Commentary

What Explains the Negative Consequences of Adverse Childhood Experiences on Adult Health?

Insights from Cognitive and Neuroscience Research

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When we first heard the initial findings reported by Felitti et al. (this volume)[1] indicating relations between adverse childhood experiences (ACE) and subsequent health problems in adulthood, our reaction was "of course." These findings are, no doubt, due to multiple factors. However, these findings would be of little surprise to cognitive and neuroscience researchers in that they are consistent with a vast confluence of data from studies of central nervous system (CNS) "plasticity"—the study of CNS organization as a function of experience. A converging body of evidence from a wide variety of disciplines suggests that the structure, organization, and activity of the human brain is dramatically affected by early experience. The effects of these vary as a function of what parts of the brain subserve the human faculty in question. For example, deprivation in visual experience will affect the visual cortex differentially, depending on when the deprivation occurs. Deprivation of emotional contact and linguistic input will differentially affect the limbic system and left temporal plane, depending on when and for how long the deprivation occurs. This means that there are different times during which different areas of the CNS are organizing and, therefore, either require (critical periods) or are most sensitive to (sensitive periods) organizing experiences (and the neurotrophic cues related to these experiences). Disruptions of experience-dependent neurochemical signals during these periods may lead to major abnormalities or deficits in neurodevelopment.[2]

Much like working on clay, which becomes more difficult as the clay hardens, age and time harden the plasticity of the central nervous system. In some systems (such as the visual and auditory systems) the clay is hard by the end of the first year. For others, the opportunity to adjust the developmental trajectory persists into later childhood (language, cognitive subsystems). The central point that we make in the following discussion is that the construct of "plasticity" is operative at every level of organization, from a single neuron and neuronal networks, to overt behavior such as language acquisition—sensory experience from the environment has a profound and, regrettably, sometimes irreversible impact.

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Neuron as a Self-Organizing System

It may be useful to begin this brief review with some examples of the plasticity of a single neuron. Indeed, some of the basic mechanisms of how a single neuron organizes itself seem to be the basis upon which higher levels of CNS plasticity may function. Some of the best illustrations of research on neuronal plasticity have been reported by Kandel and his associates who studied the underlying mechanisms associated with habituation of the *Aplysia* gill withdrawal response.[3] They found that the decreased synaptic transmission that resulted in behavioral habituation is due to the inactivation of Calcium (Ca^{++}) channels in the presynaptic terminal, which control the amount of neurotransmitter available for release. Short-term memory for a learned task may be due to a functional change in the strength of previously existing synapses. Similarly, Kandel attributed increased synaptic transmission associated with sensitization to be the result of increased levels of cyclic AMP in the presynaptic cell (presynaptic facilitation). It is clear that changes at the neuronal level are not simply transient effects in these non-associative learning tasks. Rather, prolonged habituation or sensitization results in relatively permanent morphologic changes in the presynaptic terminals.[4] Similar short- and long-term alterations in cell physiology and morphology have also been found in studies of associative learning (i.e., classical conditioning).[5]

Plasticity and CNS Organization

Not only has plasticity been demonstrated on the level of the single cell, or the network of cells associated with a simple response like a gill withdrawal, but it has also been demonstrated in the organization of complex synaptic networks. Beginning with the seminal work on altered, enriched, and deprived environments reported

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by Hebb[6] and Hubel and Wiesel,[7,8] several investigators have demonstrated alterations in synaptic organization as a function of deprivation, with accompanying changes in behavior. For example, dark-reared or monocularly deprived animals were found to have decreased orientation-sensitive cells in the cortex,[7] smaller dendritic fields and branching patterns,[9,10] lower spine densities on the dendrites,[11] and reduced percentages of synapses per neuron[12] in a number of visual cortical cell types and locations. Perceptual and behavioral consequences of deprivation included significant difficulties in learning tasks specifically requiring spatial integration of visual information, such as complex maze learning or visual discrimination.[13]

Greenough and his associates have demonstrated that alterations in CNS and behavioral status occur not only from sensory deprivation, but also as a function of environmental complexity.[14,15] Following Donald Hebb's initial suppositions,[6] Greenough and his associates assessed a number of behavioral and neural indices of rats placed in one of three rearing conditions. Large groups of animals who were given a variety of environmental stimuli, such as barriers, ramps, toys that rolled or made noises, varied in their odor, and so on, were referred to as the *Environmental Complexity* group. Conversely, the two other rearing groups were housed in standard laboratory cages with none of the extra environmental stimuli, either alone (*Individual Cage* condition) or in pairs (*Social Cage* condition).

Consistent with Hebb's original findings, Greenough and his colleagues and others have reported superior performance on a variety of behavioral tasks for the *Environmental Complexity*, and in some cases the *Social Caged* animals, compared to the *Individual Caged* group. Of particular importance were the findings that the degree of environmental complexity and deprivation differentiated rats on measures of cerebral cortex weight[16] neural cell body size and amount of glial,[17] amount of dendrite and synaptic density per neuron[18] and dendritic field size in subcortical areas (i.e., hippocampus) and in the cerebellum.[19–21] The effects of enriched, compared to deprived, environments were unmistakable and evident at both behavioral and neuronal levels of organization.

Brain Plasticity Endures Through Adulthood

It has been well known for more than 20 years that cortical representation of body parts are organized into highly specific topographic maps.[22] However, some significant demonstrations of plasticity have been shown in these somatosensory cortical maps as a function of experience in adult primates. Deafferentation was performed by transections at the dorsal roots of spinal segments at spinal cord entry.[23] Subsequently, the cortical receptive areas associated with the transectioned segments were "taken over" or re-mapped by adjacent afferent inputs. These reports have profound implications concerning the enduring plasticity of the nervous system. However, the degree to which remapping has been reported in adult animals is *minimal* compared to the massive cortical reorganization found in neonatal animals.[24]

The effect of earlier compared to later experience on cortical mapping has also been demonstrated with human subjects. A recent study of stringed instrument players examined by Magnetic Resonance Imaging techniques (MRI) revealed that the amount of somatosensory cortex dedicated to the thumb and fifth finger of the left hand—the fingering digits—was significantly larger than in nonplayers. The younger the child had started to play, the larger the map (the more cortex devoted to playing), independent of the amount of time spent practicing.[25]

The relevance of these data to discussions of early adverse childhood experiences may seem indirect. However, it is essential to understand that early sensory experience has a direct and meaningful influence on the organization of a single nerve cell and complex neural networks. These experience-based alterations in neuronal activity form the basis of CNS plasticity at a higher level of organization. Though plasticity has been demonstrated to endure well into adulthood, it is clear that the CNS is far more malleable during early development. The maintenance of synapses seems to operate largely with a principle of "use it or lose it," and many essential neural networks are either formed—or significantly reduced—well before a child's entry into kindergarten.

Behavioral Correlates to CNS Plasticity: Infant Auditory Perception, the Effects of Early Intervention, and Language Acquisition

Clearly, the developing central nervous system is quite sensitive to, and dependent upon, environmental input. As we stated at the outset, this is not only true at the level of neuron or neuronal network, but it is also true at the level of overt behavior. Implied in "behavioral plasticity" is the notion of "sensitive" periods. We will briefly highlight three areas of research to illustrate the influence that experience has on development.

Infant Speech Perception

Each language of the world can be described by how it segments sounds into phonemes. Any one language uses a subset of the possible phonemes that exist across all languages. As a result, all languages possess sound contrasts that native adult speakers of the language can hear and perceive, that non-native adults are unable to perceive. For example, native Japanese-speaking adults

have a very difficult time perceiving the difference between the sounds /r/ and /l/ spoken in English. Similarly, native English-speaking adults were unable to discriminate pairs of Hindi speech contrasts that are not used in English (i.e., dental voiceless aspirated versus the voiced aspirated voicing contrast /t^ha/—/d^ha/). However, several authors have demonstrated that infants under approximately 6 to 8 months of age were able to discriminate pairs of contrasts in languages other than their native tongue, which adults in their native language were *unable* to perceive.[26] It seems that young infants—during the time in development when they have an over-abundance of synapses (i.e., at 6 to 8 months of age)—are able to discriminate many speech contrasts. However, if their native language does not utilize a specific speech contrast, the ability to discriminate the sounds will be lost by the time the child is beyond 12 months of age.

Effects of Early Intervention on Intellectual and Academic Achievement

The Carolina Abecedarian project has convincingly demonstrated that intense early-intervention with children who are at risk for mental-retardation and developmental delay can have long-term effects on achievement and intelligence.[27] The earlier the intervention, the more enduring the gain. In 1972, Ramey randomly assigned 120 poor families to one of four experimental groups: intense year-long intervention starting at ages 4 months to 8 years, 4 months to five years, 5 to 8 years, or no intervention. The two groups with the earliest intervention scored significantly higher on a variety of academic and achievement dimensions than the other two groups. The differences were extreme in the early school years and still significant (albeit smaller) by adolescence (e.g., mean IQ difference of 5 points). What was both surprising and cause for great concern were the findings that intervention after 5 years of age conferred no long-lasting benefit in terms of intelligence (IQ) and academic achievement.

Language Acquisition

The debate surrounding the issue of a sensitive period for language acquisition has raged for years. The data come from a variety of sources including: naturally occurring cases of extreme neglect (the so-called "wild-child" studies), deaf children who learn ASL late in childhood, children who undergo head-trauma and develop aphasia, and autistic non-speakers who are exposed to intensive language therapy. We will review only some of the relevant issues here.

Nature occasionally provides us with extraordinary case studies in experiential deprivation. Nature, however, is a poor experimentalist and the implications that can be drawn from these studies are limited. The two most famous studies in the literature are the cases of Genie[28] and Victor.[29] In both of these cases, it is likely that the two children (who were "rescued" at 13 and around 10 years of age, respectively) had almost no exposure to language prior to their discovery. After years of intensive language intervention, they learned many words and could communicate thoughts and feelings, but they never mastered the essence of human language: syntax. These results are consistent with those of Newport and her colleagues[30,31] who have studied the acquisition of American Sign Language (ASL) in deaf children of hearing parents who are exposed to ASL at different points in development. If children are exposed to ASL up to about 6 years of age (all other things being equal), then they can achieve "native ASL" status. Between 6 and about 11 years of age they can become fluent signers, but there are distinguishable differences in their use of syntax. After this age, they do not acquire true ASL. These data reflect a similar pattern seen with children acquiring a second language. After about 11, people cannot possess a second mother-tongue (although they can attain fluency).

Further evidence for the sensitive period for language acquisition, comes from McEachin et al.'s work with a sample of young autistic children who at age 3 appeared to have little or no language.[32] Intensive therapy approaching 40 hours a week for 2 years remediated the language deficit as well as the autistic symptomatology in about half of the sample. No such findings have been systematically identified for children receiving intensive therapies at older ages. This is stunning evidence for behavioral (and presumably neuronal) plasticity in very young children diagnosed as autistic.

In summary, there appear to be roughly three distinct phases of language development. The first lasts roughly up to about 6 years of age. If children are given access to language during this period they *can* develop normally. The second phase lasts roughly until 11 or the onset of puberty. During this phase, children can still learn language but it will be "non-native." After 11, language learning seems to be restricted to very limited development centering on communication (semantics) rather than grammar (syntax). When children are deprived of language during the first 6 years, they will *never* be equal to normal language users, no matter what their native intelligence, no matter what rehabilitation they are subjected to. For language, experience writes in indelible ink.

Final Thoughts

Infants are born with approximately 100 billion neurons. That is about all we need to be Einsteins or

Beethovens. But what differentiates Einstein and Beethoven from a neonate, is not the number of neurons, but the connections that these neurons make (the synaptic connections). By adulthood, these neurons branch out to each other to form on the order of 100 trillion connections. This thousandfold increase is due almost solely to the effects of experience. Experience not only creates connections, it also prunes connections. Pathways that are not used get used by others. There are thousands of studies documenting the unequivocal effect of early experience on development. The conclusions from these studies are obvious: deprivation or abuse of early experience leads to less optimal development and enriched experience can lead to enhanced development.

The brain is never so malleable as during the first few years of development. This is both a curse and a blessing. It is during this sensitive period that much of the damages of birth and negative experience are the most reversible. Yet funding for research and intervention programs for young children as a percentage of federal and state support is far less than for any other period of life. It is tragic that during the period of development where we can do so much, we do so little; and during the period of development where the interventions of society can have the least long-term effect, we spend so much.

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