month after the intervention and found that the improvement in reading skills was maintained. However, while most reading functions were improved, phonological errors increased. They suggested that after the training, dyslexic children may have learnt to use the lexical information (i.e., whole word form) and rely less on the sublexical information (i.e., phonological segments and their sequence), which may have temporarily worsened their phonological skills. However, fewer phonological errors were observed when testing was repeated a month after the intervention.

Action video games (AVG) are highly demanding visual tasks that has been applied to provoke neural plasticity of visual temporal processing skills and improve visuospatial attention.[29, 56-58]

Thus, AVG have been adopted as an indirect approach to enhance magnocellular-dorsal function. Recent studies have investigated whether the improvement of the magnocellular-dorsal system through AVG training can be transferred to reading performance and whether improvements in reading skills are associated with AVG performance and levels of attention demanded.[59-61]

Bertoni et al.[59] investigated the treatment effect of AVG on DD, adopting a partial crossover intervention paradigm. Participants received either a 9-day AVG training followed by a 9-day non-AVG training or these in reversed sequence, with a 10-day wash-out period between the two types of training. Compared to non-AVG training, AVG significantly enhanced dyslexic children's visual searching skills, a common measure for visual magnocellular function. In addition to magnocellular-dorsal function, the training also improved pseudoword reading speed, confirming the application of AVG as a training tool for DD.

Franceschini and Bertoni[60] hypothesized that if AVG had direct benefits to reading, those with more pronounced improvement in game-playing skills could learn how to read more effectively. To test this hypothesis, they divided the dyslexic children who received AVG training into high and low learning players according to the game score enhancement. Following their hypothesis, high learning players showed significant improvement in their pseudoword reading rate and phonological short-term memory, while the low learning players did not. Thus, game score enhancement can be considered as an evaluation index when applying AVG for DD treatment.

Lastly, Peters et al.[61] investigated whether increasing the attentional demand in AVG playing could further improve dyslexic children's reading performance. This study divided the treatment group into the regular (AVG-R) and increased attention AVG (AVG+) groups. Both groups played the same AVG but with different game controlling methods: the AVG-R group used a computer mouse, whilst the AVG+ group used the players' eye movements tracked by an eye-tracker to increase the attentional demands. However, while AVG training improved reading accuracy, rate, comprehension, and rapid naming skills, there were no significant differences between the AVG-R and AVG+ groups. They proposed that the treatment efficacy relied more on the automatic attentional control required by the AVG rather than conscious attention and eye movements, but it was also possible that the AVG+ training was too challenging and affected children's motivation to play the game.

Given the encouraging evidence mentioned above, magnocellular-dorsal training can be considered as a treatment approach to improve reading performance in dyslexics. However, most intervention studies reported have been small scale. Larger-scale clinical trials are needed to confirm the treatment efficacy. It has also been suggested that because the test-retest correlation for reading tests is low in dyslexics, the reading tests before and after the interventions should be repeated, preferably thrice, to increase the statistical power.[62]•

Other factors to be considered

The accumulated evidence from the literature strongly supports magnocellular-dorsal deficit as one of the root causes of DD. However, recent studies have also indicated additional factors worth considering when investigating this neurobiological deficit further.

Magnocellular deficits do not happen in all dyslexics

It should be noted that not all dyslexics exhibit a magnocellular deficit. By using clustering analyses, Peters et al.[63]•• classified dyslexics into two subgroups, Magnocellular-Deficit

Dyslexics (MD-Dyslexics) and Magnocellular-Typical Dyslexics (MT-Dyslexics) based on their flicker fusion threshold (FFT) performance. FFT measures the temporal frequency for rapidly modulated luminance at which the flickering light is perceived as entirely steady.[64, 65] The achromatic FFT performance is associated with the magnocellular activation observed in non-linear multifocal visual evoked potential responses[66] and is believed to reflect the ability of the primary visual cortex to process temporal visual information. Their analyses classified 53.7% of dyslexics as the MD-Dyslexics who showed a reduced FFT, while others as the MT-Dyslexics with normal FFT.

Further studies may need to investigate what factors differentiate MD- from MT-Dyslexics and if languages requiring different orthographic and phonological processing skills (e.g., English vs. Chinese) affect the proportion of these dyslexic subtypes. More importantly, whether magnocellular-dorsal training described above can be adopted to improve reading performance for both dyslexic subtypes.

Parvocellular-ventral stream should not be neglected

The magnocellular theory assumes that the parvocellular-ventral stream remains intact in dyslexics. This assumption arises because dyslexics underperform only in visual tasks that attempt to activate the magnocellular-dorsal stream. Indeed, visual stimulations used in previous studies encompassed a broad range of spatio-temporal properties that may also stimulate the parvocellular-ventral system. In addition, there is increasing evidence that the dorsal stream does not only receive magnocellular inputs, but also signals from neurons in the parvocellular-recipient layer 4Cβ of the primary visual cortex.[19] At higher cortical levels, the magnocellular-dorsal and parvocellular-ventral signal processing are not entirely isolated, but inter-mingled.[67, 68] Thus, it is hypothesized that the parvocellular-ventral stream may also be involved in DD.

Contemori et al.[69]• recently reported that typical readers had higher contrast sensitivity in visual tasks that involve activation of the parvocellular-ventral system (i.e., low temporal frequency) than in tasks specific to the magnocellular-dorsal system (i.e., low spatial & high temporal frequency). However, such facilitation in contrast sensitivity was absent in dyslexics. They therefore suggested that dyslexics may have an inefficient magno-parvo co-activation that disturbs the feedforward processing of words during reading. The same team later investigated the lateral masking effect in dyslexics and typical readers.[70]• The lateral masking task required participants to discriminate the motion direction of a Gabor target of low spatial frequency (0.5 c/deg) drifting at 16 deg/s, which was intended to stimulate the magnocellular-dorsal system. A pair of static vertical flankers (spatial frequency: 0.125, 0.5, or 2 c/deg) were located above and below the target. Theoretically, lateral masking is provoked if the target and flankers share similar spatial frequencies.[71] As expected, typical readers showed less lateral masking when the flankers' spatial frequency was higher than the target, which was expected to trigger the magno-parvo coactivation. In contrast, the lateral masking under this magno-parvo co-activation condition was not observed in dyslexics, supporting their hypothesis that unbalanced magnocellular and parvocellular activities may exist in DD.

Dyslexics have difficulties in excluding noises

One of the frequently used indicators for magnocellular-dorsal deficit is coherent motion sensitivity,[24, 29-32] a measure of global motion perception. This low-level visual motion processing is determined using the Random Dot Kinematogram (RDK), which comprises two sets of moving dots, the signal and noise dots. The signal dots move coherently in the same direction, while the noise dots move randomly. Dyslexics usually require a higher proportion

of signal dots to detect the presence of global motion.[24, 29-32] Given that perception of motion coherence is mediated by the V5/MT,[72-75] a region of the extrastriate visual cortex dominated by magnocellular input,[67, 68, 76] it is speculated that the reduced coherent motion sensitivity in DD may reflect a deficit of the magnocellular-dorsal system. However, it has been argued that rather than impaired perception of global dot motion, dyslexics might have difficulties in excluding the noise dots.[77-79] In other words, they may fail to filter out the environmental distractors and fail to properly orient visual-spatial attention to the target.

Recently, Ji and Bi[80]• tested this hypothesis by comparing the performance of dyslexics and typical readers in the coherent motion and static global form tasks under high (Signal & Noise contrast = 63.88%) and low noise levels (Signal contrast = 63.88%, Noise contrast = 58.52%). If the magnocellular deficit is the only cause of DD, dyslexics should perform worse in the coherent motion task than typical readers, but similarly in the global form task, regardless of the noise levels. Contrary to this prediction, dyslexics exhibited lower sensitivities than typical readers for both coherent motion and global form tasks in the high-noise, but not the low-noise condition. These results further support the noise cancellation theory that dyslexics have difficulties in excluding distractors. Nevertheless, as indicated by Ji and Bi,[80] the magnocellular deficit and noise exclusion theories are not contradictory. Indeed, noise exclusion is one of the mechanisms explaining visuospatial attention,[81] which, in turn, is also mediated by the magnocellular-dorsal pathway.[82, 83]

Conclusions

Recently published evidence supports the magnocellular theory and affirms the dysfunction of the magnocellular-dorsal system as the cause, rather than the consequence, of DD. Although not all dyslexics have magnocellular-dorsal deficits, a visual task with rapid temporal modality can discriminate a subtype of dyslexics from typical readers with adequate sensitivity and specificity.[63] Thus, magnocellular-dorsal functions, taken together with the magno-parvo co-activation and noise cancellation theory, should be included in the battery of tests alongside conventional phonological measurements to help identify earlier children at risk of DD.

Acknowledgements

This study was supported by the Research Centre for SHARP Vision (RCSV) from The Hong Kong Polytechnic University. We thank Dr. Maureen Boost for critical reading of the manuscript.

Human and Animal Rights

This article does not contain any studies with human or animal subjects performed by any of the authors.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

Recently published papers of particular interest have been highlighted as:
• Important
•• Very important

1. Yang L, Li C, Li X, Zhai M, An Q, Zhang Y, et al. Prevalence of developmental dyslexia in primary school children: A systematic review and meta-analysis. Brain Sci. 2022;12: 240.
2. World Health Organization. ICD-11 for mortality and morbidity statistics. 2018.
3. Goldston DB, Walsh A, Mayfield Arnold E, Reboussin B, Sergent Daniel S, Erkanli A, et al. Reading problems, psychiatric disorders, and functional impairment from mid- to late adolescence. J Am Acad Child Adolesc Psychiatry. 2007;46:25-32.
4. Mugnaini D, Lassi S, La Malfa G, Albertini G. Internalizing correlates of dyslexia. World J Pediatr. 2009;5:255-64.
5. Mammarella IC, Ghisi M, Bomba M, Bottesi G, Caviola S, Broggi F, et al. Anxiety and depression in children with nonverbal learning disabilities, reading disabilities, or typical development. J Learn Disabil. 2016;49:130-9.
6. Nelson JM, Harwood H. Learning disabilities and anxiety: A meta-analysis. J Learn Disabil. 2011;44:3-17.
7. Daniel SS, Walsh AK, Goldston DB, Arnold EM, Reboussin BA, Wood FB. Suicidality, school dropout, and reading problems among adolescents. J Learn Disabil. 2006;39:507-14.
8. Ramus F, Rosen S, Dakin SC, Day BL, Castellote JM, White S, et al. Theories of developmental dyslexia: insights from a multiple case study of dyslexic adults. Brain. 2003;126:841-65.
9. Boden C, Giaschi D. M-stream deficits and reading-related visual processes in developmental dyslexia. Psychol Bull. 2007;133:346-66.
10. Skottun BC. The magnocellular deficit theory of dyslexia: the evidence from contrast sensitivity. Vis Res. 2000;40:111-27.
11. Stein J. The magnocellular theory of developmental dyslexia. Dyslexia. 2001;7:12-36.
12. Stein J. What is developmental dyslexia? Brain Sci. 2018;8: 100.
13. Stein J. The current status of the magnocellular theory of developmental dyslexia. Neuropsychologia. 2019;130:66-77.
14. Vidyasagar TR. A neuronal model of attentional spotlight: parietal guiding the temporal. Brain Res Rev. 1999;30:66-76.
15. Livingstone M, Hubel D. Segregation of form, color, movement, and depth: anatomy, physiology, and perception. Science. 1988;240:740-9.
16. Maunsell JH. Functional visual streams. Curr Opin Neurobiol. 1992;2(4):506-10.
17. Croner LJ, Kaplan E. Receptive fields of P and M ganglion cells across the primate retina. Vis Res. 1995;35:7-24.
18. Kaplan E, Shapley RM. The primate retina contains two types of ganglion cells, with high and low contrast sensitivity. Proc Natl Acad Sci. 1986;83:2755-7.
19. Nassi JJ, Callaway EM. Parallel processing strategies of the primate visual system. Nat Rev Neurosci. 2009;10:360-72.
20. Norman J. Two visual systems and two theories of perception: An attempt to reconcile the constructivist and ecological approaches. Behav Brain Sci. 2002;25:73-96; discussion -144.
21. Goodale MA, Milner AD. Separate visual pathways for perception and action. Trends Neurosci. 1992;15:20-5.
22. Milner AD, Goodale MA. Two visual systems re-viewed. Neuropsychologia. 2008;46:774-85.
23. Lovegrove WJ, Bowling A, Badcock D, Blackwood M. Specific reading disability: differences in contrast sensitivity as a function of spatial frequency. Science. 1980;210:439-40.
24. Cornelissen P, Richardson A, Mason A, Fowler S, Stein J. Contrast sensitivity and coherent motion detection measured at photopic luminance levels in dyslexics and controls. Vis Res. 1995;35:1483-94.

25. Pammer K, Wheatley C. Isolating the M(y)-cell response in dyslexia using the spatial frequency doubling illusion. Vis Res. 2001;41:2139-47.
26. Buchholz J, McKone E. Adults with dyslexia show deficits on spatial frequency doubling and visual attention tasks. Dyslexia. 2004;10:24-43.
27. Gori S, Cecchini P, Bigoni A, Molteni M, Facoetti A. Magnocellular-dorsal pathway and sub-lexical route in developmental dyslexia. Front Hum Neurosci. 2014;8:460.
28. Leung KY, Chan HH, Leung MP. Subjective and objective evaluation of visual functions in dyslexic children with visual perceptual deficiency-Before and after ten-weeks of perceptual training. Res Dev Disabil. 2018;80:112-30.
29. Gori S, Seitz AR, Ronconi L, Franceschini S, Facoetti A. Multiple causal links between magnocellular-dorsal pathway deficit and developmental dyslexia. Cereb Cortex. 2016;26:4356-69.
30. Hill GT, Raymond JE. Deficits of motion transparency perception in adult developmental dyslexics with normal unidirectional motion sensitivity. Vis Res. 2002;42:1195-203.
31. Samar VJ, Parasnis I. Cortical locus of coherent motion deficits in deaf poor readers. Brain Cogn. 2007;63:226-39.
32. Slaghuis WL, Ryan JF. Spatio-temporal contrast sensitivity, coherent motion, and visible persistence in developmental dyslexia. Vis Res. 1999;39:651-68.
33. Benassi M, Simonelli L, Giovagnoli S, Bolzani R. Coherence motion perception in developmental dyslexia: a meta-analysis of behavioral studies. Dyslexia. 2010;16:341-57.
34. Ferretti G, Mazzotti S, Brizzolara D. Visual scanning and reading ability in normal and dyslexic children. Behav Neurol. 2008;19:87-92.
35. Iles J, Walsh V, Richardson A. Visual search performance in dyslexia. Dyslexia. 2000;6:163-77.
36. Vidyasagar TR, Pammer K. Impaired visual search in dyslexia relates to the role of the magnocellular pathway in attention. Neuroreport. 1999;10:1283-7.
37. Livingstone MS, Rosen GD, Drislane FW, Galaburda AM. Physiological and anatomical evidence for a magnocellular defect in developmental dyslexia. Proc Natl Acad Sci. 1991;88:7943-7.
38. Giraldo-Chica M, Hegarty JP, 2nd, Schneider KA. Morphological differences in the lateral geniculate nucleus associated with dyslexia. Neuroimage Clin. 2015;7:830-6.
39. Eden GF, VanMeter JW, Rumsey JM, Maisog JM, Woods RP, Zeffiro TA. Abnormal processing of visual motion in dyslexia revealed by functional brain imaging. Nature. 1996;382:66-9.
40. Heim S, Grande M, Pape-Neumann J, van Ermingen M, Meffert E, Grabowska A, et al. Interaction of phonological awareness and 'magnocellular' processing during normal and dyslexic reading: behavioural and fMRI investigations. Dyslexia. 2010;16:258-82.
41. Demb JB, Boynton GM, Heeger DJ. Brain activity in visual cortex predicts individual differences in reading performance. Proc Natl Acad Sci. 1997;94:13363-6.
42. Huettig F, Lachmann T, Reis A, Petersson KM. Distinguishing cause from effect–many deficits associated with developmental dyslexia may be a consequence of reduced and suboptimal reading experience. Lang Cogn Neurosci. 2018;33:333-50.
43. Olulade OA, Napoliello EM, Eden GF. Abnormal visual motion processing is not a cause of dyslexia. Neuron. 2013;79:180-90.
44. Gottesman, II, Gould TD. The endophenotype concept in psychiatry: etymology and strategic intentions. Am J Psychiatry. 2003;160:636-45.
45. Glahn DC, Knowles EE, McKay DR, Sprooten E, Raventos H, Blangero J, et al. Arguments for the sake of endophenotypes: examining common misconceptions about the use

of endophenotypes in psychiatric genetics. Am J Med Genet B Neuropsychiatr Genet. 2014;165B:122-30.
46.•• Mascheretti S, Gori S, Trezzi V, Ruffino M, Facoetti A, Marino C. Visual motion and rapid auditory processing are solid endophenotypes of developmental dyslexia. Genes Brain Behav. 2018;17(1):70-81. **This study indicates magnocellular deficits as an endophenotype of dyslexia.**
47.• Flint S, Pammer K. It is the egg, not the chicken; dorsal visual deficits present in dyslexia are not present in illiterate adults. Dyslexia. 2019;25:69-83. **This study proves that magnocellular deficits in dyslexics are irrelevant to the reading experience.**
48. Schiavi C, Finzi A, Cellini M. Steady-State pattern electroretinogram and frequency doubling technology in adult dyslexic readers. Clin Ophthalmol. 2019;13:2451-9.
49. Vilhena DA, Guimaraes MR, Guimaraes RQ, Pinheiro AMV. Magnocellular visual function in developmental dyslexia: deficit in frequency-doubling perimetry and ocular motor skills. Arq Bras Oftalmol. 2021;84:442-8.
50. Brusini P, Busatto P. Frequency doubling perimetry in glaucoma early diagnosis. Acta Ophthalmol Scand Suppl. 1998;227:23-4.
51. Fan X, Wu LL, Ma ZZ, Xiao GG, Liu F, Jr. Usefulness of frequency-doubling technology for perimetrically normal eyes of open-angle glaucoma patients with unilateral field loss. Ophthalmology. 2010;117:1530-7, 7 e1-2.
52. Kaushik S, Pandav SS, Ichhpujani P, Gupta A. Correlation of frequency-doubling perimetry with retinal nerve fiber layer thickness and optic disc size in ocular hypertensives and glaucoma suspects. J Glaucoma. 2011;20:366-70.
53. Prokosch V, Eter N. Correlation between early retinal nerve fiber layer loss and visual field loss determined by three different perimetric strategies: white-on-white, frequency-doubling, or flicker-defined form perimetry. Graefes Arch Clin Exp Ophthalmol. 2014;252:1599-606.
54.• Ebrahimi L, Pouretemad H, Khatibi A, Stein J. magnocellular based visual motion training improves reading in Persian. Sci Rep. 2019;9:1142. **This study provides direct evidence that training magnocellular-dorsal functions can improve the reading performance of dyslexic children.**
55.• Ebrahimi L, Pouretemad H, Stein J, Alizadeh E, Khatibi A. Enhanced reading abilities is modulated by faster visual spatial attention. Ann Dyslexia. 2022;72:125-46. **This study provides direct evidence that training magnocellular-dorsal functions can improve the reading performance of dyslexic children.**
56. Franceschini S, Gori S, Ruffino M, Viola S, Molteni M, Facoetti A. Action video games make dyslexic children read better. Curr Biol. 2013;23:462-6.
57. Franceschini S, Bertoni S, Gianesini T, Gori S, Facoetti A. A different vision of dyslexia: Local precedence on global perception. Sci Rep. 2017;7(1):17462.
58. Franceschini S, Trevisan P, Ronconi L, Bertoni S, Colmar S, Double K, et al. Action video games improve reading abilities and visual-to-auditory attentional shifting in English-speaking children with dyslexia. Sci Rep. 2017;7:5863.
59. Bertoni S, Franceschini S, Puccio G, Mancarella M, Gori S, Facoetti A. Action video games enhance attentional control and phonological decoding in children with developmental dyslexia. Brain Sci. 2021;11:171.
60. Franceschini S, Bertoni S. Improving action video games abilities increases the phonological decoding speed and phonological short-term memory in children with developmental dyslexia. Neuropsychologia. 2019;130:100-6.
61. Peters JL, Crewther SG, Murphy MJ, Bavin EL. Action video game training improves text reading accuracy, rate and comprehension in children with dyslexia: a randomized controlled trial. Sci Rep. 2021;11:18584.

62.• Toffalini E, Giofre D, Pastore M, Carretti B, Fraccadori F, Szucs D. Dyslexia treatment studies: A systematic review and suggestions on testing treatment efficacy with small effects and small samples. Behav Res Methods. 2021;53:1954-72. **This study suggests experimental methods to increase the statistical power in dyslexia treatment studies.**
63.•• Peters JL, Bavin EL, Brown A, Crewther DP, Crewther SG. Flicker fusion thresholds as a clinical identifier of a magnocellular-deficit dyslexic subgroup. Sci Rep. 2020;10:21638. **This study classifies dyslexics based on the magnocellular-dorsal function.**
64. Eisen-Enosh A, Farah N, Burgansky-Eliash Z, Polat U, Mandel Y. Evaluation of critical flicker-fusion frequency measurement methods for the investigation of visual temporal resolution. Sci Rep. 2017;7:15621.
65. Mankowska ND, Marcinkowska AB, Waskow M, Sharma RI, Kot J, Winklewski PJ. Critical flicker fusion frequency: A narrative review. Medicina (Kaunas). 2021;57: 1096.
66. Brown A, Corner M, Crewther DP, Crewther SG. Human flicker fusion correlates with physiological measures of magnocellular neural efficiency. Front Hum Neurosci. 2018;12:176.
67. Merigan WH, Maunsell JH. How parallel are the primate visual pathways? Annu Rev Neurosci. 1993;16:369-402.
68. Schiller PH. On the specificity of neurons and visual areas. Behav Brain Res. 1996;76:21-35.
69.• Contemori G, Battaglini L, Barollo M, Ciavarelli A, Casco C. Developmental dyslexia: A deficit in magnocellular-parvocellular co-activation, not simply in pure magnocellular activation. Vis Res. 2019;159:61-7. **This study indicates the involvement of magnocellular-parvocellular co-activation in dyslexia.**
70.• Ciavarelli A, Contemori G, Battaglini L, Barollo M, Casco C. Dyslexia and the magnocellular-parvocellular coactivaton hypothesis. Vis Res. 2021;179:64-74. **This study indicates the involvement of magnocellular-parvocellular co-activation in dyslexia.**
71. Polat U, Sagi D. Lateral interactions between spatial channels: suppression and facilitation revealed by lateral masking experiments. Vis Res. 1993;33:993-9.
72. Ajina S, Kennard C, Rees G, Bridge H. Motion area V5/MT+ response to global motion in the absence of V1 resembles early visual cortex. Brain. 2015;138:164-78.
73. Giaschi D, Zwicker A, Young SA, Bjornson B. The role of cortical area V5/MT+ in speed-tuned directional anisotropies in global motion perception. Vis Res. 2007;47:887-98.
74. Newsome WT, Pare EB. A selective impairment of motion perception following lesions of the middle temporal visual area (MT). J Neurosci. 1988;8:2201-11.
75. Rees G, Friston K, Koch C. A direct quantitative relationship between the functional properties of human and macaque V5. Nat Neurosci. 2000;3:716-23.
76. Maunsell JH, Nealey TA, DePriest DD. Magnocellular and parvocellular contributions to responses in the middle temporal visual area (MT) of the macaque monkey. J Neurosci. 1990;10:3323-34.
77. Conlon EG, Lilleskaret G, Wright CM, Power GF. The influence of contrast on coherent motion processing in dyslexia. Neuropsychologia. 2012;50:1672-81.
78. Conlon EG, Sanders MA, Wright CM. Relationships between global motion and global form processing, practice, cognitive and visual processing in adults with dyslexia or visual discomfort. Neuropsychologia. 2009;47:907-15.
79. Sperling AJ, Lu ZL, Manis FR, Seidenberg MS. Motion-perception deficits and reading impairment: it's the noise, not the motion. Psychol Sci. 2006;17:1047-53.
80.• Ji Y, Bi HY. Visual Dysfunction in Chinese children with developmental dyslexia: Magnocellular-dorsal pathway deficit or noise exclusion deficit? Front Psychol. 2020;11:958. **This study provides evidence on the noise exclusion theory for dyslexia.**
81. Dosher BA, Lu ZL. Noise exclusion in spatial attention. Psychol Sci. 2000;11:139-46.

82. Cheng A, Eysel UT, Vidyasagar TR. The role of the magnocellular pathway in serial deployment of visual attention. Eur J Neurosci. 2004;20:2188-92.
83. Vidyasagar TR. Attentional gating in primary visual cortex: a physiological basis for dyslexia. Perception. 2005;34:903-11.