Brain science is child's play

Dr Duncan Astle, from the Medical Research Council's (MRC) Cognition and Brain Sciences Unit in Cambridge, UK, studies the cognitive and brain mechanisms associated with attention and working memory in childhood. These skills are closely associated with children's abilities to learn and are regularly implicated in neurodevelopmental disorders, so he and his team have also explored whether these skills can be altered using cognitive exercises such as memory games.

Higher order cognitive skills, for example attention and working memory, are vital for the successful completion of many other tasks. To take one example: the ability to remember and use small amounts of information over a brief period (working memory) is closely associated with a child's capacity to learn, and is often implicated in children who struggle to learn. A goal of Dr Astle's research is to understand the brain mechanisms that underpin these cognitive skills, to understand how they can go awry in childhood, and to see whether it is possible to modify these mechanisms and reduce these difficulties.

PROBING THE BRAIN

The team's research uses non-invasive neuroimaging techniques that can measure neural activity in real time, as well as the structural connections between brain regions. This allows them to study how brain areas work together. Research in adults and animals has already shown that these connections are very important in both attention and working memory. From this, the next step is to test whether similar connections are implicated in children with cognitive difficulties, and whether these problems are reduced by altering these connections with training.

The state-of-the-art brain imaging facilities at the Cognition and Brain Sciences Unit in Cambridge – including electroencephalography (EEG), magnetoencephalography (MEG) and magnetic resonance imaging (MRI) enable the team to image the brains of children in great detail. They have used MRI to explore structural connections formed from white matter in the brain, and the EEG and MEG to explore how brain areas can become coupled with each other.

Dr Astle and his team study children who are developing typically and those who are referred by clinical and educational professionals because they are having difficulties with learning. They also collaborate with geneticists to study individuals with developmental disorders of known genetic cause. In one example they used MRI to derive a whole brain connectome (a detailed 'wiring diagram' of the brain), and used graph theory (a complex mathematical process to model networks) to demonstrate that certain brain areas are less well integrated within the network in individuals with mutations in a gene called ZDHHC9.

IT'S IN THE GENES

Any mutation in a single gene associated with a specific tissue type (such as brain tissue) will impact throughout that tissue. However, across brain areas different genes are expressed to differing extents, so a single gene mutation can have a greater impact on some brain areas than others. This ties in with the observation that different gene mutations are associated with different patterns of cognitive deficit in children. For example, mutations in ZDHHC9 are most strongly associated with problems in language, whereas mutations in other genes are associated with a different profile of difficulties. This also mirrors the group's neuroimaging findings, and what we know

Different brain areas generate oscillating electrical signals at different frequencies; these can be used to explore how activity is coupled across brain regions

about where in the brain this gene is most heavily expressed.

This matches the pattern of other neurodevelopmental disorders of known genetic cause, which exhibit both global effects alongside more specific areas of strength and difficulty. The regional expression of the genes responsible could be linked to the differing phenotypes associated with the disorders.

MAKING WAVES

In addition to studying the brain's structure, Dr Astle's group also use EEG and MEG. These are non-invasive child-friendly imaging techniques that enable the team to study the electrical activity generated by neurons. Different brain areas generate oscillating electrical signals at different frequencies. These can be used to explore how brain activity is coupled across brain regions. For example, Dr Astle's team have shown that certain brain areas provide a rhythm within which high-frequency activity, associated with local brain networks, is nested. This provides a mechanistic framework for thinking about how certain brain areas can influence the activity of other areas, or how the activity of different brain areas might be integrated across large distances in the brain.

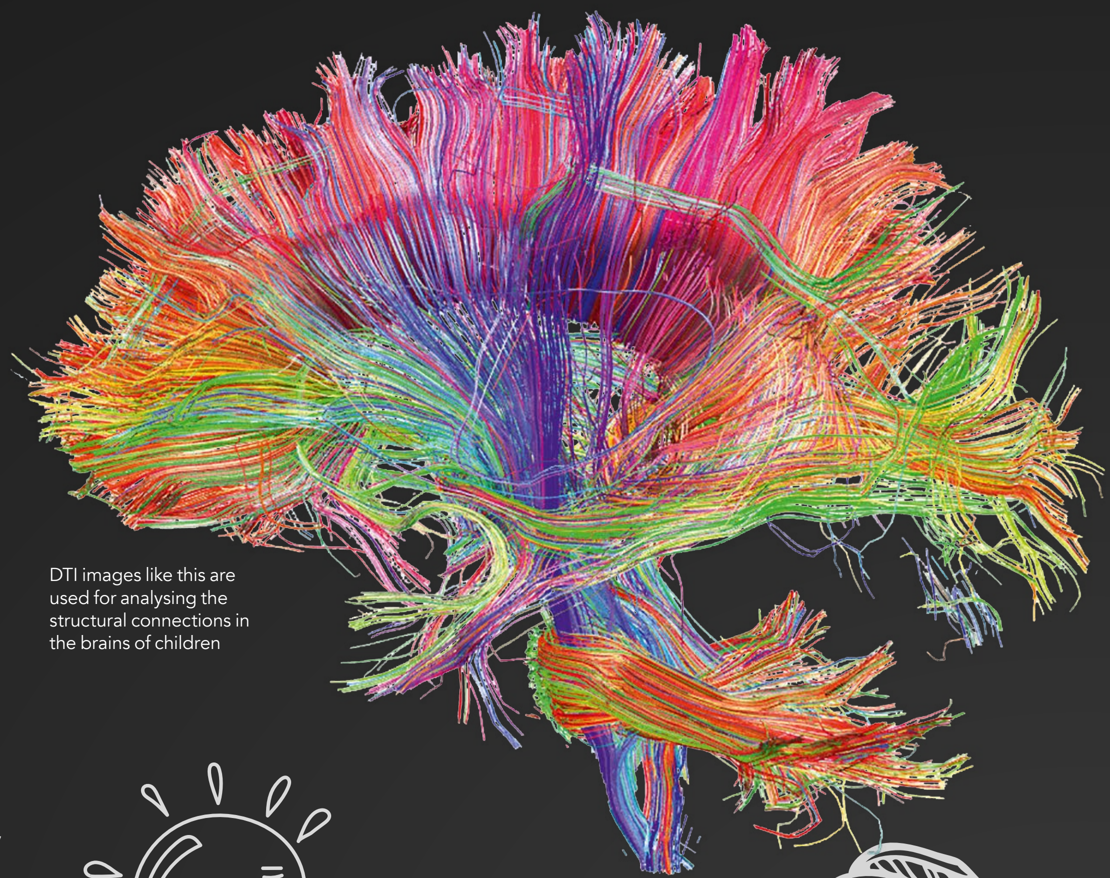
TRAINING THE BRAIN

While much of their previous research has used these techniques to understand cognitive differences across children, more recently the team have explored how developing neural networks are altered by intensive working memory training. Some of their most recent research, which uses intensive computer-based training, shows that a child's working memory can be significantly enhanced. These 'brain games' are widely available to both professionals and the general public and have received much attention in recent years.

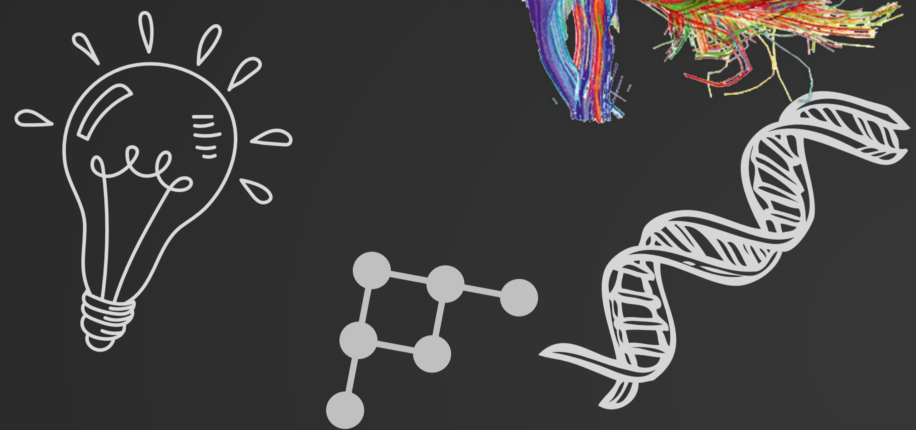
Dr Astle expresses a note of caution, however, as many studies showing an effect are poorly controlled and blinded (separating the assessor from the intervention). While there has been an effort to account for this in their studies, the nature of the research means that sample sizes are small and potential errors large. In reality we need to know much more about these interventions before they can be used to support children with difficulties in learning.

Although he says that study design is important and that, "as a field we need to ensure that future studies have active control groups, double blinding and that we include enough participants to show the effects we are looking for", Dr Astle believes that developing testable theories is the logical first step. In this way, researchers can have a collective focus and a framework that can be tested and revised – something he thinks is currently missing from this relatively new field.

The development of cutting edge techniques, and powerful statistical tools for the analysis of their data, has enabled the Astle laboratory and their collaborators to make inroads into the complex system that is the human brain. The results of these investigations, and the conclusions they draw, have the potential to impact upon our understanding of children's developing cognitive skills, and especially of those children who are experiencing difficulties in learning. Understanding why these children experience additional obstacles to learning is an important first step in helping them to realise their full potential.



DTI images like this are used for analysing the structural connections in the brains of children



Different genes are expressed to differing extents across brain areas, so a single gene mutation can have a greater impact on some brain areas than others

Q&A

What is particularly interesting about children in terms of neurophysiological research?

Differences in cognitive ability that emerge over developmental time likely reflect differences in the organisation of the brain. We think this is really interesting, and requires a new set of imaging techniques that are capable of looking at organisation (rather than activity levels within one particular brain area). I think this makes brain development in childhood particularly interesting.

What additional challenges are faced by working with this group?

Getting them to sit still can be really tricky!

How reliable are EEG, MEG and MRI as tools for probing cognitive function and structural architecture?

We always feel that no single method is sufficient to properly characterise what is happening within the brain. Where we get converging sources of evidence I think we get much greater insight into the changes that are occurring, and how they are related to cognitive development.

How might this research impact on educational strategies for children with cognitive deficits?

Current approaches to training are patchy at best. We do not really know the ways in which training is effective, or for whom it is likely to be beneficial. In fact, the majority of well-powered studies have shown that our current approach to training simply doesn't work – classroom learning isn't enhanced.

Our hope is that by studying what training does to cognition and the brain, we might be able to develop training that has broad real-world benefits.

What are the next steps in understanding the role of adaptive training in neural development?

We are becoming increasingly interested in transfer – how does this training change the organisation of the underlying system and what are the wider benefits of this? We have started applying machine learning techniques (a branch of artificial intelligence) to large datasets to explore this.

A goal of Dr Astle's research is to understand the mechanisms that underpin the cognitive and behavioural problems of children

Detail

RESEARCH OBJECTIVES

Dr Astle's research explores the cognitive and brain mechanisms associated with attention and working memory in childhood. He and his team develop and use new brain imaging methods alongside tools like machine learning. In recent years, they have been using this approach to explore how these skills are changed by cognitive training.

FUNDING

- Medical Research Council (MRC)
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COLLABORATORS

- Professor Kia Nobre (University of Oxford)
- Professor Gaia Scerif (University of Oxford)
- Dr Kate Baker (University of Cambridge)
- Professor Mark Woolrich (University of Oxford)

BIO

Dr Astle completed fellowships at the Universities of Oxford, Cambridge and Royal Holloway (University of London), as well as a stint as a visiting scholar at Yale. He now runs an intramural programme at the MRC's Cognition and Brain Sciences Unit in Cambridge.

CONTACT

Dr Duncan Astle
Programme Leader
MRC Cognition and Brain Sciences Unit
University of Cambridge
UK

E: duncan.Astle@mrc-cbu.cam.ac.uk
W: https://www.mrc-cbu.cam.ac.uk/people/duncan.astle/
Blog: https://forgingconnectionsblog.wordpress.com/
@DuncanAstle