“Does He Like Kippers?”

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This article first appeared (under a different title) in the Times Higher Education Supplement (www.thes.co.uk) on 29 March 2002 and won the THES/Oxford University Press science writing prize. It is reproduced with permission, copyright TSL Education Ltd 2002.

At three years old, Jamie is a bright and adorable toddler whose parents love his enthusiasm and zest for life. They hope he’ll follow them into their profession, the law. He’s endearingly clumsy, a little slow to walk and talk perhaps, but they’re sure, even at this early stage, that he has the intelligence and empathy to make a formidable lawyer. And, as his father teases his mother, “he can certainly talk well enough. He talks more than you do!”

Five years later, Jamie’s parents’ hopes for him are being abandoned. Bright though he is, he isn’t doing well at school. The teachers can’t seem to connect with him; and Jamie himself, initially bubbling over with ideas, has withdrawn into a bored, frustrated silence. Jamie’s parents know the reason for his misery. Their fluent, charming, creative little boy is unable to express himself in writing. His reading is poor, his handwriting abysmal, his spelling worse, and he can’t concentrate. He still hasn’t learnt to ride a bike. His classmates torment him, calling him clumsy and stupid. Teachers’ reports express their bafflement at how such a bright child can be so inept in class.

Jamie’s parents will be at their wits’ end by the time they receive the diagnosis of dyslexia. And the label itself will mean very little. Whatever dyslexia is, there seems to be no cure. The news that it is partly genetic will leave them stricken with guilt, casting about desperately for answers. In a society so dependent on the written word, Jamie – unless he’s lucky, his parents are well-off and his teachers extremely sympathetic – may never fulfil his potential.

Still, his parents can tell themselves it could have been worse. Not so the family of the dyslexic boy whose agonies at school came to light in his (pitiably badly-written) suicide note.

Fortunately, that level of tragedy is rare. Developmental dyslexia is not the stuff of melodrama. It's not severe like autism, not terrifying like cancer or CJD. Help is available in principle once the diagnosis has been made, and the condition is now officially recognised by government and the teaching profession. Children are less likely to be labelled stupid, lazy or difficult. But there is still little understanding of a condition estimated to affect around five in every hundred people, nor of the negative impact dyslexia can have on self-esteem, socioeconomic status and life chances.

Intensive tuition can help with some dyslexic symptoms: poor reading, spelling, handwriting and concentration. But there is much more to dyslexia than this. Dyslexics often have problems with co-ordination and with learning complex movements, as if their brains are somehow less efficient than they should be. Reading may hurt the eyes because letters blur or move about, leading to headaches and fatigue. Short-term memory can be so poor as to make everyday organisation an exhausting chore. And many dyslexic individuals report unusually high levels of minor, but ongoing, physical complaints: dry skin and dandruff, migraines, stomach upsets, thirst, allergies and intolerances.

Among scientists dyslexia remains a specialist subject. It is not a psychiatric disorder, nor a medical condition, so psychiatrists and doctors have both traditionally ignored it. Educationalists have often disapproved of "medicalising" what they see as a cognitive problem, a learning disability pure and simple. For many years dyslexia was therefore treated with tuition in phonics and reading. However, the success level of these treatments remained low. And a few scientific mavericks kept remarking on oddities of this "educational" problem: the tendency of dyslexia to run in families, the associated physical symptoms, the creativity, the clumsiness and attentional difficulties. Then, in the 1980s, neuroscience gained the technologies to look inside the living brain. What had been a radical hypothesis – proposed by an American research group who analysed brains donated by dyslexic individuals – edged slowly

towards scientific consensus. The brains of dyslexics are subtly but undeniably different from those of non-dyslexics.

Dyslexia is one of a group of conditions known as neurodevelopmental disorders (NDDs), which includes autism, dyspraxia, attention deficit hyperactivity disorder (ADHD), schizophrenia, and possibly depression and manic depression as well. In NDDs abnormal changes take place in the brain at the time when it is growing fastest. Precisely because the brain is growing so fast, it is much more vulnerable to damage than the far more slowly-changing brain of an adult. Alcohol poisoning, for example, can be tolerated for years by adult humans, but can cause terrible and permanent disability to an unborn child.

In dyslexia, as in other NDDs, there seem to be changes in brain organisation and connections which lead to problems later on; parts of the brain seem to work less efficiently. These changes are thought to be due to a disruption of neuronal migration, the process by which growing brain cells (neurons) make their way to their final positions. Migration takes place during the second and third trimesters (thirds) of pregnancy. This is when researchers think the changes happen which lead to dyslexia.

What could cause these changes? Dyslexia, like other NDDs, is partly genetic: it runs in families, but in a complicated way. Dyslexia in the parents could mean a dyslexic child. It might mean a child with autism or ADHD, since NDDs often cluster in families. But the child might be unaffected. And NDDs can arise without any clear family history. So genes can't be the whole story. There must be some environmental factor or factors which trigger the development of NDDs in certain children.

The idea that environmental factors are important is confirmed by something that sounds wacky: dates of birth. But this is science, not astrology. NDD individuals are more likely than the general population to be born at particular times of year; for dyslexics, it's spring and early summer. This implies that environmental factors which vary with the seasons – such as light levels and infectious diseases, to name but two – may affect dyslexic individuals in the womb. This isn't a new idea; we know that the seasons affect human behaviour. Seasonal affective disorder (SAD, or "winter blues") can range from mild lethargy to debilitating despair, and can be treated by raising

light levels. Deaths, suicides and hospital admissions for mental illness all rise at certain times of year. The brain appears particularly sensitive to seasonal variation.

In the womb, the foetal brain is protected from the direct effects of many environmental changes: for instance, it sees no light. But infectious disease can penetrate the safety of the womb, sometimes causing brain damage or even death. And many infectious diseases peak during winter months. For dyslexics born in spring or early summer, this means that the chance of infection is highest during the second or third trimesters of their foetal life: peak time for neuronal migration. Some researchers have thus been led to propose that infection could be the environmental "missing link" between a genetic predisposition and becoming dyslexic.

When something foreign (like an infectious disease) enters the body, specialised cells detect the alien and react with the "inflammatory response", a complicated series of events in which many molecules are released. These act as alarm signals, calling security (specialised "killer" blood cells) to deal with the intruder. In the resulting melee, nearby cells are often casualties.

For genetic reasons, some people's immune systems seem distinctly trigger-happy. They respond with aggressive inflammation to inconveniently common substances like pollen, causing asthma or other allergies. People with a genetic risk for dyslexia may have genes that predispose them towards an over-enthusiastic immune system. Too much inflammation can do real damage, particularly to that supremely delicate organ, the developing brain. At the research lab where I work, we suspect that this is what may happen in dyslexia: an infection during pregnancy causes an inflammatory response in the foetal brain, disrupting the intricate arrangements of the neurons. If the infection is severe, then the inflammation may be enough to cause the changes associated with dyslexia even in a foetus with no genetic risk. But if the foetus is already "primed" with a genetic predisposition towards vigorous inflammatory responses, then even a mild infection may be enough to affect the growing neurons.

Because I'm writing science, not fiction, I can't tie up the story neatly at this point. The infection hypothesis is still to be fully explored; much more needs doing before it begins to be accepted even by other scientists. It has made some radical predictions

which we are currently testing. So far the results are positive. Whether it will reach that goal of scientific hypotheses – to be taken for granted and regarded as blindingly obvious – only time will tell. If it does, we may gain the ability not only to treat but perhaps even eventually to prevent dyslexia. If we can work out which infections are responsible, for example, doctors may be able to use vaccination to protect parents at risk from transmitting that risk to their children. But that is for the future. At present there is still a lot we just don't know.

In the meantime, however, we have another approach which may help ease some of the symptoms of dyslexia. The reasoning behind it is as follows: if too much inflammation contributes to NDD symptoms, then what we need to lessen those symptoms is something which reduces inflammatory responses, rebalancing an overly-aggressive immune system. Ideally that something should be as natural and harmless a substance as possible, and it should not impair our bodies' ability to defend itself against infections.

And is there such a substance? More than one. Step forward omega-3 PUFAs, and take a bow.

PUFAs (polyunsaturated fatty acids) are a natural component of a decent diet, and a vital ingredient in the recipe for building healthy brains. There are two major groups of PUFAs, the omega-3s and the omega-6s. Our bodies make the specific fatty acids they need from other ('precursor') fatty acids (one for each group), but these precursors can't be made by humans; we need them in our food. Omega-3 fatty acids have recently been shown to reduce inflammatory responses without reducing the ability to fight infections.

This is exciting because of a long-standing observation in the research literature on neurodevelopmental disorders. Some individuals with NDDs find that their symptoms improve dramatically when they take dietary fish oil supplements containing high levels of omega-3s. Numerous though these anecdotal reports are, they must be backed up by controlled scientific testing. PUFAs of various types have therefore been tested against a placebo in randomised clinical trials, just as doctors would test a new medicine. In ADHD, dyslexia, depression and manic depression we already have

evidence that omega-3 PUFAs provide significant improvement. More trials are underway for these and other NDDs. The results are particularly encouraging for ADHD, depression and manic depression, because the standard treatments for these conditions are powerful drugs with often severe side effects. PUFAs seem remarkably safe; the only known problems, on high-dose PUFA trials, have been occasional slight stomach upsets from taking large quantities of oil.

To understand what PUFAs do, we need to think about what the body is made of: cells. Each cell is like a tiny plastic bag full of water, except that the plastic bag isn't plastic, but made of fat. If this seems odd, remember that fats and water don't mix. If you drop melted butter onto a glass of water you get a slimy layer of fat on top of the water, like a skin (contrast this with adding orange juice, which mixes thoroughly). Imagine that layer surrounding a droplet of water, and you have a picture of a cell. The "skin" of fat is called the cell membrane, and it is essential to the survival of each and every cell in our bodies.

The fat which makes up a cell membrane can't be just any old fat. It has to be a particular kind called a phospholipid (lipid is the technical term for fat, and "phospho" means that these molecules have phosphorus in them). Phospholipids are long stringy molecules with a very clever feature: one end likes water, the other hates it. If you drop phospholipid molecules into water, the ends which like water will be attracted to water molecules. But the ends which hate water like fat, so they will be attracted to each other and repelled by the water molecules. The best way to deal with all these conflicting demands is to put two phospholipid molecules with their water-hating ends together, and this is what happens in practice. The phospholipid molecules arrange themselves into a double layer, with water on either side.

Cell membranes are made up of these phospholipid double layers; but they contain many other things as well. Think back to the buttery skin on your glass of water. If you scatter dust or flour over the top, the particles will become embedded in the fat. Or you could stick a straw through the skin to suck out the water beneath. Similarly, a fatty cell membrane can contain lumps of proteins and other foreign material. Some of the proteins straddle the cell membrane and form complex shapes with holes in. Like a straw, this allows water (and other molecules) to travel in and out of the cell. By

changing its shape, a protein can make the hole open and close depending on what else is happening. Regulating what goes in and out, the cell can affect other cells nearby. It can also learn what's going on in its environment, what it's just done and what to do next. Cells learn by receiving messages (in the form of many different molecules) which must pass through their membranes. Because so much of us is water, these messages must be able to dissolve in water in order to be carried from cell to cell. But water can't penetrate fatty phospholipid layers. So if membranes were pure fat cells would have severe communication problems. Not a great recipe for building complex organisms.

Phospholipid molecules are essential: without them, there would be no membranes and therefore no cells. However, the type of phospholipid matters immensely because it affects the "oiliness" of the membrane. How? Well, phospholipids are shaped a little like the capital letter "E", with a long backbone of carbon and three clusters of molecules branching off. One of those clusters is a fatty acid. The type of fatty acid affects the shape of the phospholipid, which in turn affects the membrane. Why does this matter? Because if phospholipids are tightly packed together the membrane will be stiff and inflexible. The proteins trapped in it, which need room to change shape when opening and closing, won't have space to move, and the cell will not be able to work properly.

If you're in a supermarket, and you pause to read the little label that tells you in detail how bad that cream cake is for you, you will find references to saturated and unsaturated fat, or perhaps to monounsaturates and polyunsaturates. These are all types of fatty acids, made up of a number of atoms which hold together by way of chemical bonds. Each atom has a particular number of bonds it can make with other atoms. Saturated fatty acids have no "spare bonds" in any of their atoms. Monounsaturated fatty acids have one spare bond. Polyunsaturated fatty acids (PUFAs) have more than one. Spare bonds cause a molecule to kink. So a saturated fatty acid is straight, while a PUFA is crinkly.

We can see why this affects membranes because fatty acids are attached to phospholipids. If those fatty acids are straight, the phospholipids can pack tightly together, making the membrane stiff and cramping the style of the proteins. Crinkly

fatty acids prevent this tight packing. So PUFAs help cells – and therefore brains – to work more efficiently.

We all have cells, so we all need PUFAs to build them. But if our immune systems are to stay nicely balanced between inflammation and failing to deal with infections we also need omega-3 PUFAs to regulate them. If omega-3 levels are low, the first people to feel it will be those genetically predisposed to overactive immune systems. But why should omega-3 levels be so low?

In a typical Western diet, we take in large quantities of saturated fat along with our PUFA precursors. Unfortunately, the mechanisms which convert dietary fatty acids to the PUFAs used in cells are a limited resource for which saturated fats, omega-6 PUFAs and omega-3 PUFAs all compete. So the more saturated fat and/or omega-6s you eat, the less benefit you'll get from your omega-3s. Worse still, the kinds of foods rich in omega-6s are foods like meat and milk, which also have high levels of saturated fat; whereas the foods rich in omega-3s are low-fat delicacies like broccoli and kippers. Not always the popular choice, especially with children, and especially with a nearby burger bar selling (you got it) meat and milk(shake). Many people are therefore hugely deficient in omega-3 fatty acids. Taking fish oil supplements is not adding something artificial to your food. It's putting back something taken out by modern life.

So if the infection hypothesis is correct we know *why* omega-3 PUFAs can help in dyslexia (and perhaps in other NDDs too). Even if it isn't, we know *that* omega-3s can help, and help less harmfully than standard medical alternatives. We know that dyslexia is not merely due to lack of PUFAs (we suspect infection during pregnancy also plays a part). But ensuring that children and pregnant mothers at risk get adequate PUFAs may help to lessen the impact of dyslexia. And the symptoms which omega-3s treat aren't restricted to people with dyslexia (just as many people can't read well who aren't dyslexic). Even as adults, many of us show signs of fatty acid deficiency: dry hair, dandruff, brittle nails, allergies and intolerances. Perhaps we should all think more seriously about what exactly we are – and are not – eating in our technological, convenient and PUFA-deficient world.