JACOBS FOUNDATION
Our Promise to Youth

Human Brain Plasticity: Future Research Directions and Implications for Children's Learning and Development

Kate A. McLaughlin, PhD
Allyson Mackey, PhD
Gelgia Fetz Fernandes
Karen Brown
Jessica C. Bühler, PhD
Silvia A. Bunge, PhD

Content

Layout und Design
BLYSS Brand Identity, Zürich

I. Executive Summary

Is it ever too late—or too early—to acquire basic abilities like speech or vision? Or specialized ones, like virtuosity on the piano? How about reasoning and the ability to memorize obscure details?

And if so, can the brain's timeline be manipulated by experience or intervention?

Thanks to advances in neuroscience, researchers have come much closer to answering such questions. This paper aims to summarize recent research into brain plasticity and implications for children's learning and development.

First, it is important to understand the terminology. There are specific times in life when the brain is primed to develop critical abilities, such as language and visual perception, in response to environmental input. Those times, marked by heightened neuroplasticity, are called sensitive or critical periods—we refer to them throughout as sensitive periods.

The timing of sensitive periods differs across neural circuits and behavioral systems, but they generally occur during periods of rapid brain development.

Brain malleability can lead to both positive and negative outcomes, depending on individuals' environments and experiences. During windows of heightened plasticity the brain is receptive to learning a native language, as well as facts and skills taught in school. However, the brain is also more vulnerable at this time to adverse social experiences, physical illness, and early trauma.

The way individual children's brains are shaped by their unique experiences, termed experience-dependent brain plasticity, is often the target of educational interventions. We know that children can learn new sensory or motor skills with practice and training. Whether they can hone general cognitive skills, such as the ability to pay attention or inhibit inappropriate thoughts and actions, is more controversial. Evidence for cognitive plasticity in adults is mixed. Most recent findings suggest that cognitive training helps adults improve on specific tasks but does not transfer more generally beyond those tasks.

To improve children's well-being and academic success, there is a clear need for more research on brain plasticity at younger ages. Priorities for future investigation include exploring the mapping between behavioral and neural manifestations of plasticity; explaining brain changes in the absence of behavioral changes; understanding individual differences and age-related changes in brain plasticity; and predicting children's responses to interventions.

Although the science on brain plasticity has broad implications for children's development, we have much to learn about how this evolving science can best inform policies to protect children and capitalize on sensitive periods as windows of heightened educational opportunity.

II. Brain Plasticity—The Brain's Capacity to Change in Response to Changing Environments

Throughout life, humans encounter and act on changing environmental stimuli that require them to learn and adapt. The term *neuroplasticity* describes the capacity of the brain to change in response to these environmental experiences. Neuroplasticity allows humans to adapt to changing circumstances by reconfiguring brain structure and function to accomplish new patterns of thought and behavior.

The brain is most sensitive to experience during childhood, when it is changing most dramatically. For example, it is considerably easier to learn a second language as a toddler than as an adult. Although language acquisition is not impossible in adulthood, achieving fluency requires much more exposure and practice than in childhood.

During childhood, the brain undergoes three types of plasticity: *experience-independent, experience-expectant,* and *experience-dependent* (Kolb & Gibb, 2014). Experience refers to the interaction of a child with his or her environment. In humans, such experience begins before birth. This early experience influences the basic architecture of circuits that mature during fetal development. After birth, experience plays an increasingly important role in shaping the architecture of developing neural circuits so that they function optimally for each individual. Experience fine-tunes the development of the brain and shapes the architecture of its neural circuits according to the distinctive needs and environment of the individual (National Scientific Council on the Developing Child).

Experience-independent plasticity involves brain changes that take place regardless of the environment and unfold over time through a tightly regulated series of molecular events. Fetal brain development is an example of experience-independent plasticity: humans—indeed, all mammals—experience a series of brain changes in the womb that are remarkably similar across individuals.

Experience-expectant changes, by contrast, do not unfold until they are triggered by specific environmental cues that the brain expects to encounter. For example, the visual cortex is not fully functional until infants open their eyes for the first time, and children do not learn language until they hear speech.

Experience-dependent brain plasticity refers to ways neural pathways are strengthened through repeated engagement, via multiple cellular mechanisms, so that they become more efficient over time. In contrast with the largely predictable forms of brain maturation that most people share, experience-dependent changes are unique to each person, reflecting the remarkable range of human social environments and cultures and the particular activities in which individuals engage.

For example, children who learn to read show fine-tuning of brain networks involved in language processing, and those who practice the piano show changes in networks involved in motor skills and auditory processing.

Individual experience exerts the most pronounced influence on the brain's architecture when the neural circuit is maturing most rapidly. The genetic plans and architecture of mature circuits can still be modified by human experience, but the extent of later modifications tends to be far more limited.

The period of heightened sensitivity to environment and experience is called a sensitive period for that circuit. Because it is far more difficult to alter neural circuits substantially after these periods, experiences during these windows play a very important role in shaping the brain. Behavioral capacities that develop during sensitive periods include vision, hearing, language, and even attachment to a caregiver.

Different cognitive capacities mature during different and partially overlapping time periods in a child's development. Cognitive functions are carried out by different hierarchies of neural circuits in the brain. The hierarchies of circuits that analyze visual information are different from those that process auditory information, learn language, remember recent events, plan future actions, or generate emotional responses. Because these various hierarchies mature at different times, the same environmental conditions will produce different cognitive and emotional experiences for children, depending on their age of exposure.

Circuits that process lower-level information mature earlier than those that process higher-lever information. For example, in the neural hierarchy that analyzes visual information, low-level circuits that process color, shape, or motion are fully matured long before the higher-level circuits that interpret complex stimuli, such as facial expressions. For the developing brain, this means that the ability to perceive simple aspects of the world and to make basic emotional and social judgments develops long before the ability to engage in sophisticated reasoning and decision-making.

Because brain networks mature at different rates, the windows of malleability differ across brain systems (Werker & Hensch, 2015). Indeed, there is evidence about multiple sensitive periods in human brain development. For example, visual system development happens rapidly during the first six months of life and is driven by visual experience—specifically, patterned light input to the eye—once a baby opens his or her eyes. After six months of age, the visual system is much less likely to change in response to visual experience. Another example is language acquisition, which occurs rapidly and, seemingly, without effort during the first few years of life. Children learn the sounds, words, and structure of languages they hear repeatedly during this period of time. After the age of around seven years, learning a second language becomes more difficult (Kuhl, 2010).

It is not yet known whether there is a period during development after which it is more difficult to develop higher cognitive skills like memory, reasoning, or social decision-making, although there may be a sensitive period during which the underlying networks are most easily modified. Research shows the neural circuitry behind these skills does not mature fully until early adulthood and differs widely among individuals (Kilford, Garrett, & Blakemore, 2016; Lindenberger, 2018; Luna, Marek, Larsen, Tervo-Clemmens, & Chahal, 2015; Shaw et al., 2008; Wendelken et al. 2017). Furthermore, practicing reasoning skills in adulthood can strengthen this network (Mackey, Miller Singley, & Bunge, 2013; Mackey, Whitaker, & Bunge, 2012). Thus, if there is a sensitive period for developing reasoning skills, it most likely extends through early adulthood and differs across individuals.

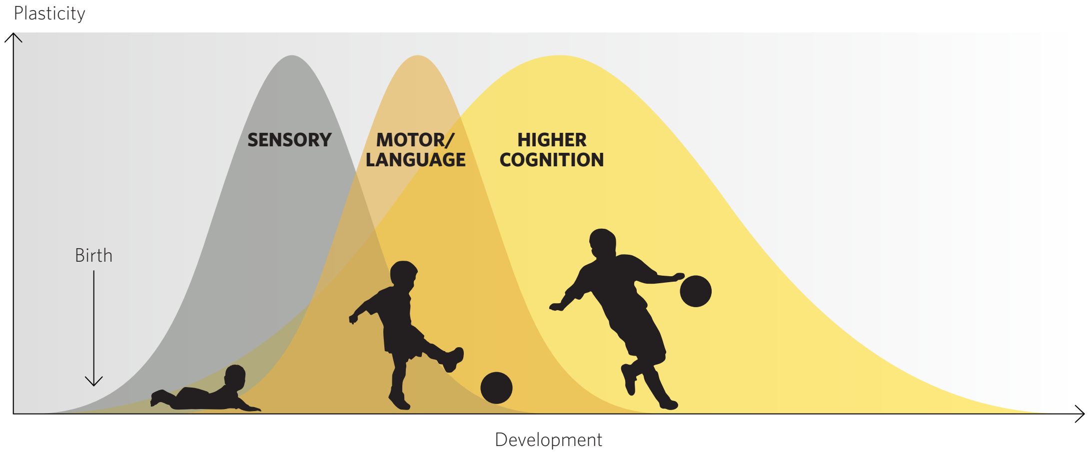

Fig 1: Windows of plasticity in brain development

Adapted from Hensch, T.K. (2005). Critical period plasticity in local cortical circuits.
Nature Reviews Neuroscience, 6(11), 877–888

Although brain plasticity continues throughout life, it declines rapidly with age, at least in part due to molecular processes that actively suppress brain plasticity, leading to the closure of sensitive periods (Werker & Hensch, 2015). The specific cellular and molecular mechanisms that regulate the opening and closing of sensitive periods have been discovered in studies of rodents, whose developmental milestones are more stereotyped than humans', but they also shed light on human brain plasticity.

These findings raise a fundamental question: Why are there sensitive periods, and why are they arranged in a temporal sequence? Would it not be better if our brains remained plastic and responsive to environmental input throughout life?

In fact, there may be drawbacks to ongoing brain plasticity after an individual has reached adulthood and learned to survive independently. The neural restructuring that underlies brain plasticity is energetically expensive and can leave the brain vulnerable to negative environmental experiences. Efforts to change the brain in later life must contend with these molecular brakes on plasticity. It's a trade-off.

The brain's remarkable plasticity, or malleability in response to experience, is simultaneously a source of its power as well as its vulnerability. On the positive side, it is this feature of the nervous system that enables children to learn the facts and skills taught in school, and to build expertise in specific domains. On the negative side, there are numerous ways in which brain development and behavior can be undermined by factors beyond a child's control, such as a physical illness, head injury, or exposure to violence or poverty.

Next, we provide some detailed examples of brain plasticity following different types of environmental experiences in order to identify promising future research directions and broader implications for children's learning and development.

III. Examples of How the Brain Changes with Experience

A. Adapting to Environmental Adversity
Children are routinely confronted with stressful experiences. Many of these experiences represent normal developmental challenges that most children can adapt to without difficulty (e.g., problems with peers, the death of a grandparent). But some stressors are so severe or chronic that they overwhelm the coping resources of most children.

Common experiences of environmental adversity, sometimes referred to as *toxic stress*, include chronic exposure to violence, chronic poverty, and the absence of a stable and responsive caregiver. Mounting research suggests that these types of adverse experiences can influence the developing brain. Without buffering support from adult caregivers, toxic stress can have lasting effects on the architecture of brain circuits, including regions involved in the regulation of emotion, language skills, and multiple forms of learning and memory. Below, we discuss two damaging forms of adversity: exposure to violence and neglect.

Many children grow up in environments characterized by violence or the threat of violence. Examples include children who are abused, witness domestic violence, live in neighborhoods where violence is common, or grow up in areas affected by war or armed conflict.

Children who have been exposed to violence experience brain changes that might help them adapt to living in a dangerous environment, at least in the short term. Specifically, a brain network involved in identifying potential threats and learning to predict danger becomes highly sensitive. In other words, these children's internal alarm system is easily triggered. For example, in children who have experienced violence, the amygdala—a central node in this network—responds more strongly to negative emotions in other people (McCrory et al., 2011; McLaughlin, Peverill, Gold, Alves, & Sheridan, 2015). This brain response suggests that the emotional cues are interpreted as more threatening by children who have experienced violence compared with children who have not.

As a result of this neural adaptation to an adverse environment (Nettle, Frankenhuis, & Rickard, 2013), children who have experienced violence can identify anger in a face more quickly than children who have never been exposed to violence, and they pay more attention to anger (Pollak & Kistler, 2002). In dangerous environments, this strong alarm signal allows children to predict threats and react in a way that keeps them safe. But it also causes them to react equally strongly to cues that present no danger.

For example, children exposed to violence are more likely to perceive hostility from peers in ambiguous situations, such as another child bumping into them at school. As a result, they are more likely to respond aggressively (Dodge, Pettit, Bates, & Valente, 1995). This can make it more difficult for them to form supportive friendships. Heightened vigilance for threat can also interfere with children's ability to focus at school and it may predict the onset of mental health problems such as anxiety and post-traumatic stress disorder. While a highly attuned alert system is a reasonable—and protective—tool in dangerous environments, it can be harmful in the long-term.

Of course, violence is just one type of adversity experienced by children. Another is growing up without a supportive and responsive caregiver. This is common in children who are neglected by parents, raised in institutions, and, in some cases, living in chronic poverty.

Early in life, caregivers provide safety, nutrition, nurturing, and opportunities to learn. Caregivers determine the complexity of sensory, motoric, linguistic, and social experiences through physical contact, speech, and interactions with the child. The absence of such interactions deprives children of many forms of cognitive and social stimulation that shape early learning.

This type of early deprivation influences brain development differently than exposure to violence. Whereas children exposed to violence identify anger more readily than their peers and are more likely to interpret ambiguous facial expressions as threatening, neglected children have difficulty distinguishing among emotions in other people. For example, they may not be able to tell if a face is angry or fearful, happy or sad. (Pollak, Cicchetti, Hornung, & Reed, 2000). These shortcomings likely stem from limited exposure to nurturing caregiver relationships.

Children who have been neglected or deprived early on may also exhibit delays or difficulties in cognitive development, including language, executive functions, and other forms of learning and memory (McLaughlin, Sheridan, & Nelson, 2017). At the neural level, studies have shown a thinner cortical layer and less activity in the cortical regions that underlie these cognitive skills (Mackey et al., 2015; McLaughlin et al., 2014; Noble et al., 2015). For example, children who have been neglected or raised in poverty show different patterns of prefrontal cortex activity when using language (Noble, Norman, & Farah, 2005; Romeo et al., 2018) and performing working memory tasks (Finn et al., 2016; Rosen, Sheridan, Sambrook, Meltzoff, & McLaughlin, 2018) than their non-deprived peers.

Similar to deficits in emotional perception, it is possible that children without early, consistent caregiver relationships have never received the environmental input to learn these cognitive skills. As a result, the associated brain circuits did not develop properly. Behaviorally, this means the children were not exposed to the sensory, linguistic, or social experiences the brain expects for normal development (e.g. language learning).

At the neural level, one central mechanism underlying brain plasticity is synaptic pruning; that is the process of eliminating specific connections between neurons that are underused. In typical development, synaptic pruning allows the brain to become more efficient. In the case of early deprivation—where children experience dramatic reductions in environmental inputs that the brain expects for development—these connections might be pruned too drastically or too early. Such mechanisms at a cellular level could explain the frequently observed patterns of cortical thinning in regions that underlie complex cognition (McLaughlin et al., 2017). It is important to note, however, that synaptic pruning and other molecular processes cannot currently be measured in humans, so it's hard to say whether pruning plays a greater or lesser role than other neural mechanisms in guiding the brain development of neglected children.

Adverse early life experiences may not only shape the brain during sensitive periods. They may actually alter the *timing* of these periods in brain maturation. For example, exposure to violence appears to speed up development of threat detection circuitry (Gee et al., 2013), which could accelerate the opening of a sensitive period. By contrast, the development of other neural circuitry, including those underlying language and executive functions, may be delayed by adversity.

Animal research has shown that complete visual deprivation can prolong the window of a sensitive period for visual development (Timney, Mitchell, & Giffin, 1978). The same may be true for other forms of deprivation, such as lack of exposure to language or to a stable, nurturing caregiver. These ideas are speculative, as it is not possible to carry out in children the types of controlled, environmental experiments that are conducted with animals. However, these working hypotheses are informed by cases involving children who have experienced severe neglect.

B. Targeted Cognitive Training and Educational Experiences

The brain's plasticity means that negative experiences, like injury and trauma, can leave their mark in potentially lasting and harmful ways. But that same plasticity also allows for learning new skills.

Research, primarily in adults, has shown that something as simple as motor training—such as learning how to juggle with balls—changes the brain's architecture, after even a short period of practice (Draganski et al., 2004). In children, there have been a few studies on brain changes after practicing specific skills, such as playing a musical instrument (Kraus & Chandrasekaran, 2010). Another growing area of research focuses on broader experiences, like school-based education.

Scientists generally agree that children acquire specific skills and knowledge through experience and practice, and that such learning is reflected in neural changes—even though research on experience-dependent brain plasticity in children remains limited. A more disputed question is whether, and to what extent, experience and practice shape general cognitive skills, such as the ability to pay attention, think quickly and flexibly, or inhibit inappropriate thoughts and actions. The implications of this question are important. Given that higher cognitive skills are associated with better educational outcomes, improving those skills—i.e. helping students think more quickly, retain information longer, and solve problems more efficiently—could lead to better academic performance (Mackey, Park, Robinson, & Gabrieli, 2017).

Evidence for such cognitive plasticity in adults is mixed. Recent findings suggest that cognitive training helps adults improve on tasks in a very specific way but that does not necessarily transfer to other tasks (Lindenberger, Wenger, & Lövdén, 2017).

It's unclear whether findings about task-specific transferability apply to children. For one, children's brains are more flexible than those of adults. Children are also less expert, and less strategic, so their brains may change more broadly, and less efficiently, to learn a new task. Moreover, children and adults use different approaches to get through cognitive training. Adults use rote, computerized practice—an approach that also works in children (Jaeggi, Buschkuehl, Jonides, & Shah, 2011; Melby-Lervåg & Hulme, 2013). However, children benefit most from immersive play-based curricula implemented in early grades (Diamond & Lee, 2011; Lillard et al., 2013). In general, cognitive training approaches for children seem to be much more diverse and comprehensive than those for adults, ranging from socially-interactive, modular programs (Mackey, Hill, Stone, & Bunge, 2011; Mackey et al., 2017) to curriculum overhauls (Blair & Raver, 2014; Diamond, Barnett, Thomas, & Munro, 2007).

The nature of the cognitive training is also important. At present, a broad-spectrum cognitive training program targeted at students with low scores on tests of academic achievement is a promising path forward (Mackey et al., 2017). For example, cognitive training approaches to improve attention, which started as a way to help rehabilitate adults with brain injuries, have since been adapted for children with attention deficits, showing a particular benefit in school age and preschool children.

An early study revealed brain and behavior changes in four- and six-year-olds after they performed attention training exercises for five days, as compared with a control group (Rueda, Rothbart, McCandliss, Saccomanno, & Posner, 2005). For example, in one exercise, children were asked to remember a complex cartoon portrait and then pick it out of an array. They later showed gains on an untrained measure of reasoning. They also showed a more mature pattern of brain activity after training, as measured via scalp electrode recordings. Four-year-olds who did the training showed brain activity profiles similar to untrained six-year-olds, and trained six-year-olds showed a more adult-like pattern of brain activation.

In another study, an integrative intervention involving both parents and children produced changes in brain activity, as well as higher scores on general cognitive measures (Neville et al., 2013). Children aged three to five from low socioeconomic status (SES) backgrounds were assigned to one of three study groups. The first participated in an existing preschool program for socioeconomically disadvantaged children (treatment as usual). The second group engaged in interactive sessions aimed at boosting their attention skills (child attention training). The third group did these same activities while their parents took classes over eight weeks to learn how to guide their children's attention and manage their behavior (a two-generation approach). The children in this latter group showed improved reasoning, language ability, and social skills, and reduced problem behaviors. The attention training in and of itself, as tested in the second group, was not effective.

The cognitive and social changes observed in the two-generation intervention were accompanied by brain changes linked to children's greater ability to ignore distracting information while trying to pay attention to relevant information. Similar to the attention training study by Rueda and colleagues, the two-generation intervention produced a more mature pattern of brain activation in children—that is, one that resembled an adult-like pattern. This study showed that a program that targets child-specific attention, using a family-based model, is highly effective in changing children's neurocognitive functioning as well as their parents' caregiving behaviors in a relatively short period of time. This evidence suggests that programs targeting multiple pathways, including the home environment, have the potential to narrow the large and growing gap in school readiness and academic achievement between higher and lower SES children.

An additional study of eight to eleven-year-olds examined cognitive training that targets short term working memory (Astle, Barnes, Baker, Colclough, & Woolrich, 2015; Barnes, Nobre, Woolrich, Baker, & Astle, 2016). Children who completed this computer-based training over 20—25 sessions performed better on tests of working memory while also showing changes in the frontoparietal network, a brain network that supports attention, working memory, and reasoning. These findings are particularly exciting, because the learning-related changes in the brain happened in a neural network specifically targeted by the intervention—that is, the intervention was designed to tax the cognitive functions supported by this brain network.

A future challenge will be to make use of those brain networks, through cognitive training, in a way that could produce therapeutic benefits for diverse populations with developmental or acquired deficits in everyday tasks.

Another way to study positive environmental influences on brain development is to measure changes resulting from educational opportunities, such as an academic course or instructional program. Such experiences are multi-faceted and provide the opportunity to practice a broad set of skills, typically with an element of human interaction. For example, children whose reading scores improved following a reading intervention showed greater cortical thickening than children who did not respond to the intervention (Romeo et al., 2017). Responders were more likely to come from socioeconomically disadvantaged backgrounds than non-responders.

The most immersive, nearly universal, learning experience that exists is formal education. Because all children in industrialized nations are required to attend school, it is difficult to study how education influences brain development because there is no easy comparison group. It is therefore hard to say whether the well-documented age-related improvements in a child's attention, self-regulation, memory, reasoning, and other cognitive capacities are the direct result of sitting and listening to a teacher, doing homework, and engaging in other scholastic activities.

Recently, however, researchers have designed studies that take advantage of different cut-off ages for starting school. They compare behavior and brain activity between children of a similar age who are at different grade levels due to the fact that their birth dates fall on either side of a cutoff for first grade enrollment (Grammer, Gehring, & Morrison, 2018). One such study (Brod, Bunge, & Shing, 2017) showed that five- to six-year-olds enrolled in first grade showed more improvement over the course of a year on an attention-demanding task (responding to images of a heart or a flower on a computer screen), compared to children of the same age who were still in kindergarten.

In addition, the first graders had more brain activation in a region involved in attention—the right parietal cortex—while performing a "Go/No-Go" task, in which they had to press a button every time they saw a dog and withhold a response when they saw a cat. This task, like the attention-demanding "Hearts and Flowers" task described above, bears no resemblance to what the children were asked to learn in school, where they did not even have access to computers. Thus, the experience of schooling itself hones attention skills. These studies serve as a good starting-point for future research comparing the effects of different school curricula on cognitive functioning, and for teasing apart maturational and education-related changes that vary widely depending on the age at which children start school.

The programs that are most likely to have a significant, lasting impact on a child's well-being and academic success are intensive (multiple times per week), protracted (over one or more years), multifaceted (targeting multiple skills in multiple ways, ideally exercising children's cognitive, socioemotional, and physical skills (Diamond & Ling, 2016)), and family-based (focusing not only on children and classroom instruction, but also on caregivers and the home environment (Burger, 2010)). However, the most scientifically rigorous intervention studies tend to be quite narrowly focused, both in terms of duration and types of skills targeted, as this is the best way to identify the key ingredients of a successful program. Both approaches are valuable—and, indeed, complementary. Programs that are too broad are likely to include ineffective components that could be eliminated or replaced with elements from the most promising targeted interventions, resulting in more effective and cost-efficient interventions.

Currently, there are still more questions than answers on the effects of cognitive interventions and schooling on the brain. To improve children's well-being and academic success, we need substantially more research on experience-dependent brain plasticity in children. Despite evidence from animal research that the developing brain is more plastic than the mature brain, most research on the effects of cognitive or physical interventions on the human brain have been conducted in adults. Indeed, we are aware of only a handful of studies examining brain plasticity in children following interventions or education. We also do not yet know the best design for an intervention. How many weeks should it be, how many minutes per day, and how many days per week? What are the best metrics of the success of an intervention? And at what point should the programs be assessed to understand their long-term effects? Do interventions simply speed up developmental changes that would naturally occur later on, without altering the level and the rank order of individual differences in adult proficient performance?

IV. Future Research Directions

Above, we have provided an overview of research to date on human brain plasticity, with an emphasis on the small number of studies involving children. Below, we outline important areas for further investigation (see also Benasich and Ribary, 2018).

A. Exploring Relations between Behavioral and Neural Manifestations of Plasticity
Several recent intervention studies involving children have shown changes in the brain even when the behavior stays the same (Brod et al., 2017; Neville et al., 2013). There are several scenarios that could explain this puzzling pattern. One possibility is that neural changes do not manifest as behavioral changes unless or until they are sufficiently large or sufficiently protracted. In other words, initial brain changes could be a sign that learning is starting to occur, and that behavioral benefits will follow. Imagine planting a seed and watering it. You can detect growth more rapidly if you peer into the soil and see the seed sprouting than if you wait for a shoot to emerge above ground. That is what brain imaging allows us to do: To measure plasticity and learning sooner than we would with behavioral measures alone. As such, brain imaging is a good way to assess whether a new behavioral intervention holds promise, or whether an established intervention is likely to be helpful for a particular child.

A second, and equally plausible, scenario is that some studies are using the wrong measures of transfer of learning: That is, the outcome measures, or transfer tasks, may not be the appropriate ones with which to assess experience-dependent plasticity. After all, researchers handpick just a couple of outcome measures out of a vast array of possibilities. Also, researchers may not always select transfer tasks that rely on the cognitive processes that have been honed by the intervention. In such a situation, brain imaging of both the trained tasks and possible transfer tasks would help researchers to gauge the degree of overlap in the brain networks engaged by each, to determine whether the candidate transfer tasks could be appropriate measures of the transfer of learning.

B. Understanding Individual Differences and Age-related Changes in Plasticity
In addition to helping us resolve the puzzle of why behavioral and brain changes do not always go hand in hand, brain imaging can provide a tool to understand why some children benefit from an intervention while others do not. The standard approach in intervention studies is to test whether the group receiving the treatment improves more, *on average,* than the group not receiving the treatment. If it doesn't, the intervention is considered a failure. However, the devil is in the details: it could well be that a few children improve dramatically while the majority are unaffected. If we can pinpoint the specific brain changes in children who respond most dramatically to an intervention, we should be able to predict whether an individual child is likely to benefit from a particular program (Basak, Voss, Erickson, Boot, & Kramer, 2011; Mathewson et al., 2012; Supekar et al., 2013). Thus, neuroimaging could help individualize treatment by predicting which techniques are most likely to help a particular child to learn, based on specific biomarkers related to his or her brain structure and function. Insights from such studies could also help develop alternative approaches for children who do not respond at first. And more broadly, brain imaging could help us predict which interventions will show benefits that are likely to transfer to the real world (Gabrieli, Ghosh, & Whitfield-Gabrieli, 2015).

As noted previously, the brain system is most malleable while it is still developing. However, we do not know the best time to attempt to modify specific brain networks. Is it ever too late to make a meaningful change in a network that has already fully matured? Is it ever too early to have an enduring impact on a network that is still poised to undergo significant developmental functional and structural changes? By testing the same intervention with children of different ages, we can learn how the type, magnitude, and extent of brain plasticity varies across development.

C. Pushing the Boundaries of Brain Plasticity

As we have discussed, the effectiveness of an intervention is limited by the fact that there are active brakes on brain plasticity as we age. However, research on animals shows that certain pharmaceuticals can shift windows of plasticity, or sensitive periods, to be earlier or later, or prevent them from opening or closing (Hensch & Bilimoria, 2012). There is even preliminary evidence that it is possible to boost learning in the adult brain by combining pharmacological treatments with intensive practice (Rokem & Silver, 2010, 2013).

Another approach is to pair cognitive training with neurofeedback to teach individuals to modulate brain activity (Hanslmayr, Sauseng, Doppelmayr, Schabus, & Klimesch, 2005; Zoefel, Huster, & Herrmann, 2011). Yet another approach is to pair cognitive training with non-invasive brain stimulation techniques such as transcranial direct current stimulation (Pisoni et al., 2018; Ruf, Fallgatter, & Plewnia, 2017; Snowball et al., 2013) and transcranial random noise stimulation (Cappelletti et al., 2013). However, this work is still highly preliminary, and some scientists question whether these forms of electromagnetic stimulation even penetrate the brain sufficiently to modulate neural activity (Vöröslakos et al., 2018). Thus, the efficacy and safety of these approaches must be further explored.

There are also subtler, less risky ways to enhance plasticity. Neurotransmitters that exist naturally in the brain, such as dopamine and acetylcholine, promote plasticity. And it is possible that their levels can be fine-tuned with behavioral interventions that boost motivation and attention, such as those focused on mindfulness, physical activity, and sleep. Mindfulness practice may lead to changes in neurotransmitters, thereby promoting plasticity. Physical exercise has been shown to improve learning and memory and could potentially be combined with cognitive training (Ward et al., 2017). Sleep is also critical for learning and memory (Walker & Stickgold, 2004), so controlling nightly sleep schedules or adding naps after cognitive trainings might enhance memory consolidation.

D. Anticipated Contributions from Brain Imaging Research

To make substantive progress in understanding brain plasticity in humans, we will need to tackle several important questions: Can neuroimaging data help elucidate the mechanisms of cognitive change, rather than simply identifying the brain regions and pathways that change as a result of an experience? By the same token, can more advanced brain imaging techniques provide deeper insights into the biological mechanisms underlying structural and functional brain changes? Finally, can brain imaging methods be used to predict who will improve the most as a result of an intervention—both on the tasks that were and were not explicitly trained? The studies described above suggest the answer may be yes, but this is just the beginning.

V. Broader Implications for Children's Learning and Development

Pushing the boundaries of brain plasticity provides great hope for enhancing lifelong learning, as well as treating brain injuries and a broad range of disorders. At the same time, it is imperative to be cautious when translating laboratory findings, often derived from animal studies, to interventions for adults, let alone for children. There are biological, clinical, and ethical risks to consider. First, there is likely a biological reason for the natural reduction in brain plasticity during development (Fawcett & Frankenhuis, 2015; Werker & Hensch, 2015). Consider what might happen if our environment was to forever have the same dramatic impact on the brain as it does during development: Our brains would likely be in a constant state of flux, with new experiences undoing the wiring laid down by previous experiences. We might not be able to retain any of the major lessons we had previously learned. This sort of failure to stabilize neural circuits may well underlie the pathology of some neurodevelopmental disorders.

Research continues on the biological mechanisms controlling brain plasticity as well as on the safety and efficacy of pharmaceuticals to shift windows of plasticity, and that is likely to be a long road. Meanwhile, there is an arena that can benefit in the short term from what we already know about the subject: childhood policies and programs. As outlined above, there is ample evidence that early childhood adversity experienced during sensitive periods of brain development, has lifelong consequences for health, learning, and behavior. Adverse childhood experiences increase the risk of engaging in harmful behaviors and are associated with a variety of chronic illnesses. Further, they have been linked to cognitive deficits, including difficulties with memory and executive function, and affective deficits such as problems with reward processing and emotion regulation (McLaughlin, 2016).

And yet, despite all that is known about the developmental harms of early adversity, it remains a challenge to translate the science into social policies to protect children. Since there are so few studies on how interventions affect brain plasticity in children, it is equally challenging to develop policies that capitalize on the knowledge of sensitive periods as windows of heightened educational opportunity. For example, although there is clear evidence that children can attain fluency in any language if they are exposed to it starting at birth, the teaching of second languages is still often delayed until early adolescence, and bilingual programs for young children are insufficiently valued. And while educational reforms dedicate resources to the training, recruitment, and retention of teachers from kindergarten to high school, they do not invest sufficiently in preschool teachers (Doyle, Harmon, Heckman, & Tremblay, 2009).

In sum, there are four central messages that have come from the research on sensitive periods. First, children's brain development and behavior are shaped by experience over time. Second, the time course of plasticity varies across brain systems. Third, both the architecture of the brain and established patterns of behavior are increasingly difficult to change as individuals get older and brain plasticity declines. And finally, it is more effective and more efficient to get things right the first time than to try to fix them later.

With those tenets in mind, the science on brain plasticity is sufficiently mature to support a number of broader implications for children's development. We hope it reaches those who develop and implement policies that affect children's health and well-being.

References

Astle, D. E., Barnes, J. J., Baker, K., Colclough, G. L., & Woolrich, M. W. (2015). Cognitive training enhances intrinsic brain connectivity in childhood. The Journal of Neuroscience: The Official Journal of the Society for Neuroscience, 35(16), 6277–6283.

Barnes, J. J., Nobre, A. C., Woolrich, M. W., Baker, K., & Astle, D. E. (2016). Training Working Memory in Childhood Enhances Coupling between Fronto-parietal Control Network and Task-Related Regions. The Journal of Neuroscience: The Official Journal of the Society for Neuroscience, 36(34), 9001–9011.

Basak, C., Voss, M. W., Erickson, K. I., Boot, W. R., & Kramer, A. F. (2011). Regional differences in brain volume predict the acquisition of skill in a complex real-time strategy videogame. Brain and Cognition, 76, 407–414.

Benasich, A. A., & Ribary, U. (Eds.) (2018). Emergent brain dynamics: Prebirth to adolescence Strüngmann Forum Reports, 25.

Blair, C., & Raver, C. C. (2014). Closing the achievement gap through modification of neurocognitive and neuroendocrine function: results from a cluster randomized controlled trial of an innovative approach to the education of children in kindergarten. PloS One, 9(11), e112393.

Brod, G., Bunge, S. A., & Shing, Y. L. (2017). Does One Year of Schooling Improve Children's Cognitive Control and Alter Associated Brain Activation? Psychological Science, 28(7), 967–978.

Burger, K. (2010). How does early childhood care and education affect cognitive development? An international review of the effects of early interventions for children from different social backgrounds. Early Childhood Research Quarterly, 25(2), 140–165.

Cappelletti, M., Gessaroli, E., Hithersay, R., Mitolo, M., Didino, D., Kanai, R., ... Walsh, V. (2013). Transfer of cognitive training across magnitude dimensions achieved with concurrent brain stimulation of the parietal lobe. The Journal of Neuroscience: The Official Journal of the Society for Neuroscience, 33, 14899–14907.

Diamond, A., Barnett, W. S., Thomas, J., & Munro, S. (2007). Preschool program improves cognitive control. Science , 318(5855), 1387–1388.

Diamond, A., & Lee, K. (2011). Interventions shown to aid executive function development in children 4 to 12 years old. Science, 333(6045), 959–964.

Diamond, A., & Ling, D. S. (2016). Conclusions about interventions, programs, and approaches for improving executive functions that appear justified and those that, despite much hype, do not. Developmental Cognitive Neuroscience, 18, 34–48.

Dodge, K. A., Pettit, G. S., Bates, J. E., & Valente, E. (1995). Social information-processing patterns partially mediate the effect of early physical abuse on later conduct problems. Journal of Abnormal Psychology, 104(4), 632–643.

Doyle, O., Harmon, C. P., Heckman, J. J., & Tremblay, R. E. (2009). Investing in early human development: timing and economic efficiency. Economics and Human Biology, 7(1), 1–6.

Draganski, B., Gaser, C., Busch, V., Schuierer, G., Bogdahn, U., & May, A. (2004). Neuroplasticity: changes in grey matter induced by training. Nature, 427(6972), 311–312.

Fawcett, T. W., & Frankenhuis, W. E. (2015). Adaptive explanations for sensitive windows in development. Frontiers in Zoology, 12 Suppl 1, S3.

Finn, A. S., Minas, J. E., Leonard, J. A., Mackey, A. P., Salvatore, J., Goetz, C., ... Gabrieli, J. D. E. (2016). Functional brain organization of working memory in adolescents varies in relation to family income and academic achievement. Developmental Science. https://doi.org/10.1111/desc.12450

Gabrieli, J. D. E., Ghosh, S. S., & Whitfield-Gabrieli, S. (2015). Prediction as a humanitarian and pragmatic contribution from human cognitive neuroscience. Neuron, 85(1), 11–26.

Gee, D. G., Gabard-Durnam, L. J., Flannery, J., Goff, B., Humphreys, K. L., Telzer, E. H., ... Tottenham, N. (2013). Early developmental emergence of human amygdala-prefrontal connectivity after maternal deprivation. Proceedings of the National Academy of Sciences of the United States of America, 110(39), 15638–15643.

Grammer, J. K., Gehring, W. J., & Morrison, F. J. (2018). Associations between developmental changes in error-related brain activity and executive functions in early childhood. Psychophysiology, 55(3). https://doi.org/10.1111/psyp.13040

Hanslmayr, S., Sauseng, P., Doppelmayr, M., Schabus, M., & Klimesch, W. (2005). Increasing individual upper alpha power by neurofeedback improves cognitive performance in human subjects. Applied Psychophysiology and Biofeedback, 30(1), 1–10.

Hensch, T. K., & Bilimoria, P. M. (2012). Re-opening Windows: Manipulating Critical Periods for Brain Development. Cerebrum: The Dana Forum on Brain Science, 2012, 11.

Jaeggi, S. M., Buschkuehl, M., Jonides, J., & Shah, P. (2011). Short- and long-term benefits of cognitive training. Proceedings of the National Academy of Sciences of the United States of America, 108(25), 10081–10086.

REFERENCES

Kilford, E. J., Garrett, E., & Blakemore, S.-J. (2016). The development of social cognition in adolescence: An integrated perspective. Neuroscience and Biobehavioral Reviews, 70, 106–120.

Kolb, B., & Gibb, R. (2014). Searching for the principles of brain plasticity and behavior. Cortex; a Journal Devoted to the Study of the Nervous System and Behavior, 58, 251–260.

Kraus, N., & Chandrasekaran, B. (2010). Music training for the development of auditory skills. Nature Reviews. Neuroscience, 11(8), 599–605.

Kuhl, P. K. (2010). Brain mechanisms in early language acquisition. Neuron, 67(5), 713–727.

Lillard, A. S., Lerner, M. D., Hopkins, E. J., Dore, R. A., Smith, E. D., & Palmquist, C. M. (2013). The impact of pretend play on children's development: a review of the evidence. Psychological Bulletin, 139(1), 1–34.

Lindenberger, U. (2018). Plasticity beyond early development: Hypotheses and questions. In A. A. Benasich & U. Ribary (Eds.), Emergent brain dynamics: Prebirth to adolescence Strüngmann Forum Reports, 25, 207–223.

Lindenberger, U., Wenger, E., & Lövdén, M. (2017). Towards a stronger science of human plasticity. Nature Reviews. Neuroscience, 18(5), 261–262.

Luna, B., Marek, S., Larsen, B., Tervo-Clemmens, B., & Chahal, R. (2015). An integrative model of the maturation of cognitive control. Annual Review of Neuroscience, 38, 151–170.

Mackey, A. P., Finn, A. S., Leonard, J. A., Jacoby-Senghor, D. S., West, M. R., Gabrieli, C. F. O., & Gabrieli, J. D. E. (2015). Neuroanatomical correlates of the income-achievement gap. Psychological Science, 26(6), 925–933.

Mackey, A. P., Hill, S. S., Stone, S. I., & Bunge, S. A. (2011). Differential effects of reasoning and speed training in children. Developmental Science, 14(3), 582–590.

Mackey, A. P., Miller Singley, A. T., & Bunge, S. a. (2013). Intensive reasoning training alters patterns of brain connectivity at rest. The Journal of Neuroscience: The Official Journal of the Society for Neuroscience, 33(11), 4796–4803.

Mackey, A. P., Park, A. T., Robinson, S. T., & Gabrieli, J. D. E. (2017). A Pilot Study of Classroom-Based Cognitive Skill Instruction: Effects on Cognition and Academic Performance. Mind, Brain and Education: The Official Journal of the International Mind, Brain, and Education Society, 11(2), 85–95.

Mackey, A. P., Whitaker, K. J., & Bunge, S. A. (2012). Experience-dependent plasticity in white matter microstructure: reasoning training alters structural connectivity. Frontiers in Neuroanatomy. https://doi.org/10.3389/fnana.2012.00032

Mathewson, K. E., Basak, C., Maclin, E. L., Low, K. a., Boot, W. R., Kramer, A. F., … Gratton, G. (2012). Different slopes for different folks: Alpha and delta EEG power predict subsequent video game learning rate and improvements in cognitive control tasks. Psychophysiology, 49, 1558–1570.

McCrory, E. J., De Brito, S. A., Sebastian, C. L., Mechelli, A., Bird, G., Kelly, P. A., & Viding, E. (2011). Heightened neural reactivity to threat in child victims of family violence. Current Biology: CB, 21(23), R947–R948.

McLaughlin, K. A. (2016). Future Directions in Childhood Adversity and Youth Psychopathology. Journal of Clinical Child and Adolescent Psychology: The Official Journal for the Society of Clinical Child and Adolescent Psychology, American Psychological Association, Division 53, 45(3), 361–382.

McLaughlin, K. A., Peverill, M., Gold, A. L., Alves, S., & Sheridan, M. A. (2015). Child Maltreatment and Neural Systems Underlying Emotion Regulation. Journal of the American Academy of Child and Adolescent Psychiatry, 54(9), 753–762.

McLaughlin, K. A., Sheridan, M. A., & Nelson, C. A. (2017). Neglect as a Violation of Species-Expectant Experience: Neurodevelopmental Consequences. Biological Psychiatry, 82(7), 462–471.

McLaughlin, K. A., Sheridan, M. A., Winter, W., Fox, N. A., Zeanah, C. H., & Nelson, C. A. (2014). Widespread reductions in cortical thickness following severe early-life deprivation: a neurodevelopmental pathway to attention-deficit/hyperactivity disorder. Biological Psychiatry, 76(8), 629–638.

Melby-Lervåg, M., & Hulme, C. (2013). Is working memory training effective? A meta-analytic review. Developmental Psychology, 49, 270–291.

Nettle, D., Frankenhuis, W. E., & Rickard, I. J. (2013). The evolution of predictive adaptive responses in human life history. Proceedings. Biological Sciences / The Royal Society, 280(1766), 20131343.

Neville, H. J., Stevens, C., Pakulak, E., Bell, T. A., Fanning, J., Klein, S., & Isbell, E. (2013). Family-based training program improves brain function, cognition, and behavior in lower socioeconomic status preschoolers. Proceedings of the National Academy of Sciences of the United States of America, 110(29), 12138–12143.

Noble, K. G., Houston, S. M., Brito, N. H., Bartsch, H., Kan, E., Kuperman, J. M., … Sowell, E. R. (2015). Family income, parental education and brain structure in children and adolescents. Nature Neuroscience, 18(5), 773–778.

Noble, K. G., Norman, M. F., & Farah, M. J. (2005). Neurocognitive correlates of socioeconomic status in kindergarten children. Developmental Science, 8(1), 74–87.

REFERENCES

Pisoni, A., Mattavelli, G., Papagno, C., Rosanova, M., Casali, A. G., & Romero Lauro, L. J. (2018). Cognitive Enhancement Induced by Anodal tDCS Drives Circuit-Specific Cortical Plasticity. Cerebral Cortex , 28(4), 1132–1140.

Pollak, S. D., Cicchetti, D., Hornung, K., & Reed, A. (2000). Recognizing emotion in faces: developmental effects of child abuse and neglect. Developmental Psychology, 36(5), 679−688.

Pollak, S. D., & Kistler, D. J. (2002). Early experience is associated with the development of categorical representations for facial expressions of emotion. Proceedings of the National Academy of Sciences of the United States of America, 99(13), 9072−9076.

Rokem, A., & Silver, M. A. (2010). Cholinergic enhancement augments magnitude and specificity of visual perceptual learning in healthy humans. Current Biology: CB, 20(19), 1723–1728.

Rokem, A., & Silver, M. A. (2013). The benefits of cholinergic enhancement during perceptual learning are long-lasting. Frontiers in Computational Neuroscience. Retrieved from http://www.frontiersin.org/Journal/Abstract.aspx?s=237&name=computational_neuroscience&ART_DOI=10.3389/fncom.2013.00066

Romeo, R. R., Christodoulou, J. A., Halverson, K. K., Murtagh, J., Cyr, A. B., Schimmel, C., … Gabrieli, J. D. E. (2017). Socioeconomic Status and Reading Disability: Neuroanatomy and Plasticity in Response to Intervention. Cerebral Cortex , 1–16.

Romeo, R. R., Leonard, J. A., Robinson, S. T., West, M. R., Mackey, A. P., Rowe, M. L., & Gabrieli, J. D. E. (2018). Beyond the 30-Million-Word Gap: Children's Conversational Exposure Is Associated With Language-Related Brain Function. Psychological Science, 956797617742725.

Rosen, M. L., Sheridan, M. A., Sambrook, K. A., Meltzoff, A. N., & McLaughlin, K. A. (2018). Socioeconomic disparities in academic achievement: A multi-modal investigation of neural mechanisms in children and adolescents. NeuroImage, 173, 298−310.

Rueda, M. R., Rothbart, M. K., McCandliss, B. D., Saccomanno, L., & Posner, M. I. (2005). Training, maturation, and genetic influences on the development of executive attention. Proceedings of the National Academy of Sciences of the United States of America, 102(41), 14931–14936.

Ruf, S. P., Fallgatter, A. J., & Plewnia, C. (2017). Augmentation of working memory training by transcranial direct current stimulation (tDCS). Scientific Reports, 7(1), 876.

Shaw, P., Kabani, N. J., Lerch, J. P., Eckstrand, K., Lenroot, R., Gogtay, N., … Wise, S. P. (2008). Neurodevelopmental trajectories of the human cerebral cortex. Journal of Neuroscience, 28(14), 3586−3594.

Snowball, A., Tachtsidis, I., Popescu, T., Thompson, J., Delazer, M., Zamarian, L., … Cohen Kadosh, R. (2013). Long-Term Enhancement of Brain Function and Cognition Using Cognitive Training and Brain Stimulation. Current Biology: CB, 1–6.

Supekar, K., Swigart, A. G., Tenison, C., Jolles, D. D., Rosenberg-lee, M., & Fuchs, L. (2013). Neural predictors of individual differences in response to math tutoring in primary-grade school children. Proceedings of the National Academy of Sciences of the United States of America, 110(20), 8230−8235.

Timney, B., Mitchell, D. E., & Giffin, F. (1978). The development of vision in cats after extended periods of dark-rearing. Experimental Brain Research. Experimentelle Hirnforschung. Experimentation Cerebrale, 31(4), 547−560.

Titz, C., & Karbach, J. (2014). Working memory and executive functions: effects of training on academic achievement. Psychological Research, 78(6), 852−868.

Vöröslakos, M., Takeuchi, Y., Brinyiczki, K., Zombori, T., Oliva, A., Fernández-Ruiz, A., … Berényi, A. (2018). Direct effects of transcranial electric stimulation on brain circuits in rats and humans. Nature Communications, 9(1), 483.

Walker, M. P., & Stickgold, R. (2004). Sleep-dependent learning and memory consolidation. Neuron, 44(1), 121–133.

Ward, N., Paul, E., Watson, P., Cooke, G. E., Hillman, C. H., Cohen, N. J., … Barbey, A. K. (2017). Enhanced Learning through Multimodal Training: Evidence from a Comprehensive Cognitive, Physical Fitness, and Neuroscience Intervention. Scientific Reports, 7(1), 5808.

Wendelken, C., Ferrer, E., Ghetti, S., Bailey, S. K., Cutting, L., & Bunge, S. A. (2017). Frontoparietal Structural Connectivity in Childhood Predicts Development of Functional Connectivity and Reasoning Ability: A Large-Scale Longitudinal Investigation. The Journal of Neuroscience: The Official Journal of the Society for Neuroscience, 37(35), 8549−8558.

Werker, J. F., & Hensch, T. K. (2015). Critical periods in speech perception: new directions. Annual Review of Psychology, 66, 173−196.

Zoefel, B., Huster, R. J., & Herrmann, C. S. (2011). Neurofeedback training of the upper alpha frequency band in EEG improves cognitive performance. NeuroImage, 54(2), 1427–1431.

Jacobs Foundation
Seefeldquai 17
P.O. Box
CH-8034 Zurich

www.jacobsfoundation.org