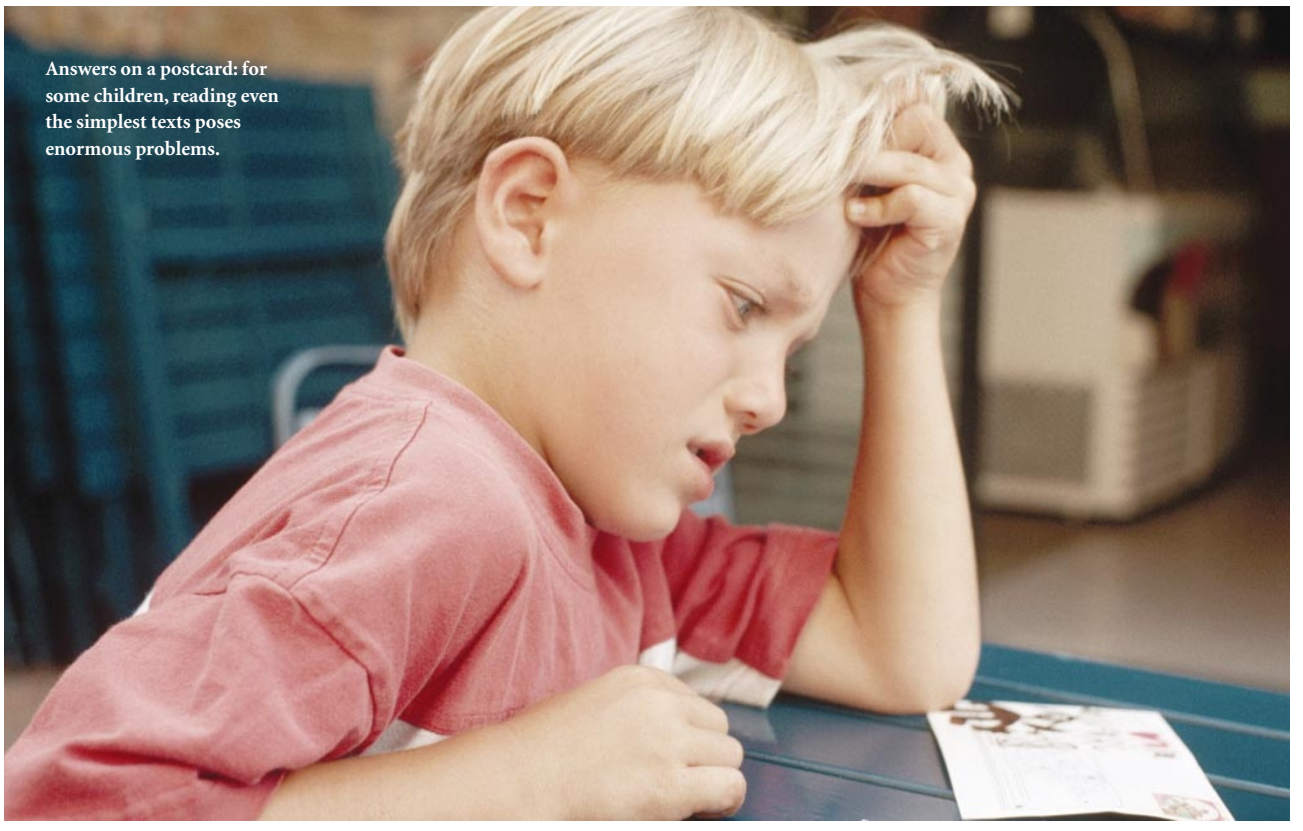


OWEN FRANKEN/CORBIS

Answers on a postcard: for some children, reading even the simplest texts poses enormous problems.

Lost for words

Thanks in part to brain-imaging technology, researchers are now homing in on the root cause of dyslexia. But research into strategies for treating the condition is still in its infancy, says Glenn Murphy.

Most people have a vague idea of what it is, or know someone who has it, or have heard about famous sufferers such as actor Tom Cruise, who seem to get by well enough despite their problems with reading. But for most of the past century, researchers have been unable to agree on what causes dyslexia.

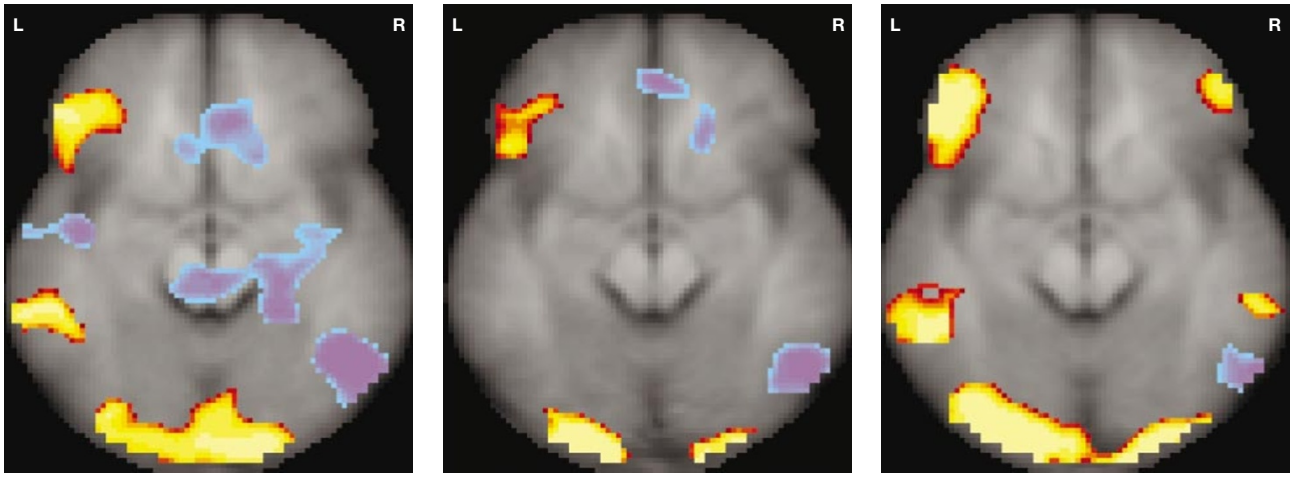
When children or adults fail to learn to read fluently — despite normal intelligence, instruction and opportunities to do so — they are diagnosed with developmental dyslexia. Exactly why they should fail has led to speculation about a host of possible causes. Over the past few years, however, brain-imaging studies have supplied fresh evidence that the fundamental problem lies in the brain's ability to process 'phonemes'. These are the speech sounds that enable us to tell one word from another — 'pet' and 'bet', for instance, are distinguished by the sounds of their initial consonants.

For all of us, decoding the arbitrary symbols of written language is a complex skill that requires instruction and considerable effort to attain. And for the world's dyslexics — around one in ten people — it presents almost insurmountable problems. Their plight first attracted attention in the late nineteenth century. Then studied mostly by ophthalmologists, speculation about the cause of this 'word blindness' centred initially on problems with vision — a view that still has its adherents today. In the 1980s, for instance, physiologist John Stein of the University of Oxford, UK, developed a theory that blames dyslexia on problems with focusing on text and with the scanning eye movements that we perform while reading[1].

> "My parents found out I was dyslexic when I was five. My aunt was training to be an educational psychologist, and she pointed out that something wasn't quite right."
> Jess, 25, from London

Other researchers have argued that the underlying problem lies with auditory processing. In 1980, Paula Tallal at Rutgers University's campus in Newark, New Jersey, proposed that dyslexics suffer from a defect that hampers their perception of short or rapidly varying sounds[2]. The defect is not disruptive enough to prevent dyslexics from learning to understand speech, but Tallal argues that it prevents them from associating short bursts of phonemes with their respective letters as they are learning to read. Some dyslexics also have problems with movement and balance, which has led psychologist Roderick Nicholson of the University of Sheffield, UK, to argue that dyslexia is caused by defects in the cerebellum, at the base of the brain[3].

In recent years, these ideas about visual, auditory and cerebellar defects have become part of a larger, 'magnocellular' theory of dyslexia[4]. This stems from post-mortem evidence — provided in 1991 by Margaret Livingstone and Albert Galaburda of Harvard Medical School in Boston[5] — showing that dyslexics have abnormalities in the magnocellular visual pathway, which is involved in processing fast-changing visual information. Other magnocellular systems handle similarly fleeting auditory and tactile information, and they each feed into the cerebellum during learning — so an extensive magnocellular dysfunction could explain



S. & B. SHAYWITZ

During reading, persistently poor readers (right) use similar brain areas to normal subjects (left), most notably in the back of the brain (bottom of images), although with markedly less success. Dyslexics who have to some extent overcome their disability (middle) show a different pattern of activity.

many of the defects observed in dyslexics.

Many dyslexia researchers, however, belong to a rival camp that argues that the fundamental problem lies not in visual or auditory processing, but is instead caused by a more specific defect in the brain's ability to decode phonemes. In tests, for example, dyslexics might swap the first letters of a pair of arbitrarily chosen words — turning 'basket-lemon' into 'lasket-bemon', for instance.

Over the past two decades, supporters of this phonological theory have amassed evidence documenting dyslexics' problems with phoneme processing, and confirming that these defects are the most commonly observed symptom of dyslexia[6]. In an attempt to close the case, Uta Frith of the Institute of Cognitive Neuroscience at University College London (UCL) and her postdoc Franck Ramus have recently completed the first study to test the competing theories of dyslexia in the same experimental subjects.

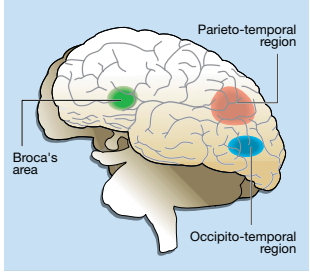
Frith, Ramus and their colleagues subjected 16 dyslexic volunteers and an equal number of non-dyslexic controls — all students at UCL — to a barrage of tests of hearing, vision, balance, motor coordination, intelligence and phoneme awareness. "Each person got at least ten hours of testing," explains Frith, "using tests that the proponents of the various theories themselves invented and suggested."

The results, published in April, revealed that all of the dyslexics had phonological deficits, and five showed none of the symptoms implicated in the rival theories[7]. "While only some dyslexics have abnormal vision and hearing, all have problems with tasks that specifically require them to manipulate phonemes," says Frith. This, she argues, indicates that dyslexia is essentially a disorder of phoneme processing; visual, hearing and cerebellar problems may often be associated with the condition, but they are not its direct cause.

Supporters of the magnocellular theory maintain that poor phonological processing is just one of many symptoms of dyslexia. But most experts now see it as the defining symptom, and the phonological theory has come to dominate. "There is more and more supporting evidence piling up for the phonological model, and conflicting evidence piling up against the others," says Maggie Snowling, a dyslexia researcher at the University of York, UK.

> "Spoonerism. I did that a lot when I was little — 'par cark' instead of 'car park' — all that kind of stuff. I still do it, but not so much. You find yourself about to say things, and you think: 'Err … no, that's not right.'" Jess

Some of the most persuasive evidence comes from studies using functional magnetic resonance imaging (fMRI), which allows researchers to study activity in the brain while it performs specific tasks, by monitoring changes in blood flow. "Functional imaging is a wonderful tool," says neuroscientist Sally Shaywitz of Yale University in New Haven, Connecticut. "It allows you to use fewer subjects and target different neural systems."



Map reading: the brain regions that are involved in deciphering text.

Results from fMRI suggest that there are at least two pathways for reading in the brain: inexperienced readers use one pathway, whereas a second, faster pathway takes over in more skilled readers. Both involve three key areas in the left side of the brain: a region at the front of the brain known as Broca's area; and at the rear, the parieto-temporal and occipito-temporal regions (see diagram, above). Broca's area has long been known, from studies of patients with brain lesions, to be required for normal speech and writing. Novice readers seem to use the parieto-temporal region to dismantle words for step-by-step phonological analysis; more experienced readers apparently rely on the occipito-temporal region to recognize whole words instantly[8].

With her husband Bennett and other Yale colleagues, Shaywitz has used fMRI to compare the brains of dyslexics to those of normal, healthy readers as they perform reading tasks such as trying to identify nonsensical words in rhyming pairs and real words in non-rhyming pairs. When the words used were nonsensical ('jeat' and 'lete', for example), they could not instantly be recognized, and so all the volunteers were forced to sound out the words in their heads, phoneme by phoneme. In 1998, Shaywitz and her colleagues reported that dyslexics and non-dyslexics differ in their patterns of brain activity[9]. "We found a clear neurological signature for dyslexia," she says.

As expected, the brains of normal readers lit up on the left side, activating areas mostly at the back, in particular the parieto-temporal region. But dyslexics showed a different pattern: the back of the brain remained dim in the scans, whereas the front, around Broca's area, was highly active. The dyslexic volunteers were apparently trying to compensate for their inactive parieto-temporal region by overactivating other parts of the brain's reading circuitry.

The dyslexic volunteers in this study were adults, which left open the possibility that their distinctive patterns of brain activity were the consequence of years of struggling with reading, rather than being the cause of their problems. But Shaywitz has since repeated the work with 144 children — half of them dyslexic, the rest normal readers.

Word processor: the Fast ForWord program helps dyslexics associate sounds with letters.

Last year, her team reported that the telltale fMRI signature had appeared once again[8], bolstering the idea that the underactivation of the parieto-temporal region seen in the brain scans is a key component of the underlying neurological deficit that causes dyslexia.

Shaywitz's research has also yielded insights into the processes by which some dyslexics are able to overcome, at least partially, their difficulties with reading. Although the fMRI scans of Shaywitz's older and younger dyslexic volunteers were broadly similar, there were some subtle differences: the overactivation of the front of the brain was more pronounced in older readers, who also activated regions on the right side of their brains. Could this mean that the older dyslexics were able to offset their faulty phonological processing systems by using other pathways?

> "As you get older, you try to make an effort to improve, and you do. I'm nowhere near as bad as I used to be, because I have to make a conscious effort to get things right — for fear of looking daft at work." Jess

To investigate the issue more thoroughly, Shaywitz looked at a group of young dyslexics who had managed to become accurate, if not fluent, readers, and compared their brain activity with that of another group whose reading had remained persistently poor. The two groups had been monitored since they were five years old, and assessed annually as part of a wider study of the acquisition of reading skills.

Shaywitz examined these young adults using fMRI, and again discovered distinct patterns of brain activity in each group. Those who could partially compensate for their reading problems had similar fMRI patterns to the dyslexic signatures identified in Shaywitz's earlier studies, with reduced activity at the rear of the brain. Persistently poor readers also gave similar results for tests involving nonsensical words. But when tested with real words, their brains became active in the occipito-temporal region. This was different from the pattern of activity in this area in normal readers, and seemed to be connected to activity in areas that are involved in general visual memory, rather than those that deal specifically with reading and language[10].

Shaywitz argues that many dyslexics learn to compensate for their poor phonological processing ability by increasing the activity of Broca's area. The persistently poor readers, on the other hand, try to rely more on general rote memory.

For researchers who are devising methods to help dyslexic children learn to read, this is an important result. First, it suggests that there may be at least two subgroups of dyslexics, one of which will respond more effectively to treatment. Second, it provides hope that the new consensus on the importance of phoneme processing, combined with the ability of functional brain imaging to monitor the activity of dyslexics' brains as they learn to overcome their difficulties, will help to put research into treatment strategies on a sounder scientific footing.

One study has already used fMRI to help monitor the effectiveness of a popular computer program used to treat dyslexia. Fast ForWord, developed by Tallal in collaboration with John Gabrieli of Stanford University in California, was devised in the light of Tallal's auditory theory of dyslexia, and therefore focuses on helping dyslexic children to process speech by exaggerating words and slowing them down.

> "It annoys me, to a certain extent, that nobody helped me. I know that they didn't have the resources to do it, and that annoys me more. We have an educational system that's missing a percentage of its students." Jess

Tallal and Gabrieli trained 20 dyslexic children, aged between 8 and 12 years, for eight weeks, giving them 100 minutes of tuition with Fast ForWord each day. In February, the researchers reported that the children's reading skills were significantly improved, and that these changes correlated with visible changes in brain function, viewed by fMRI as the children tackled a series of rhyming exercises[11]. There were "huge differences", says Gabrieli, including activation of the brain areas deployed by normal readers, and of the areas that are implicated in compensation for dyslexia by Shaywitz.

It's an encouraging result, but one that should be greeted cautiously, says Guinevere Eden of the Center for the Study of Learning at Georgetown University in Washington DC. She points out that Tallal and Gabrieli's study omitted a necessary control group, meaning that the placebo effect cannot be ruled out. "You need to involve another group of dyslexics that don't get the treatment," Eden says.

This sort of problem is common in research into dyslexia treatment, she says, as even studies with appropriate control groups have failed to match dyslexic and non-dyslexic subjects for general intelligence, socio-economic status and other factors. Eden also argues that more work will need to be done on the neurological basis of ordinary reading before improved treatment methods can be developed for dyslexia. "We're operating in a vacuum," she says. Functional brain-imaging studies are improving our understanding, she adds, but a great deal more groundwork remains to be done before the results can be integrated into education programmes[12].

Another difficulty for the field is that many current treatment strategies are linked to commercial products such as the Fast ForWord program. In this business-oriented climate, it is difficult for researchers, who may have a stake in the products they are testing, to remain objective, Eden says.

But the stage should now be set for more rigorous studies using brain imaging and other tests to evaluate the success of the various products on the market — especially those that focus specifically on improving phonological processing — and to help devise better treatment methods. "The big news," says Shaywitz, "is that science has come into education. It's amazing that it has taken so long to do so." ■

Glenn Murphy is a student in science communication at Imperial College, London.

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