THE ROLE OF EARLY EXPERIENCE IN INFANT DEVELOPMENT

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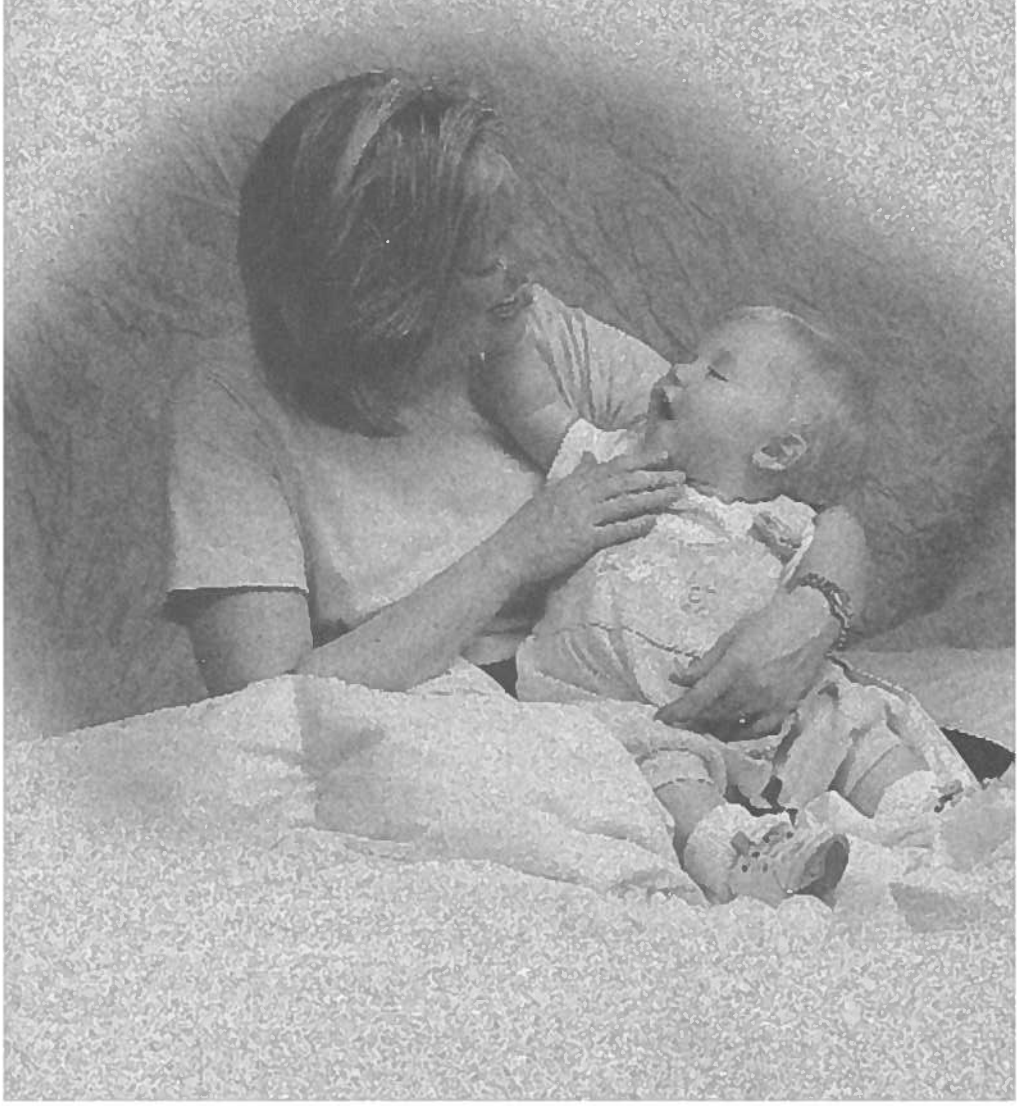
Sponsored by

Johnson & Johnson
pediatric
institute
Division of Johnson & Johnson Consumer Companies, Inc.

1999

Section 3: Cognitive Development



Abstracts From Section 3. Cognitive Development

Development of Cognitive Functions Is Linked to the Prefrontal Cortex

Adele Diamond, PhD

The prefrontal cortex is involved in "executive functions" critical for higher-level problem solving, creative thought, and focused, sustained attention. Although full maturation is achieved by puberty or early adulthood, the prefrontal cortex makes possible important cognitive functions in infants as young as 9 months, and contributes to their ability to solve spatial problems and memory problems in creative ways. Cognitive deficits related to impaired or immature prefrontal cortex function may contribute to subtle learning and behavioral problems.

Born to Learn: What Infants Learn From Watching Us

Andrew N. Meltzoff, PhD

Imitation is a powerful form of learning commonly used by children, adults, and infants. A child's enthusiasm for imitative behavior prompts parental attention and interaction, and provides a mechanism for transmitting appropriate cultural and social behavior. Although simple imitative behavior is evident in the postnatal period, by around 14 months infants remember and repeat actions they observe in adults, other children, and on television. Imitation games provide early experience in mapping the similarities between self and other. Behavioral imitation, empathy, and moral sentiments may be part of the same developmental pathway.

Early Experience Matters for Spatial Development (But Different Kinds at Different Times)

Nora S. Newcombe, PhD

This paper reviews competing theories of cognitive/spatial development (as proposed by nativists, and followers of Piaget and Vygotsky) and discusses

their salient features and shortcomings relative to each other and new research findings. Normal spatial development in the first year of life requires only a typical predictable environment in which children can explore and play. Beginning at 2 or 3 years of age, it is likely that children rely on cultural transmission to acquire understanding of symbols systems and mapping.

Development of Cognitive Functions Is Linked to the Prefrontal Cortex

Adele Diamond, PhD

Introduction: Babies Are Smarter Than People Thought

About a quarter of all cortex in the human brain is prefrontal cortex, located in the front of the brain, behind the forehead and in front of the motor areas. This is the region of the brain that has increased the most in size during the course of primate evolution and the region thought to be involved in "executive functions" critical for higher-level problem solving and creative thought. It is needed for focused, sustained attention, working memory, and inhibition of prepotent but inappropriate action tendencies. Not long ago, people thought that babies were not capable of these high-level abilities and that the prefrontal cortex did not function during the first few years of life. We now know, however, that even during the first year of life infants are capable of sophisticated cognitive operations, and there is a growing body of evidence that the prefrontal cortex makes possible important cognitive functions even during infancy (as early as 9 to 12 months of age).[1-4]

It is incorrect to assume that because the prefrontal cortex is not fully mature until puberty or early adulthood, it does not have any important cognitive functions during early life. Even though the prefrontal cortex will not be fully mature until years later, it is capable of performing cognitive operations before a child's first birthday. It would also be incorrect to assume that the prefrontal cortex is fully mature by 12 months of age in humans just because some of its functions begin to emerge by then. The prefrontal cortex continues to mature over the next 10, or even 20, years of a person's life, just as a person's cognitive development, while remarkable by 1 year, continues to unfold over the next 10 to 20 years.

Infants Are Creative Problem Solvers

Creativity and ingenuity are already evident before an infant's first birthday. For example, we all have a tendency to reach on a straight line for something we see that we want. If there is a barrier in the way, we have to detour around it. If a toy is placed in a transparent box open on one side, babies 6 to 8 months of age persist in trying to reach straight through the side of the box through which they are looking, instead of detouring around to the open side. By 8.5 to 9 months of age, infants start to get the idea of reaching through the open side. It is quite complicated, however, for an infant to plan a reach that goes off to the side and curves back around through an opening, and there is still the strong tendency to reach through the side through which they are looking.

Fig 1. Example of an "awkward reach" on both sides of box.

Left side open, the young girl leans over and looks at the toy through opening.

She reaches awkwardly with far hand. (In this way, she can continue to look in opening and keep her hand in view.)

She leans down and looks into the right side.

She reaches in awkwardly with her LEFT hand, keeping her eye on her hand and toy through opening.

To cope with these problems, infants of 8.5 to 9 months of age come up with a very clever and creative solution. They lean all the way over so they can look into the open side (Fig 1). This enables them to look along the line they will need to reach. Once down in that position, for instance if they are leaning to look into the right side of the box, their right arm is crumpled underneath them and is ready to help support them should they start to fall, so again they come up with a creative solution: They recruit their left hand to reach into the right side of the box and, similarly, their right hand to reach into the left side of the box. It looks very contorted and unusual (we call it the "awkward reach"), but it is a brilliant solution to their need at this age to be looking through the side into which they are reaching (AD, unpublished data).[1-3]

Infants Have Robust Memories

For years it was assumed that the memory support that is impaired when a person has amnesia matures late because children less than 2 years of age perform poorly on a test called the "delayed nonmatching to sample test,"which requires that memory system.[5,6] But that memory system functions quite well very early in infancy; it is another ability required for this test that matures late.

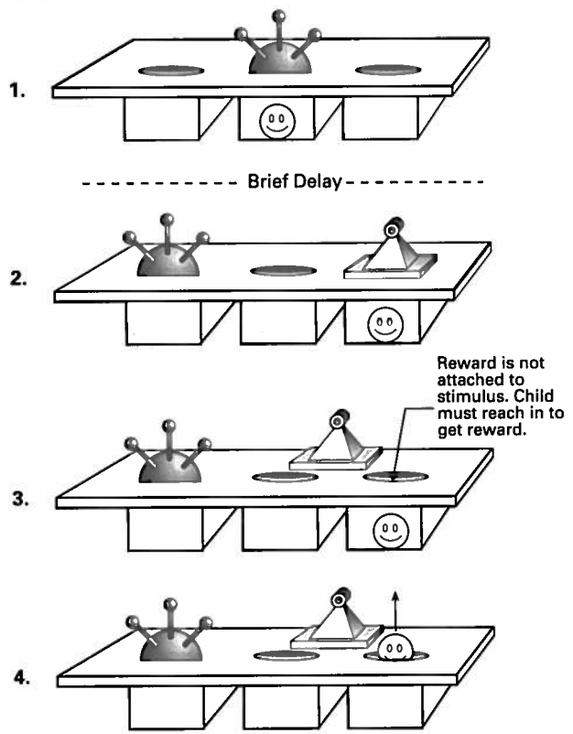
Earlier work with infants on the delayed matching to sample test – a classic test of the medial temporal lobe memory system that requires the ability to remember what you have just seen – revealed that toddlers cannot succeed on the test until they are almost 2 years old.[5,6] (See text box for details of the test.)

The delayed nonmatching to sample task

Here, a sample object is presented over a shallow "well" in the center of the testing table. The subject being tested displaces the sample to retrieve a reward from inside the well. A delay follows, then the familiar sample is presented to one side and a new object is presented to the other side, each over a well. The correct choice is to select the novel object, ie, the object that does not match the previously presented sample – hence the task's name (Fig 2). The well under the novel object contains a reward; the other well is empty. On each trial, new objects are used, and which side the novel one appears on is varied randomly over trials.

Fig 2. The delayed nonmatching sample test.

The test subject is expected to choose the novel stimulus object; that is, the stimulus that does not match the sample presented in 1. The smiley face indicates the location of the reward.



Given that success on this test appears so late in development and given that it has been shown convincingly and repeatedly that success requires proper functioning of the medial temporal lobe, it had been argued that the medial temporal lobe memory system must mature late.[7] The logic seemed reasonable: Here is a behavioral task that requires the functions the medial temporal lobe, but children cannot succeed on this task until quite late (21 months of age). Conclusion: This neural system must not be mature enough to subserve memory until about 21 months of age. That conclusion turns out to be incorrect, however. We now know that during the first year of life, infants can remember objects or actions they have seen for minutes, hours, days, and even weeks.[8-10]

But it is important to look at the *characteristics* of performance, not just success or failure rates, because a given test can be failed for many different reasons. Problems on a test can occur for various reasons, and different kinds of problems implicate different brain regions.

Similarly, developmental improvements on a task do not necessarily correspond to maturational changes in a particular neural region. In a broad sense, failure does not always mean a deficit in the single specific ability one was hoping to measure – success usually requires multiple abilities, not just the ability in which one is interested.

Consider the performance difference in human infants and in adult macaque monkeys with damage to the medial temporal lobe on the delayed nonmatching to sample test. Adult macaque monkeys with bilateral lesions of the medial temporal lobe (especially the rhinal cortical areas [perirhinal and entorhinal cortex]) do poorly on this task.[11-15] They appear to fail because they forget what the sample was. Consistent with this, their performance is better when there is a brief delay between sample and test (delays of 5, 10, or 15 seconds), and their performance progressively worsens as the delay increases to 60 seconds, 5 minutes, 10 minutes, and longer. Intact adult monkeys perform extremely well even after very long delays.

In contrast, human infants do not perform well, even with brief delays of 5 or 10 seconds.[5,6] Moreover, unlike adult macaques with medial temporal lobe lesions, whose performance progressively worsens with longer delays, when infants first succeed with the 5-second delay, they also succeed with delays of 30 and 60 seconds.[5]

If the developmental improvement on this test were measuring an improvement in memory, one would expect that young infants would succeed with brief delays and older, more mature children would succeed with longer delays. However, once children solve the task, they succeed after both long and short delays. Thus, one problem with making the leap from "performance on delayed nonmatching to sample is linked to the medial temporal lobe," to "therefore the developmental progression of performance on delayed nonmatching to sample must indicate the developmental progression of the medial temporal lobe" is that the performance characteristics of intact human infants are quite different from the performance characteristics of adult monkeys with damaged medial temporal lobes. Again, it is crucial to look at the characteristics of performance, and not just at success and failure rates.

A final argument against the theory of late medial temporal lobe memory system development is the large body of evidence of robust memory in very young infants. Indeed, if infants are not required to displace stimulus objects to receive the reward in the shallow well underneath but are allowed simply to explore the new stimulus objects themselves, infants as young as 6 months of age succeed on the task with delays as long as 3 minutes.[10]

Temporal vs Spatial Relationships

In being able to understand the relationship between one thing and another, a very small temporal separation can make a surprisingly large difference.

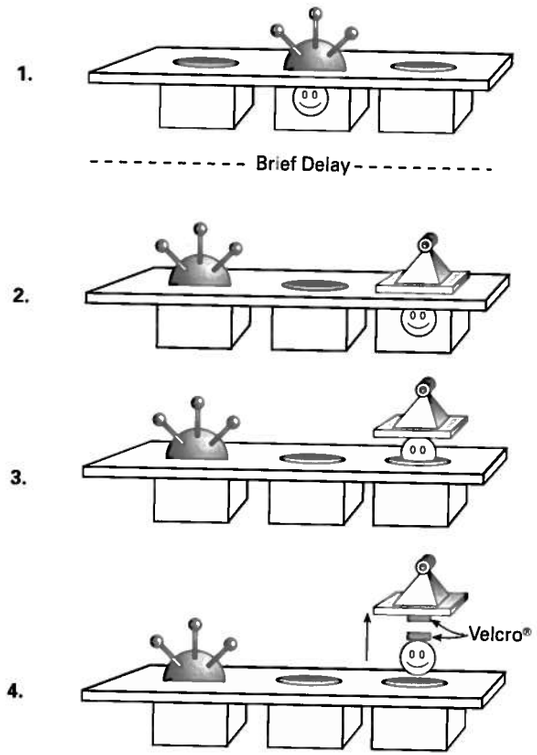
If infants have excellent memories even early in life, why then do they generally fail the delayed nonmatching to sample task until almost 2 years of age? The answer appears to be that infants do not understand the relationship between the reward in the shallow well and the stimulus object sitting on top of the well. For example, infants of only 9 to 12 months of age succeed on this test if the rewards are *attached* to the base of the sample (with Velcro®) instead of placed in wells *beneath* the sample (A. Diamond et al, In press, *Developmental Psychology*, see Fig 3). In the Velcro® condition, just as in the standard condition, the stimuli are placed atop wells, the rewards are in the wells below, and the rewards are separate objects from the stimuli; however, attaching the rewards to the stimuli with Velcro®, a seemingly minor variation in the procedure, appears to alter infants' understanding of the task dramatically.

Something very similar was observed in chimpanzees back in 1965 by Jarvik,[16] who asked why it takes a smart creature like a chimpanzee 100 to 200 trials to learn a simple color discrimination (eg, always choose red or always choose blue). Color discrimination is normally tested in primates by placing, for example, a red plaque over one shallow well and a blue plaque over another shallow well. The left-right placement of the two plaques is varied randomly over trials, but the reward is always under the plaque of a given color. Jarvik varied whether the reward was placed in the well under the plaque or taped to the underside of the plaque. When the reward was attached to the plaque, Jarvik found *one* trial learning.

In the Velcro® condition, the reward is physically closer to the stimulus than in the standard procedure. Is it that spatial proximity is that critical? Perhaps even a tiny spatial separation between stimulus and reward makes a task

Fig 3. Modified delayed nonmatching to sample.

In this test, the reward is affixed to the base of the novel object with Velcro®. The infant picks up the object and then pulls off the reward.



In the classic procedure, infants pick up the stimulus and then look into the well for the reward. There is thus a temporal gap between choosing a stimulus and seeing its reward. In the Velcro® procedure, when the rewards are attached to the base of stimuli, infants see the reward as soon as they lift and turn the stimulus. Instead of the reward remaining in the well, the reward moves with the stimulus. Could the critical factor be the close temporal proximity between displacing the stimulus and seeing the reward?

Is the Velcro® condition easy because of the close *spatial* proximity of the reward and stimulus or because of the close *temporal* proximity? To answer

We constructed an apparatus in which moving the correct stimulus triggered a jack-in-the-box to pop open behind it. The reward (the jack-in-the-box) was farther from the stimulus than in the classic procedure, but it was temporally closer, because it popped open immediately with the slightest movement of the stimulus.

Infants 9 and 12 months old perform every bit as well in the jack-in-the-box condition as they do in the Velcro® condition (Diamond & Lee, unpublished data). The tight temporal coupling of "reach-for-stimulus" and "jack-pops-up" almost makes it appear as if the stimulus is a trigger that causes the jack-in-the-box to pop open. This temporal proximity may enable infants to conceptualize the stimulus and the jack-in-the-box reward as connected, as two parts of a single unit. In both the Velcro® and jack-in-the-box conditions, the reward was temporally close to the stimulus. In the jack-in-the-box condition, however, the reward was spatially farther away from the stimulus than in even the standard condition. Thus, it appears that it is close temporal proximity between stimulus and reward that enables infants in the first year of life to begin to grasp the relationship between stimulus and reward.

Training, Experience, and Thresholds

Training and experience often have little effect until a child is at the threshold of acquiring a competence on his or her own. Thus, for example, Overman and colleagues tested infants every weekday, day after day, week after week, month after month, on the delayed nonmatching to sample test from 12 months of age onward.[6] Those infants succeeded at the same age (21 months on average) as the toddlers tested for the first time at 21 months by either Overman or Diamond, toddlers who had no prior experience with the task.[5,6]

On the task of reaching around a transparent barrier mentioned previously, I tried to see whether training experiences or cues would help infants succeed.[17] I found that cues or training helped only when infants were at the border of progressing to the next higher level of performance. Cues or training helped infants progress to the next level perhaps 2 weeks before they would have otherwise. When an infant was not near the border between one level and the next, however, nothing I tried made any difference. Infants could not profit from the cues or training until they were ready.

Measuring Function and Deficit

A global insult (such as lower or higher levels of a dietary amino acid) can have specific effects that do not show up on standard cognitive or behavioral tests.

Global measures, such as IQ tests, are poor indices of *specific* cognitive functions and poor indicators of what particular neural system might be affected if there is a problem. Developmental cognitive neuropsychologists now have precise measures of specific cognitive functions that are sensitive to the functions of particular neural subsystems. These measures can help in the study and treatment of diverse developmental disorders.

For example, cognitive deficits in children treated early and continuously for phenylketonuria (PKU) went officially unrecognized for many years because the children performed within the normal range on IQ tests, despite the protestations of parents and teachers that something was wrong. The global cognitive measures that were being used in the clinic were too imprecise.

The core problem in PKU is an inability to convert one amino acid, phenylalanine, into another amino acid, tyrosine. This is caused by a defect in the gene that codes for an enzyme, phenylalanine hydroxylase.[18,19] When a person who has PKU eats protein containing phenylalanine, it builds up in the bloodstream to levels that may be 20 to 30 times normal. Also, because phenylalanine is not converted to tyrosine, tyrosine levels are low (although not absent, because some tyrosine is also available in protein). Widespread brain damage and severe mental retardation result.[20,21] The treatment for PKU consists of limiting the amount of foods containing phenylalanine one eats. Eating a diet low in this amino acid succeeds in averting gross brain damage and produces children who have IQ scores in the normal range.[22,23] This is an example of an environmental, behavioral alteration that affects one's biochemistry and one's brain: Changing what children with PKU eat has a dramatic effect on the amino acid levels in their bloodstreams and, because of that, on the development of their brains.

Important cognitive problems are still evident, however.[24-26] The reason for this is that a diet low in phenylalanine rarely results in normal blood levels of this amino acid, because the diet must balance the need to minimize phenylalanine intake with the need for protein. The compromise diet reduces phenylalanine levels but not to normal concentrations, and does little to

ameliorate the low blood levels of tyrosine. The consequence is that phenylalanine levels are mildly elevated and tyrosine levels are mildly reduced. Given that the levels of these amino acids in the bloodstream are not normal, it is perhaps not that surprising that there might be a problem. More surprising were the observations that the problems seemed to be *limited* to the cognitive functions dependent on the prefrontal cortex.[27] The clinical question became how could an amino acid imbalance affecting the entire body produce a specific effect limited to one region of the brain? The following model provides an explanation.

Because phenylalanine and tyrosine compete to cross into the brain, a moderate elevation in bloodstream phenylalanine results in a moderate reduction in the amount of tyrosine that reaches the brain.[28,29] Tyrosine is needed by the brain to make the neurotransmitter dopamine. Most dopamine systems in the brain can cope with modest changes in the level of tyrosine with no ill effects; however, the dopamine neurons that project to the prefrontal cortex are different from most other dopamine neurons – they fire faster and turn over dopamine faster.[30,31] This makes them sensitive to changes in the level of tyrosine that are too small to affect other regions of the brain.[32,33] Indeed, reductions in tyrosine too small to affect other dopamine systems in other neural regions profoundly reduce dopamine levels in the prefrontal cortex.[34] Reductions in dopamine in the prefrontal cortex have severe consequences on the cognitive functions that depend on this area of the brain.[35] In fact, drastically depleting the prefrontal cortex of dopamine produces cognitive deficits comparable to those caused by destroying the prefrontal cortex altogether.[36]

In a large, longitudinal study of children treated early and continuously for PKU, we found that children whose blood phenylalanine levels were 6 to 10 mg/dL (3 to 5 times normal), previously considered within the acceptable range, were impaired on tasks that required both holding information in mind (working memory) and inhibiting a dominant response (inhibitory control), tasks linked to dorsolateral prefrontal cortex.[4] The higher a child's current levels of phenylalanine, the worse that child's performance on these tests. These deficits were evident in all age groups (infants, toddlers, and young children) and remained significant even after we controlled for IQ, sex, health variables, and background characteristics. The deficits were clear whether the children were compared to other PKU children with lower phenylalanine levels, their own siblings, matched controls, or children from the general population. Children with PKU whose blood phenylalanine levels were 3 to 5 times normal were not impaired on any of the large battery of control tasks, which required functions dependent on other regions of the brain, such as the posterior parietal cortex or the medial temporal lobe. Because the functions of these areas were spared, the cognitive deficits appear to be selective.

How can children with serious deficits in their prefrontal cognitive abilities perform within the normal range on general IQ tests? It depends on how one defines "normal." "Within the normal range" means only IQs of 80 or better. Most children with PKU whose phenylalanine levels are 6 to 10 mg/dL have IQ scores in the 80s and 90s – as do most patients with damage to or destruction of the prefrontal cortex.[37] The prefrontal cortex is needed, for example, for problem solving, creativity, and manipulating several pieces of information at the same time. It is needed most when changed circumstances require some alteration of normal practice, or when new goals demand the modification of existing routines.[38] IQ tests, however, largely measure accumulated or stored knowledge. They test one's memory and past learning, and only in small measure, one's problem solving or creativity.

To investigate the biological mechanism more directly, my colleagues and I developed and characterized the first animal model of early- and continuously treated PKU.[39] This enabled us to study directly the effect of moderate, chronic phenylalanine elevations in the bloodstream on neurotransmitter levels in different brain regions. We found cognitive deficits (impaired performance on a behavioral task dependent on the prefrontal cortex) and reduced dopamine in the prefrontal cortex in the PKU animal model. In contrast, other neurotransmitters and other brain regions were much less affected.

Conclusion: The Prefrontal Cortex and Behavior

Young children can sometimes get stuck in a behavioral rut from which they cannot easily extricate themselves – despite their best intentions and despite knowing what correct performance entails. It is important to bear this in mind before mistakenly labeling a young child "bad," "intentionally difficult," or "willful."

It is not enough to know something or remember it; one must translate that knowledge into behavior. Infants and young children, in whom the prefrontal cortex is not yet mature, sometimes do the wrong thing even though they know what they should do and *are trying to do it.* For example, consider a child who has just been sorting a deck of cards by color and then is instructed

to sort the cards by shape but continues sorting the cards by color – even though on each and every trial the child *correctly tells you what the new rule is and shows you where that means each card should be sorted.*[40] Because young children can sometimes have difficulty getting their actions to reflect their intentions, they may be labeled as "bad," "intentionally difficult," or "willful," when that is not the case.

The inhibitory ability dependent on the prefrontal cortex is important for many cognitive tasks. Consider that to sustain the focused concentration required for a difficult task, one needs to be able to resist distraction; to act in new ways, one needs to resist falling back into usual ways of acting or thinking; that is, one needs the inhibitory control ability that depends upon the prefrontal cortex. To relate several ideas and facts together, one must be able to resist focusing exclusively on just one idea or fact; to recombine ideas and facts in new, creative ways, one needs to be able to resist repeating old thought patterns; again, one needs the inhibitory control ability that comes from the prefrontal cortex.

It is easier for people to continue doing what they have been doing rather than to change, and it is easier to go on "automatic pilot" than to consider carefully what to do next. Sometimes, however, we need to change; sometimes we need to act differently than might have been our first inclination. The ability to exercise inhibitory control, which prefrontal cortex makes possible, frees us to act according to what *we choose to do* rather than being "unthinking" creatures of habit.

The ability to hold information in mind, which also depends on the prefrontal cortex, enables us to consider alternatives, to bring conceptual knowledge (and not just perceptual input) to bear on our decisions, and to consider our remembered past and our future hopes when planning our present actions. These two abilities, working memory and inhibitory control, make it possible for us to be creative problem solvers and to exercise free will and self-determination. Such capabilities are not needed all the time, but when they are needed, we would all like to be able to exercise them, and we would like the same for our children.

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