Opinion TRENDS in Cognitive Sciences Vol.9 No.3 March 2005

Influencing brain networks: implications for education

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In our view, a central issue in relating brain development to education is whether classroom interventions can alter neural networks related to cognition in ways that generalize beyond the specific domain of instruction. This issue depends upon understanding how neural networks develop under the influence of genes and experience. Imaging studies have revealed common networks underlying many important tasks undertaken at school, such as reading and number skills, and we are beginning to learn how genes and experience work together to shape the development of these networks. The results obtained appear sufficient to propose research-based interventions that could prove useful in improving the ability of children to adjust to the school setting and to acquire skills like literacy and numeracy.

Introduction

There is growing interest in the possibility that brain research can have implications for the education of children, and many commercial packages have been designed to improve aspects of education for children with and without special difficulties. In our view the way to approach applications of brain research is to understand as fully as possible the nature of neural systems underlying subjects taught in schools, how these networks differ among people, and the role of genes and experiences in shaping the networks. In this brief article, we consider what is known about each of these issues.

Thanks to pioneering studies using primates, it is now widely understood that even primary sensory systems can be altered by experiences that include training [1]. Evidence for brain plasticity in learning is basic to applications of brain studies to education. In addition, imaging studies have shown that specific anatomical areas differ between tasks such as reading, listening, music, number, and emotions such as fear and empathy [2]. These findings encourage efforts to influence the development of networks underlying cognition and emotion. In this article, we first examine evidence that individuals differ in the functional activation of brain networks. These differences reflect the combination of genetic differences and differences in experience. We document these influences with respect to training attention, and illustrate efforts to apply our current knowledge to school subjects such as literacy and numeracy. A continuous dialogue between educators and brain researchers will be needed to enhance the application of brain research to education.

Individual differences in brain networks

Although there is strong evidence of common networks underlying cognitive processes, there are also individual differences in their details that influence the efficiency of the network. These differences are likely to reflect both genes and experience. The rapid development of fMRI methods has begun to provide a basis for understanding differences among individual brains both anatomically and in terms of functional activations. These differences are to be expected, because people are not identical in their thoughts, feelings or behaviors. Several studies have shown that individual differences in functional activation can be reliably assessed [3,4]. Studies have also examined the role of genetic differences in the strength of activation of networks involved in attention and memory (see Box 1). These studies demonstrate that at least part of the

Box 1. Imaging and genetic alleles

Studies in animals have identified a gene called brain-derived neurotrophic factor (BDNF) that plays a crucial role in long term potentiation, thought to be a model of memory. One study examined the role of differences in two forms (alleles) of the BDNF gene [28]. The behavioral part of the study compared performance of two groups with different forms of the gene performing a test of learning and memory. The two groups performed differently on the test, with the difference among alleles accounting for ~25% of individual differences on the test. When the test was run in the scanner on much smaller groups, significant differences between them was found in the hippocampus. As the hippocampus is an important node in the network underlying explicit storage and retrieval in memory, these findings supported the importance of the BDNF gene in that function.

In our work we measured individual differences in attention using the Attention Network Test (see Figure 1 in main text). The test provides a measure of the efficiency of attentional networks related to maintaining the alert state, orienting to sensory information, and controlling conflict between competing responses. Work on attention has examined candidate genes related to chemical neuromodulators of these networks. Studies on alert monkeys have shown that the orienting system is modulated by cholinergic input [29], whereas dopamine is the principle modulator of the frontal areas important for monitoring conflict [30]. Alleles of two cholinergic genes have been fund to influence a visual search task related to the orienting network [31], whereas alleles of two dopamine genes influenced performance in the flanker task and produced a significant difference in activation in the anterior cingulate [32].

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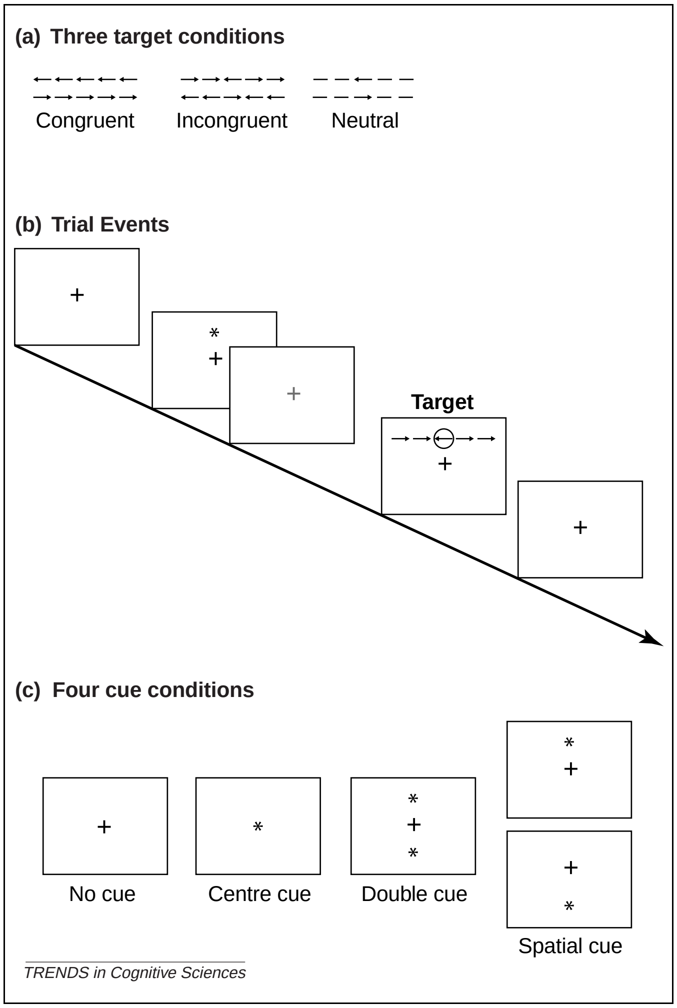

Figure 1. A schematic view of the Attention Network Test designed to measure the efficiency of the three attentional networks: maintaining the alert state, orienting to sensory information, and controlling conflict between competing responses. **(a)** The targets used; **(b)** the events during each trial (an incongruent target and center cue is shown); **(c)** the four cue conditions. The 'alerting network' score is obtained by subtracting the mean Double cue reaction times (RTs) from the mean No cue RTs. An 'orienting' score is found by subtracting the mean Spatial cue RTs from the mean Center Cue RTs; and an 'executive attention' score by subtracting the mean Congruent RTs from the mean Incongruent RTs. Adapted with permission from [27].

variability in strength of activation is due to having different versions (alleles) of genes related to the network.

Genetic differences observed to date account for only a small part of the variance found in behavior and imaging. However, a major contribution of these differences is that they serve as clues to the genes involved in network development. These genes can be examined in comparative animal studies to address questions like how genes related to hippocampal development may have affected behavior in species even before there was a hippocampus. These genes can also be examined in species for which the hippocampus plays a role in forms of memory that might be precursors of the explicit recollection found to be its role in humans. In the case of the DRD4 gene, which in humans is related to attention deficit disorder [5] and to the normal monitoring of conflict [6], in the mouse seems to be related to exploration of the environment [7]. These studies have the potential to improve our understanding of the role of genes in shaping the networks common to all humans. They might also eventually help us understand which children are likely to benefit from the kinds of interventions discussed below and in Box 2.

Gene–environment interactions

One reason for the relatively modest effect of genetic alleles in accounting for behavioral differences may be that they interact with experience during development of the network. The existence of gene–environment interaction is not controversial [8], and it is well known that gene expression can be influenced by the microenvironment in the brain area where it is expressed. Moreover, there is ample evidence that in primates, gene expression can be influenced by events, which, like maternal separation, can be a part of human development [9]. Whereas there is evidence that interventions can influence performance and change networks as revealed by imaging, we lack evidence that the mild environmental differences involved in normal education or even behavioral intervention of a clinical nature can have their influence through expression of genes or by the functioning of underlying neural networks.

We do not know if educational experiences alter gene functioning, but there is already evidence that educational experience can influence the functional anatomy displayed by children after training. For example, fMRI studies of reading [10,11] have demonstrated greater activation in areas related to word sound (phonology) and

Box 2. Imaging can improve clinical and educational interventions

Studies of treatment for depression [33] have examined two methods of remediation, anti-depressive pharmaceutical therapy and cognitive behavioral therapy, which involves retraining the person's ideas about their life. Both of these methods proved to be moderately effective in relieving depression. Imaging studies suggest that the two methods worked by improving the functioning of very different pathways. The retraining methods operated on cortical areas related to attention and comprehension, including the anterior cingulate, which are changed during the depressive state. The pharmaceutical strategy operated on subcortical areas that are also altered during the depressive state. This imaging result provides a basis for considering how to use both methods to remediate or even prevent depression in those who are most vulnerable to it.

Dyslexia is defined as a low level of reading skill that cannot be accounted for by general intelligence or poor educational opportunity [34]. Imaging studies have shown dyslexia to involve underactivation in two brain areas important in normal reading [10], a posterior phonological area, and an area of the visual system called the visual word form area. The visual word form area is thought to be involved in chunking the letters into unified whole words. In normal readers, these two areas appear to work automatically to convert visual words to appropriate sounds, but in dyslexic children they show little or no activation until after training. It appears that phonological training is an optimal way to induce activation of the phonological area, but we do not as yet know what methods will prove optimal for training of visual word form. One study did show a change in the word form area after one year of phonological training [10], but it was unclear whether it was the phonology or extra reading that was more effective in producing the change. One set of studies [35] suggests that word form activation in children occurs only for words that the child already knows, whereas in adults, activation is based upon orthography and shows similar activation for unfamiliar but pronounceable nonsense words as it does for familiar words. This might suggest that word form development occurs as a part of practice in reading.

in areas related to chunking visual letters into words (visual word form) following training in reading. It remains to be seen if these involve changes in underlying genetically controlled networks, or reflect the learning of a skill that can now better activate an unchanged network. Even without knowing how functional changes following education or clinical interventions occur, it seems likely to us that significant gains in how to design interventions can result from imaging studies. Two examples are illustrated in Box 2. In the case of depression, data suggest that the ability to combine behavioral and pharmacological methods could provide a wider influence than either one alone. In the case of dyslexia, phonological interventions can provide a level of reading skill, but that level is well below fluent reading. To achieve high level fluency might require other forms of intervention in addition.

Attention training

Attention is a cognitive system that is particularly important for acquiring many forms of learning and for regulating one's own emotion and behavior [12]. We have examined the development of attentional networks involved in self regulation from infancy through childhood [13,14]. Executive attention shows a strong period of development beween 2 and 7 years of age. Changes in this network can be observed from tasks that involve conflict between sensory dimensions, such as a child version of the adult Attention Network Test (ANT) illustrated in Figure 1. The developmental and genetic findings related to the ANT raise the issue of whether this network could be influenced during its development. The idea would be to improve attention and determine whether the changes generalize to the many domains influenced by attention.

For children who suffer from attention deficit hyperactivity disorder (ADHD), training attention and working memory can produce improvement in the ability to concentrate and in performance in general intelligence tests [15–17]. These studies all involve children eight years or older with known difficulties in attention. In our studies, we have worked with normal 4-year-old children to determine if attention training might serve as a component of preschool education. Our studies were designed mainly to test the general concept and used small samples of children for a very limited period of training [18].

Four-year-olds were chosen because our previous studies had shown improvements in performance between 4 and 7 years of age in the ANT, a test designed to survey the efficiency of performance related to attentional networks [13,14]. The exercises were patterned after those used to train rhesus macaques for space travel [19]. The exercises begin by training the child to control the movement of a cat animated on a computer screen by using a joystick. The children are also given experience predicting where an object would move, given its initial trajectory. Other exercises emphasize the use of working memory to retain information in a matching to sample task and the resolution of conflict. Each of the exercises progresses from easy to difficult in seven levels, with the requirement that children perform each level correctly three times to proceed to the next level. Most of the children were able to complete the exercises within the five days allotted and if not, we abbreviated some of the exercises to allow completion.

Our results suggest that training improves executive attention in a way that also generalizes to aspects of intelligence [18]. The use of EEG allowed us to determine if we could find changes in the underlying brain network. The data suggested that the training altered activity in the anterior cingulate so that it more closely resembled what is found in adults [20]. Of course this is only a very small scale study designed to show the possibility of attention training. It would be a large task to adapt these and other methods in a form that might improve preschool education.

As the number of children who undergo our training increases, we will be able to examine aspects of their temperament and genotype to help us understand who might benefit from attention training. To this end, we are currently genotyping the children in an effort to examine the candidate genes found previously to be related to the efficacy of the executive attention networks. We are also beginning to examine the precursors of executive attention in even younger children, with the goal of determining whether there is a sensitive period during which interventions might prove most effective.

We hope also to have some preschools adopt attention training as a specific part of their preschool curriculum. This would allow training over more extensive time periods, and testing of other forms of training such as those that could occur in social groups [21]. Although we do not yet know whether our specific program is effective, much less optimal, we believe that the evidence we have obtained for the development of specific brain networks during early childhood provides a strong rationale for sustained efforts to see if we can improve the attentional abilities of children. In addition, it will be possible to determine how well these methods might generalize to preparation for school and for learning the wide variety of skills that must be acquired there, as discussed in the next two sections.

Social and emotional development

Success in school depends on how well one can control one's own behavior and get along with others. Imaging studies of adults have shown that adjacent areas of the anterior cingulate are involved in regulation of cognition and of emotion [22]. Attention training might also be important for establishing better regulation of emotion. Several imaging studies have implicated the anterior cingulate when adult subjects are asked to control their reactions to positive and negative emotions [23,24]. During childhood, performance on conflict tasks is correlated with parental reports of their child's effortful control on temperament questionnaires. In turn, effortful control is associated with the ability to delay gratification, empathy towards others and the development of conscience (for a review see [25]).

During their training studies of monkeys, Rumbaugh and Washburn [19] observed that the animals' mastery of cognitive training also led to decreases in their aggression and increases in emotional control. Research is needed to translate these findings into aspects of the curriculum that might influence the child's ability to adapt to the school surroundings. Moreover, a better understanding of the child's developing control systems might also lead to better environments for the early school years in which children of different temperaments and initial levels of self regulation will be comfortable.

School subjects

Because of the strong interest in educational applications, several commercial companies and public agencies have begun to provide information to the public on educational innovation based on brain research. We have worked with the Organization for Economic Cooperation and Development (OECD) representing 22 developed countries, which arose among the Marshall plan countries as an effort to exchange information about national policies, and to provide a vehicle for exchange on issues of economic and social development. One of its constituents, the Center for Educational Research and Innovation, has been holding meetings on brain and education for the last two years [26]. From these meetings, networks of researchers on Literacy, Numeracy and Life Long Learning have been developed. These networks of researchers have supported forums on the OECD website (www.OECD.org) for researchers and for the general public.

It has been agreed to make available results of the research we have been describing on literacy, numeracy and attention training on free websites starting in 2005. The goal is developing a vehicle to convey findings in the form of actual exercises, first in English and later in many of the world's languages. We plan to provide menus of interventions that have sound support in research along with documentation on the strengths and limitations of each intervention. We will eventually have these programs in interactive form to provide material to teachers, administrators, parents and children, and to provide information to researchers on which methods are effective with specific groups. If our initial efforts succeed, we hope to eventually move to more advanced forms of knowledge, allowing comprehension of scientific documents requiring reading, number and graphical skills. All of these efforts need to be shaped by an ongoing dialogue between educators, educational researchers and cognitive and brain scientists.

The study of neural networks underlying thought and emotion is not at all limited to the specific skills of reading, number and attention. In the future, increased understanding of how networks are developed and shaped by experience could allow many school subjects to benefit from research. Moreover, the methods need not be limited to cognitive development, but can promote children's social adaptation and moral development as discussed above.

Summary and conclusions

It is now possible to examine aspects of developing neural networks underlying many school subjects. These networks are shaped by genes, but can also be influenced by specific experiences such as educational interventions. In some cases, such as attentional networks, the influence seems to change the underlying network in ways that might lead to extensive generalization. We hope the websites created by OECD and others will be open to creative exchanges between educators and brain researchers to direct efforts on questions about where research might be the most helpful (see also Box 3). Although it is clear that we do not know all that is needed to design optimal environments for every child, we believe that the ability to study networks of brain activation provides a unique opportunity to turn experimental findings into curricular improvement.

Box 3. Questions for future research

- What are the effective ingredients for achieving generalized improvement in attention?
- Can attention training be adapted for use with the large variety of different disorders that involved deficits in attentional networks?
- Can aspects of the temperament or genome of individual subjects be used to predict who will benefit from various forms of training-related interventions?
- Will neuroimaging be effective in allowing us to determine the impact of different forms of therapy or intervention, and thus lead to better treatments?
- How long will interventions that do succeed in altering networks be effective and how widely will they generalize?

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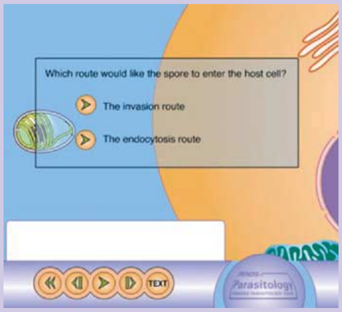
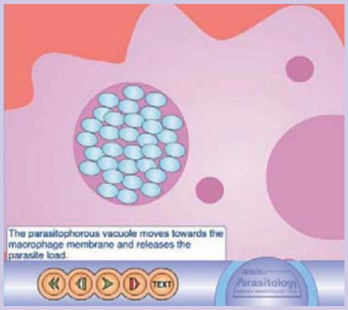


Which route would like the spore to enter the host cell?

The invasion route

The endocytosis route



The parasitophorous vacuole moves towards the macrophage membrane and releases the parasite load.