Early adverse experiences: what does the latest brain research tell us?

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This article provides an overview of brain development. Starting with four basic principles, it goes on to explain why early experiences have such a powerful role in shaping developmental trajectories and draws attention to the deleterious impact of early adverse experiences on the developing brain. It concludes by discussing evidence suggesting the potential for recovery, both at the level of the brain and in behaviour, and implications for prevention and intervention.

Recent advances in neuroimaging have led to a more nuanced and richer understanding of how the brain develops, starting from the first weeks after conception and continuing until the last years of life. We also know more about how the brain functions and have identified various neural systems that support higher-level emotional, cognitive, and behavioural functioning.

Principle 1: Brain development is a protracted process

Brain development begins shortly after conception and does not reach full maturity until the third decade of life. The neural tube forms a few weeks after conception. Shortly thereafter, cells begin to form, proliferate, and finally migrate to designed locations, which eventually form the various regions of the brain. Once cells reach their final destination, they differentiate into fully functioning neurons and become specialised to their designated brain region. Dendrites, the fibre-like reception areas that support neuronal communication, begin to arborise, allowing nerve cells to communicate with each other. Around the 23rd week of gestation starts a massive overproduction of synapses, or neurochemical signalling points between neurons. This overabundance of synapses eventually becomes reduced through a process known as 'pruning', which is heavily based on input from the environment. Here, unused synapses are eliminated, allowing for a fine-tuning and specialisation of the brain. Myelination of axonal fibres is the last stage of brain development. As part of this process, fatty glial cells wrap around axons to insulate neurons, allowing for more efficient neuronal transmission and signalling. The timing of this process varies, with some areas (sensory and motor regions) becoming fully myelinated in the first five years of life and others (frontal regions of the brain) reaching full myelination during early adulthood. For a more detailed review of the processes of brain development, see Tierney and Nelson (2009).

Principle 2: Brains develop within the context of experience

As discussed in the previous section, brain development occurs over decades of life through various stages that build on one another. While genetic forces drive initial stages of prenatal brain development, postnatal brain development occurs via a constant interaction between genes and the environment. Here, genes establish the basic 'blueprint' of development, setting the foundation and basic structural plan for the brain. However, the actual 'construction' of this plan depends heavily upon signals from the environment. Two of the most experience-dependent processes in the developing brain include the arborisation of dendrites and the pruning of synapses. The density of dendritic branches depends on the amount of and intensity of input from other neurons, with greater dendritic density occurring with greater use. Synaptic connections that are used more often become strengthened, whereas those that are unused are retracted (a phenomenon referred to as 'use it or lose it').

While the experience-based nature of brain development is advantageous from an evolutionary perspective, allowing for the brain to develop in the context of the surrounding environment, this degree of 'plasticity' comes at a cost if environmental exposures exceed that which brains are designed to handle. Exposures to extreme stress and/or early deprivation are examples of such adverse circumstances. We will discuss specific consequences of each of these atypical experiences in the sections that follow.

Principle 3: Brain development occurs in a hierarchical fashion

Each phase of brain development sets the stage for the subsequent phase; accordingly, more advanced systems depend on the more basic. Therefore, the development of the least complex systems (the brainstem) supports the more complex systems (the circuitry involved in

Figure 1 Periods of functional development

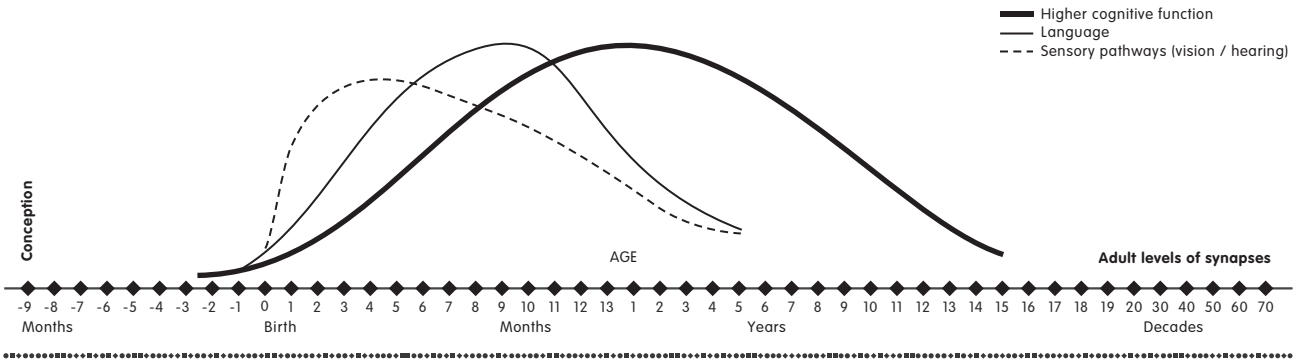

Image: Courtesy Center on the Developing Child at Harvard University. Data source: Nelson, C.A. (2000)

sensory and motor processing) and end with the most sophisticated (cortical and limbic functioning). This has critical implications for development: if adequate signals are not provided for the more basic systems, then the more complex systems, such as those that support emotion and cognitive control or language and memory, cannot develop to their full potential.

Principle 4: The first years of life mark an especially sensitive point in brain development.

Although the brain is moulded by experiences at all phases of life, the experiences during the first years of life have an especially powerful role in influencing the developing brain. Because brain regions vary in the maturation rates, they also vary in the point(s) at which they are maximally sensitive to the environment, or pass through 'sensitive periods'. Despite varying time courses, the majority of sensitive periods arise during early childhood, making the input received (or not received) during this stage in development critical for ongoing development.

Consequences of early life stress on the developing brain

Healthy brain development depends on expected input from the environment in order to reach its full genetic potential. For example, it is expected that human infants will have access to patterned light and a range of auditory cues, which support the development of visual and auditory systems. It is also expected that infants will have access to a responsive, stable caregiver, which supports the development of a number of systems, including emotional, cognitive, and physical growth. Species-atypical violations of these expected experiences have deleterious consequences for brain development.

One example involves exposure to chronic stress or excessively threatening stimuli, such as when children are reared in maltreating families or exposed to high levels of violence. Prolonged exposure to threat is associated with the activation of the Hypothalamus Pituitary Adrenal (HPA) axis, a primary stress response system in the body. Animal work has shown that chronic exposure to glucocorticoids, the end product of the HPA axis, can have adverse effects on regions of the brain that support memory and learning (the hippocampus), and stress regulation, fear response, and detection of threat (the amygdala). Excessive glucocorticoid exposure has been associated with hyperactivation of the amygdala (Lee *et al.*, 1994; Hatalski *et al.*, 1998) and reduced dendritic spines and dendritic arborisation, resulting in eventual apoptosis of neurons in the hippocampus (Sapolsky, 1996; Kim and Yoon, 1998; Brunson *et al.*, 2001; Ivy *et al.*, 2010). Convergent findings in humans have also been observed in adults with histories of childhood maltreatment (for a review see Hart and Rubia (2012)) and there is some evidence that these neural changes can be observed during childhood (Mehta *et al.*, 2009; Tottenham *et al.*, 2010; McCrory *et al.*, 2013). Human research also suggests that extreme childhood stress leads to alterations in the structural and functional development of portions of the prefrontal cortex, a brain region that supports emotional and cognitive control (Hanson *et al.*, 2010; Edmiston *et al.*, 2011; De Brito *et al.*, 2013).

Psychosocial deprivation is a second form of adversity that can negatively interfere with brain development, especially when it occurs early in life. Childhood exposure to neglect is typically investigated with children reared by neglecting parents in family settings, or at a more extreme level in institutional rearing facilities. Under neglecting circumstances, the brain does not receive adequate environmental input to carry out the normal course of neurodevelopment. This results in an 'under-wired' or 'mis-wired' brain, which confers risk for a number of cognitive, emotional

Under neglecting circumstances, the brain does not receive adequate environmental input to carry out the normal course of neuro-development. Photo • Courtesy Michael Carrol

and behavioural problems that persist throughout development. Animal models have shown that exposure to chronically depriving or understimulating environments leads to decreased dendritic arborisation and spines in various regions of the cerebral cortex, and is also associated with global reductions in brain volume (Diamond *et al.*, 1966; Globus *et al.*, 1973; Bennett *et al.*, 1996). Parallel findings in humans have also been observed. For example, children reared in depriving circumstances show reductions in overall brain volume (Mehta *et al.*, 2009; Sheridan *et al.*, 2012) and reduced thickness in the cortex (McLaughlin *et al.*, 2014), which may signal atypical trajectories of experience-dependent synaptic pruning. White matter changes are also observed in children exposed to institutional rearing, both on a global level (Sheridan *et al.*, 2012) and in specific axonal bundles associated with emotional and cognitive control (Eluvathingal *et al.*, 2006; Kumar *et al.*, 2014; Bick *et al.*, 2015), suggesting developmental delays in the degree to which neurons become myelinated across development.

Potential for recovery

On a more promising note, the high degree of neural plasticity early in life also allows the brain to be highly sensitive to positive or enriching environments. Therefore, removal from early adversity and entry into a therapeutic context can support recovery. This has been demonstrated on a cellular level in animal work. More complex environments have been shown to lead to more sophisticated dendritic branching and synaptic density in cortical areas (Altman and Das, 1964; Bennett *et al.*, 1964), and have also been associated with larger brain volumes (Rehkamper *et al.*, 1988). Human

work involving children removed from conditions of extreme neglect has shown similar findings; for example, institutionally reared children placed into enriching, responsive family settings show structural (Sheridan *et al.*, 2012; Bick *et al.*, 2015) and functional (Vanderwert *et al.*, 2010) improvements of the brain, and associated improvements in cognitive and emotional adjustment (Rutter, 1998; Nelson *et al.*, 2007). For many outcomes, the greatest improvements, both neurally and behaviourally, are typically observed for children who are removed from neglect and provided with enriching environments at the earliest ages (Vanderwert *et al.*, 2010; Rutter, 1998; Nelson *et al.*, 2007).

In summary, there is converging evidence across human and animal studies that early adverse exposure negatively interferes with the developing brain. While excessive exposure to stress may lead to neural alterations due to prolonged exposure to stress hormones, exposure to extreme deprivation may interfere with the brain's ability to reach its full developmental potential, due to insufficient input. Animal studies have been critical for understanding the consequences of these adverse experiences on a neuronal level. Human studies showing similar morphological and functional alterations have elucidated the consequences for emotional and cognitive functioning. Recent evidence points to the potential for recovery, both in terms of brain structure and function, in early intervention contexts. These studies reinforce the notion that prevention, and early intervention that occurs as early as possible, are likely to lead to the healthiest outcomes in the long term.

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