Wobbles, warbles and fish - the neural magnocellular basis of dyslexia

Supported by The Dyslexia Research Trust (www.dyslexic.org.uk), Dyers & Colourists, Esmee Fairbairn, Garfield Weston and Wellcome Trusts, BBC Children in Need
Reading is difficult!

Reading is a painful task.
It extinguishes the light from the eyes.
It bends the back.
It crushes the viscera and the ribs.
It brings forth pain to the kidneys and weariness to the whole body.

13th C. Florentine monk or 20th C dyslexic!
• 20% of UK population cannot look up the word ‘plumber’ in the yellow pages

• ½ these may have developmental dyslexia

• May be less of a problem in more ‘transparent’ languages such as Italian or Norwegian

• 20% of boys have some degree of dyslexia; 5% of girls

• Very important that teachers learn to recognise it, because treatment is most successful, the earlier it is instituted
Reading is difficult because it requires:

1. Rapid **visual** identification of letters and their order; even in experienced good readers this process is rate limiting

2. Rapid **auditory** translation into the sounds they stand for

3. Background knowledge of phonology- how words can be split down into separate phonemes

   All these processes may depend on the timing properties of magnocellular neurones
1898  Pringle Morgan  ‘Word blindness’
1930s  Samuel Orton  -  strephosymbolia
1950s  McDonald Critchley  Parietal lobe
1960s  Social denigration  -  “Middle class children are dyslexic, working class children are thick!”
1980s  Linguistic theory - phonological deficit
1990s  Development of the brain is different: planum temporale, ectopias, problems with all kinds of timing and sequencing
2000s  Magnocellular theory  impaired development of visual, auditory and motor magno-neurones
Reading is difficult!

1 in 3 of US & UK 11yr olds leave primary school unable to read.

1 in 3 of US & UK adults leave high school effectively illiterate.

Reading failure is the commonest cause of childhood misery, depression, even suicide,

OR frustration, aggression, crime; 75% of those in gaol are illiterate.

Commonest disability among College students
What is Developmental Dyslexia?
Reading and spelling significantly below that expected from subject’s age and intelligence, despite good health, teaching and cultural experience

Symptoms

1. Reading/IQ discrepancy
2. 20% of all boys
3. Poor phonology
4. Speech impairments (lisps, spoonerisms, mispronunciations
5. Unstable vision, visual confusions
6. Very bad spelling
7. Left/right confusions, mixed handedness
8. General sequencing problems
9. Clumsiness & incoordination – ‘soft’ cerebellar signs

History

11. Family History of language, literacy and psychiatric problems.
12. Difficult birth
13. Delayed milestones (crawling, walking, speech)
14. Developmental dyspraxia, dysphasia hyperactivity
15. Otitis media @ age 1-3
16. Autoimmune problems: asthma, eczema, hayfever
Dyslexia in the Classroom

- Backward reading & spelling in an otherwise bright child (reading very far behind age)
- Very common - 20% of all boys; 5% of girls
- In older pupils particularly anxious and slow at reading out loud, and very poor spelling
- Brother had the same kind

- Confusion of visual order of letters, poor visual attention & memory (poor orthography)
- Missequencing word sounds (poor phonology), days of week, months of the year; misorders doing things in his life!
- Multiplication tables make him sick!
- Confuses left and right
- Clumsy, incoordinated and inattentive. cf. developmental dyspraxia, ADHD
Neurobiological Associations of Developmental Dyslexia

- Family History of motor, language, psychiatric and immune problems – genetic linkage C 1,2,6,15,18
- Difficult birth
- Delayed crawling, walking, speaking
- Speech impairments (eg lisps, spoonerisms)
- 2/3rds male; 1/3 female
- Overlap with developmental dysphasia, ADHD, autistic spectrum
- Unstable visuomotor control and auditory perception and attention

- Abnormal hemispheric symmetry, unstable cerebral dominance, mixed handedness, left/right confusions
- Clumsiness, ‘soft’ cerebellar signs
- Immune system (allergies, asthma, eczema, hayfever)
- Deficiency of essential fatty acids – fish oils?
Overlap (comorbidity) between developmental dyslexia, dysphasia, dyspraxia, ADHD, autism – abnormal magnocellular neurones?

Dyslexia - reading and spelling difficulties, unsteady eyes, visual and auditory inattention, incoordination
Dysphasia (specific language impairment) speech impediments (mispronunciation, lisps, stuttering) auditory inattention, incoordination
Dyspraxia – incoordination, poor motor planning/execution, inattention
ADHD - hyperactivity/impulsivity, inattention, incoordination
Autism - inattention, incoordination, absent social & communication skills
But it is often argued that reading failure is just due to bad teaching, and dyslexia doesn’t really exist:

“Middle class children are called ‘dyslexic’, where working class children are called stupid”

Has dyslexia a real neurobiological basis or is it just a middle class invention?
Biological or invented?

- Genetic basis – family history, gender
- Brain differences – ectopias, smaller m-cells, cerebellum, fMRI
- Unstable visual & auditory attention - poor eye control & pronunciation
- Association with other neurodevelopmental disorders (ADHD, dyspraxia, SLI, autism spectrum)
- Often difficult birth
- Delayed crawling, walking, speaking
- Glue ear when learning to speak – impaired auditory perception - speech impairments: lisps, spoonerisms
- Association with autoimmunity
Chromosome sites linked to reading skill

C6p? KIAA gene - cell-cell recognition and immune control (MHC system)

Finnish pedigree

DYX1 gene
Reading

Motor cortex

Broca's area

Primary auditory area

Wernicke's area

Angular gyrus

Primary visual area
The brain’s reading network

• Input from eyes relays in LGN to primary visual cortex at the back of the brain
• Further visual processing moving forwards through secondary visual cortical areas
• Links with auditory processing in left angular gyrus to form lexicon (representation of visual and auditory form of words and their meaning)
• Projection forwards to left speech areas, for internal speech as well as reading out loud
Associative network (c.11 Hz) active during reading
2nd trimester ectopias in dyslexic brain. Seen also in auto immune mice.
Left hemisphere language areas that activate less in dyslexics.
Many children complain of **visual** difficulties with reading. Often their eyes **wobble** when they try to read. This may be due to weak **visual magnocellular function**.
Reading is primarily a visual process

Visual processing

DOG

visual analyser

whole word

/D/O/G/

phonological analysis

direct visual analysis

meaning (semantics)
When reading the eyes jump from word to word in the text. Each word can only be identified during very brief ‘fixations’ that last only $1/3^{rd}$ sec. Eyes must be steady during these fixations, or text will blur.
Retinal Ganglion cells

10% are large *magnocellular* cells (100x p- cells in area) - for timing visual events: fast responses, low contrast, motion, flicker, eye movements

Most retinal ganglion cells are *parvocellular* (small): for colour, fine detail, high contrast
Visual magnocellular system directs visual attention & eye movements.
The visual magnocellular system is mildly impaired in many (but not all) dyslexics

- 30% smaller LGN magnocells post mortem
- Reduced and delayed evoked brain waves
- Reduced visual motion sensitivity
- Unstable eye control
- Reduced activation of cortical motion areas (FMRI)
- Lower sensitivity to contrast
- Lower sensitivity to flicker
- Lower stereoacuity
- Reduced visual jitter
- Weaker visual attention - slower visual search
- Visual crowding
- Mini left neglect - clock drawing
- Prolonged line motion illusion
- Reduced Ternus effect
Abnormal magnocells in dyslexic brain
Delayed Brain Potentials Evoked by Moving Visual Stimulus
Visual Motion Sensitivity

Measure proportion of random dots that have to move together in the same direction to see coherent motion of the whole cloud.
Many dyslexics need stronger visual motion signals, i.e., they have lowered visual magnocellular sensitivity.
Homophone test of visual/orthographic skill

“Which one is the proper spelling?”

This task can’t be solved by sounding out the letters.

Best correlate of reading skill even in adults
Not a diagnostic test, but over 20% of individual differences in orthographic reading ability (good readers & dyslexics) can be explained just by their low level **visual magnocellular sensitivity**, independent of their cognitive skills. Thus low level visual magnocellular sensitivity helps determine how well orthographic skills develop.
The visual magnocellular system stabilises the eyes to avoid visual wobble.

- Unwanted image motion, ‘retinal slip’
- Detected by M-system
- Feedback to eye muscle control system
- Locks eyes on target
- Visual stability
- Identify letter order
- Orthographic skill
- Phonological skill
Weak magnocellular system causes unstable vision - oscillopsia

“The letters go all blurry”
“The letters move over each other, so I can’t tell which is which”
“The letters seem to float all over the page”
“The letters move in and out of the page”
“The letters split and go double”
“The c moved over the r, so it looked like another c”
“The p joined up with the c”
“d’s and b’s sort of get the wrong way round”
“The page goes all glary and hurts my eyes”
“I keep on losing my place”
DYSLEXICS’ IMPAIRED VISUOMOTOR FUNCTION

• Unsteady binocular fixation, hence unstable visual perception
• Restricted & jerky vergence control
  • Jerky pursuit eye movements
  • Slower visual search - less ‘pop out’
  • Inaccurate dot localisation
  • Slower mental rotation
  • Lose place following vertical lines
• Improving eye control can often improve reading
Wobbly eyes!
Vergence control

- The eyes have to converge for near vision when reading.
- Control of vergence eye movements is dominated by the visual magno system.
- The vergence eye movement control system is the most vulnerable to drugs and disease.
- Dyslexics have very unstable vergence control.
Magnocellular processing sharpens:

\[
\text{dog dog dog}
\]

into

\[
\text{dog}
\]
Interventions that improve m-function and eye control often improve reading

In some 9 yr old children with poor binocular control temporary blurring of left eye improves vergence control and reading by 2 months/m (proved by randomised controlled trial –RCT)

In older children exercises can stabilise binocular fixation and greatly improve reading (proved by RCT)

Blue or yellow coloured filters can often rebalance visual M-input (proved by RCT)
Blue or yellow filters can help some children to keep the letters still.
Blue & yellow filter transmission

Wavelength (nm)

Blue
Yellow
Coloured Filters

• Although they do not contribute to colour vision, retinal magnocellular ganglion cells are most responsive to yellow light.
• So in some children yellow filters can increase magnocellular and visual motion sensitivity, binocular control, hence improve reading
• Some magnocells are highly inhibited by red. Hence in other children blue filters can improve m- function and reading
Blue filters cut red most

Yellow filters cut blue most
Yellow Glasses

Before

Only 1 week later

Signatories and signatures between snow white
and blue red.

Signatures

In snow white and red:

Those have a passion

Shy - the nose bone a

Happy eating

This people trying to kill each other

1. In which county is castleton? Derbyshire village overlooked
by man for
2. Which mountain is it overlooked by? Mount Mam it has long
slides and very big.
3. When was the village first spined? In 1199 many old custo-
mers survive such as the guillem.
4. Which industries has castleton had in the past? Such as
iron rolling castle and ore mining
5. Why do you think castleton is called this? Because it has a
castle and it is on top of a hill.
6. Who built proud castle and when? William conquer it was in
1066.
7. What are the names of the seven covens? Blue Jorson speed well
black coven browl chier coven
8. What was made in black coven? Road slate used
for houses and other places.
9. Describe what blue jor looks like? Blue Jor is made from
Slasses and have similar colors like red yellow pink people.
10. Can you find out more about the old costumes that survived in
castleton? It's the most colorful since blue jor.
Elucidating the role of the visual magnocellular system in reading has enabled us to develop techniques for helping 75% of the dyslexics we see.
Magno deficit causes many dyslexics to confuse the visual order of letters!

‘He’s got a gnu.’
The visual/orthographic and auditory/phonological pathways

DOG (visual analyser)
separate letters

/ /D /O /G/ /
phonological analysis

DOG (direct visual analysis)
whole word

meaning (semantics)
2nd and 3rd formants ascend in frequency for ‘b’; but descend for ‘d’.

Subtle auditory impairments may reduce sensitivity to these changes in sound frequency.
Developmental Dyslexics are less sensitive to changes in sound frequency and intensity.

- Slow frequency changes in speech are tracked in real time by large magnocells in the auditory system.

![Graph showing detection thresholds for different frequency modulations.](image)

- **2 Hz FM**
  - Dyslexics (N=21): 2 Hz FM, Detection Threshold (Mod. Index) ≈ 1.5
  - Controls (N=23): 2 Hz FM, Detection Threshold (Mod. Index) ≈ 1.0
  - **p < 0.001**

- **40 Hz FM**
  - Dyslexics (N=21): 40 Hz FM, Detection Threshold (Mod. Index) ≈ 0.1
  - Controls (N=23): 40 Hz FM, Detection Threshold (Mod. Index) ≈ 0.05
  - **p = 0.027**

- **240 Hz FM**
  - Dyslexics (N=21): 240 Hz FM, Detection Threshold (Mod. Index) ≈ 0.008
  - Controls (N=23): 240 Hz FM, Detection Threshold (Mod. Index) ≈ 0.004
  - **p = 0.360, N.S.**

Witton, Talcott, Hansen, Richardson, Griffiths, Rees, Stein & Green, 1998
Nonsense Word Reading

Reading nonwords e.g. ‘tegwop’, ‘blint’, ‘plomt’, ‘peltip’, ‘visht’, depends on translating letters into their sounds quickly and accurately; hence they test **phonological** ability
Auditory FM Threshold (Mod. Index)

Nonword Naming (max. 30)

Meltham 10 year olds (N = 32); \( r_S = 0.7; p < 0.001 \)

FM sensitivity determines phonological skill
Impaired auditory magnocells in dyslexia?

• Large neurones in the auditory brainstem signal changes in sound frequency and amplitude
• Dyslexics have smaller magnocellular neurones in medial geniculate N.
• Lower AM & FM sensitivity
• Thus dyslexics’ poor phonology may result from impaired development of their auditory magnocells
Auditory and visual magnocellular sensitivity determines over half of the differences in children’s reading ability. Thus the most important determinant of overall reading ability appears to be low level magnocellular sensitivity. Encouraging because this can be improved by training.
The magnocellular systems also project strongly to the cerebellum – the brain’s autopilot - a magnocellular structure.
Control Head movement balancing on one leg Dyslexic
The Cerebellum & balance

- The cerebellum is the brain’s autopilot for timing, motor prediction and accurate motor programming: balance and skilled movements
- Magnocellular systems all project to the cerebellum and the cerebellum is part of the magno network
- Cerebellum is underactive in many dyslexics
- Explains their coordination problems, and may contribute to their reading difficulties
- But this is not their only cause; expensive balance exercises may improve balance but not reading
Sensorimotor Basis of Dyslexia

- Low **visual** magnocellular sensitivity → **orthographic** weakness
- Low **auditory** magnocellular sensitivity → **phonological** problems
- Lower kinaesthetic magnocellular sensitivity
- Lower **motor** magnocellular sensitivity → incoordination, poor balance
What causes this general magnocellular impairment?

Genetic
Immune System
Nutrition
Genetic linkage/association

• Are particular chromosomal markers/sites associated with poor reading?
• Analyse the DNA of father, mother and their dyslexic and normally reading children
• 300 Oxford families
• EU consortium; 1000 families, 2000 cases, 2000 controls, 50,000 markers per case
Chromosome sites linked to reading skill

C6p ? KIAA gene - cell~cell recognition and immune control (MHC system)

Finnish pedigree

DYX1 gene
C6p KIAA mutation?

- KIAA underexpression disrupts neuronal migration early in brain development
- Controls expression of cell surface recognition molecules
- Fail to respond to developmental signals, enable successful contact with other magnocells
- Could explain why the development of magnocellular neurones is impaired in dyslexia
Autoimmune conditions in dyslexics and controls

- Allergies
- Eczema
- Asthma
- Uveitis
- Migraine

Percentage affected by disease:

1. Allergies
2. Eczema
3. Asthma
4. Uveitis
5. Migraine
Dyslexia and the Immune System

• Development of magnocellular neurones is known to be regulated by the MHC cell recognition system.
• Linkage of poor reading to cell recognition genes on Chromosome 6.
• High incidence of immune anomalies in dyslexics.
• 50% of BSXB ‘autoimmune mice’ exhibit ectopias that are identical to those seen in dyslexics.
• Evidence for antimagno antibodies in serum of mothers with dyslexic children.
Cod Liver Oil Queue, 1946
Hugh Sinclair & Fish Oils
Why Fish Oils?

• Hugh Sinclair, Magdalen College, Oxford, persuaded wartime government to give cod liver oil to all pregnant mothers and children

• Omega 3 (n-3, ω3) fatty acids (derived from fish) make up 20% of the brain and heart membranes

• ω3 FAs speed nerve and muscle signalling by magnocellular neurones

• Deficiency in modern Western diets

• Treatment with ω3 FAs can improve reading
Fabulous Fish!
Fast magnocellular neurones are especially vulnerable to lack of fish oil omega 3 (n-3) fatty acids.

In order to open fast their ionic channels need flexible n-3 fatty acids in the surrounding membrane.
Fatty acid deficiency in dyslexia and young offenders?

- Many dyslexics and young offenders have signs of omega 3 deficiency: (excessive thirst, frequent urination, brittle nails, dry & bumpy skin, dry & scurfy hair)
- Low blood and brain omega-3 fatty acids
- Elevated levels of PLA2 enzyme
- Omega 3 FA (fish oil) supplements can improve m-function and reading
- Supplements can reduce offences by 1/3rd
Conclusions 1

- Fundamental auditory, visual & motor *temporal* sequencing requirements of speech and reading are mediated by *magnocellular* neuronal systems in the brain.

- **Visual** magnocellular weakness may cause visual perceptual instability, hence letter position confusions ➔ fuzzy *orthographic* representations, leading to poor orthographic skill for reading.

- **Auditory** magnocellular weakness impedes breakdown of word sounds into phonemes ➔ low *phonological* skill.

- Magno systems also involve the *cerebellum*, so that dyslexics tend to be incoordinated & clumsy.
Conclusions 2

- Weak magnocellular function may result from:
  Genetic vulnerability
  Antibody attack
  Fatty acid (fish oil) deficiency

- These weaknesses can be remedied: auditory and phonological training, eye exercises, coloured filters, fish oil supplements

BUT...
Wobbles, warbles and fish - the magnocellular neural basis of dyslexia

John Stein

Send your dyslexic students to The Dyslexia Research Trust (www.dyslexic.org.uk)