

Effects of Maltreatment (stress neglect and trauma) on Brain Structure and function

In early life (pre natally and during the first 2 years of life-1000days) toxic stress, trauma and neglect are likely to have their maximum adverse impact on the rapidly developing brain which is work still in progress at the time of birth. Toxic stress, trauma and neglect have a close relationship with each other. Their adverse impact on the developing brain and body depends on their severity, coexistence and duration of exposure. The relationship to negative impact is not absolute, since resilience serves as a strong protective influence and a good buffer. This communication highlights some effects of toxic stress, trauma and neglect on the structure and functions of the brain through constant interactive effect of nature, nurture and experience on the structure and function of the developing brain.

There is a close interaction between nurture, nature (environment and genes) as well as experience on the developing brain. Genetic influence starts very early in life but toxic stress, neglect and trauma can turn some specific genes “on” and others “off” at particular times and in different locations in the brain. This is likely to happen during the most sensitive periods of brain development. Cortisol, other hormones and neurotransmitters play a key role in affecting the brain structure and functions. The negative factors if present persistently even in a low intensity can potentially affect the expression of genes that regulate the stress response across the life course. The expression of genes can be based on their imprint and this can then affect the structure of the brain as well as neuro endocrine and immune function. This operates through the limbic structure in the brain. The effects can be protective as well as negative. The gene expression can occur through genetic transcription. This can change brain structure and have a long lasting impact.

As mentioned above, there is a close interaction between the environment, the genes and experience at all times and genetic influences are affected by environment since the baby adapts to what it sees, hears, feels and experiences. It is not surprising that structure and function would be guided by good nurturing, a favorable and stimulating environment and love and support from the caregivers in the family.

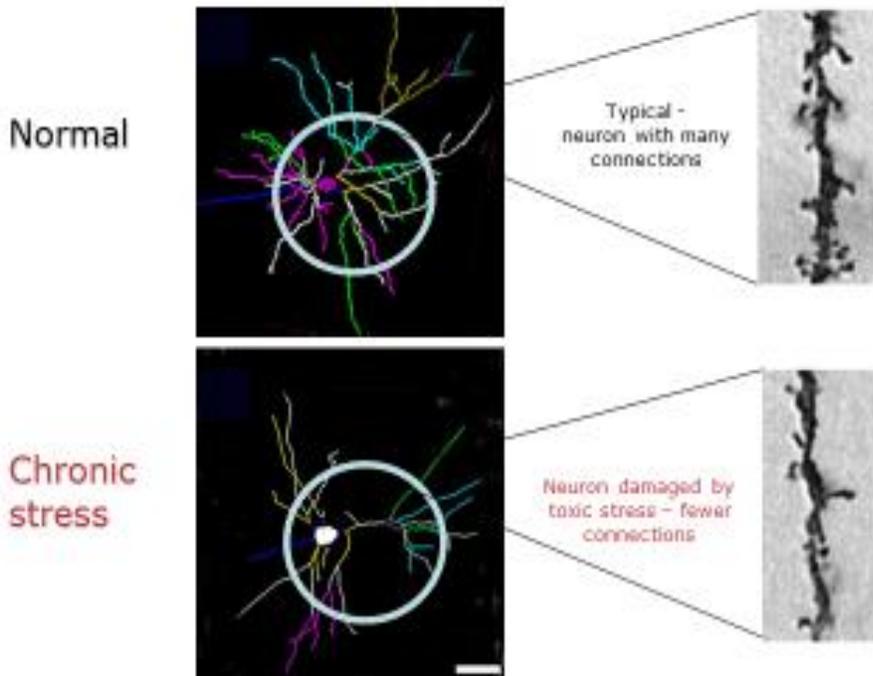
Stressful life events for a period of 3 months are associated with significant reduced grey matter volume in anterior cingulate, hippocampus and para hippocampal gyrus as shown by magnetic resonance imaging studies. Limbic hyper responsiveness and reduced hippocampal volumes could be mediators between the experiences of adversities during childhood and the development of emotional disorders later in life.

Principles of brain development have been elaborated in another communication. The implications of adverse impact of toxic stress, neglect and trauma have also been described in

another communication. As mentioned above, the brain is not structurally and functionally complete at birth. Neuronal development followed by neuronal migration is rapid pre natally and neurons are likely to be most vulnerable to adverse influences at this time. Myelination, proliferation of synaptic connections, and development of glial and circulatory support systems all continue long after a child has entered the world. These are affected by adversities during the most sensitive periods of brain development. Nature gives children a chance to adapt to the specific needs presented by the environment in which they are born. While there are a large number of environmental influences, that can affect the structure and functions of the brain, optimum development of the brain can be affected by nutrition (including micro nutrients) in quantity or quality, infectious diseases, exposure to influence of tobacco use by mother and family members or alcohol use by the mother, and exposure to toxins in the family environment like lead, mercury and toxic stress.

The effects of the childhood environment (favorable or unfavorable), are on many processes of neurodevelopment (neurogenesis, migration of neurons in utero, differentiation, apoptosis, arborization, synaptogenesis, synaptic sculpting, and myelination). These effects are mediated through ongoing genetic and environmental interactions. Synapses and synaptic pathways are affected through the process of ‘use it or lose it’.

Persistent Stress Changes Brain Architecture



Prefrontal Cortex and Hippocampus

This means there is retention and strengthening of synaptic pathways through continued use and weakening or a loss if these are not used. This depends on interaction between the caregiver and the child through a 'serve and return' function. Here the sensitivity and responsiveness of care giver as well as the child are very important. This leads to the provision of a favorable environment, support good nutrition and reduce adversities to the extent possible by care givers and all other concerned stakeholders. If these connections are lacking, brain development can be affected adversely in a lasting fashion. While the adoption of modern technology can be a great asset, the importance of retention of good practices, behaviors extended family support, caregiver child interactions cannot be underestimated.

We also know that some cases of physical abuse can cause immediate direct structural damage to a child's brain. For example, according to the National Center on Shaken Baby Syndrome, shaking a child violently can damage brain tissue and tear blood vessels. In the short term, this can lead to seizures, loss of consciousness, or even death. In the long-term, shaking can damage the fragile brain so that a child develops a range of sensory impairments, as well as cognitive, learning, and behavioral disabilities. Other types of head injuries caused by physical abuse can have similar effects.

Structural effects on the brain

Brain regions such as the hippocampus, amygdala, and prefrontal cortex are very sensitive to negative influences. They show altered patterns of activity in positron emission tomography (PET) and functional magnetic resonance imaging (fMRI). There can be changes in volume of these structures as decreased volume of hippocampus and pre frontal cortex and amygdala. The changes in amygdala volume can be variable. The other structures that are sensitive to adverse effect are corpus callosum and the cerebellum.

A Hippocampus: Adults who were maltreated or neglected in early life may have reduced volume in the hippocampus, which is central to learning and memory. Toxic stress also can reduce the capacity of hippocampus to bring cortisol levels back to normal after a stressful event has occurred. One of the ways that stress hormones modulate function within the brain is by changing the structure of neurons. The hippocampus is one of the most sensitive and malleable regions of the brain, and it is also very important in cognitive function.

B Corpus callosum: Maltreated children and adolescents tend to have decreased volume in the corpus callosum, which is the largest white matter structure in the brain and is responsible for interhemispheric communication and other important processes (e.g., arousal, emotion, higher cognitive abilities).

C. Cerebellum: Maltreated children and adolescents tend to have decreased volume in the cerebellum, which helps coordinate motor, behavior and executive functioning of the brain.

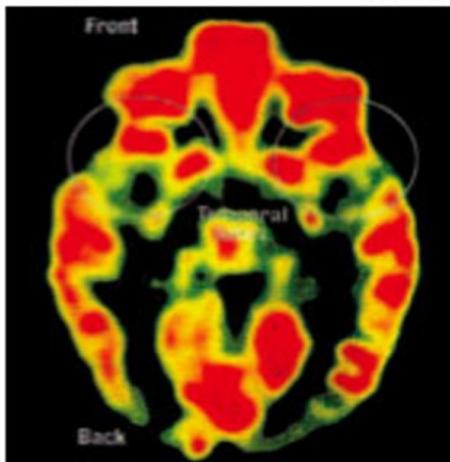
D. Prefrontal cortex: Some studies on adolescents and adults who were severely neglected as children indicate they have a smaller prefrontal cortex, which is critical to behavior, cognition, and emotion regulation. However, other studies show no differences. Physically abused children also may have reduced volume in the orbitofrontal cortex, a part of the prefrontal cortex that is central to emotion and social regulation. Repeated stress also causes changes in other brain regions.

Repeated stress causes dendritic shortening in medial prefrontal cortex but produces dendritic growth in neurons in amygdala, as well as in orbitofrontal cortex. Along with many other brain regions, the amygdala and prefrontal cortex also contain adrenal steroid receptors; however, the role of adrenal steroids, excitatory amino acids, and other mediators has not yet been studied in these brain regions adequately.

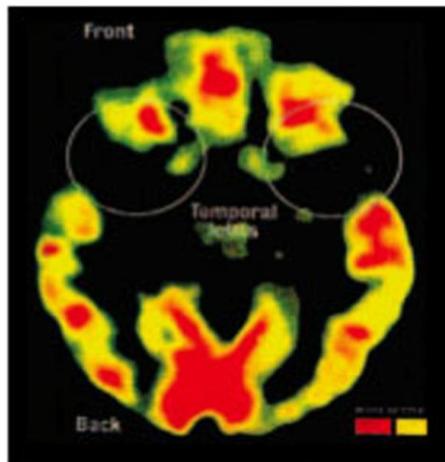
E Amygdala: Although most studies have found that amygdala volume is not affected by maltreatment, abuse and neglect can cause over activity in that area of the brain, which helps determine whether a stimulus is threatening and can trigger emotional responses.

The adoption into the UK of children who have been reared in severely deprived conditions provided an opportunity to study possible association between very early negative experiences and subsequent brain development. In a cross sectional study, done on severely deprived Romanian children who were institutionalized by using MRI studies demonstrated lower total grey and white matter volumes in the institutionalized group. The amygdala volumes were also decreased. The study shows the sensitivity of amygdala to adversity.

Comparison of the Developing Brain



Healthy Development



Development Affected by Environmental Stress

Source: Dr. H. T. Chugani, Newsweek, Spring/Summer 1997 Special Edition: "Your Child: From Birth to Three," pp 30-31.

There is an association between maltreatment and atypical development of the hypothalamic–pituitary–adrenal axis stress response, which may predispose to psychiatric vulnerability in adulthood. Functional magnetic resonance imaging (fMRI) studies have demonstrated possible structural and functional brain differences in children and adults who have experienced childhood maltreatment. Differences in the corpus callosum identified by structural fMRI have now been reliably reported in children who have experienced abuse, while differences in the hippocampus have been reported in adults with childhood histories of maltreatment. In addition, there is preliminary evidence from functional fMRI studies of adults who have experienced childhood maltreatment of amygdala hyperactivity and atypical activation of frontal regions. These functional differences can be partly understood in the context of the information biases observed in event-related potential and behavioral studies of physically abused children. There are studies that demonstrate that many of these effects occur as a result of the ongoing interaction between the genes and the environment.

Hormones

The effect of toxic stress neglect and trauma on hormones are pronounced. Through hormones, there can be an adverse impact on the structure of the brain and its functioning. Extreme exposure to toxic stress can change the hormones and the stress systems of the body. The brain can begin to respond at lower threshold levels in some individuals to events that might not be stressful to others. In these cases, the stress response system can be activated more frequently and for longer periods than is necessary. It may happen daily for variable periods of time. This leads to greater wear and tear. The effects of this wear and tear may appear immediately or show up later in life.

The neural circuits for dealing with stress are particularly sensitive or malleable (“plastic”) during the fetal and early childhood periods. Toxic stress during this early period can affect developing brain circuits and hormonal systems in a way that leads to poorly controlled stress response systems that will be overly reactive or slow to shut down when faced with threats throughout the lifespan.

Besides stress, is the body’s ability to react to such things as lack of adequate nutrition, wounds, infections, adverse environment and other threats or injuries. This can lead to undesirable outcomes in the form of depression, alcoholism and substance abuse, anxiety, or delinquency in adult life. The adverse consequences can also include early occurrence of cardiovascular disease, diabetes, or stroke in adult life. The adverse effects also occur in the immune function and metabolic functions.

Stress responses include activation of a variety of hormone and neurochemical systems throughout the body. Amongst the various systems, two hormonal systems have received extensive attention. These include: (1) the sympathetic-adreno medullary (SAM) system, which

produces adrenaline in the central part of the adrenal gland, and (2) the hypothalamic pituitary-adrenocortical (HPA) system.

Cortisol levels: Many maltreated children, both in institutional and family settings, and especially those who experienced severe neglect, tend to have lower than normal morning cortisol levels coupled with flatter release levels throughout the day. The impact of abnormal cortisol levels and patterns are variable in different individuals. This occurs because different individuals react differently to the stressors. Abnormal cortisol levels can have many negative effects. Lower cortisol levels can lead to decreased energy resources, which could affect learning and socialization; externalizing disorders; and increased vulnerability to autoimmune disorders. Higher cortisol levels could harm cognitive processes, subdue immune and inflammatory reactions, or heighten the risk for affective disorders.

Stress responses include activation of a variety of hormone and neurochemical systems throughout the body. Adrenaline production occurs in response to many forms of acute stress. Cortisol also is produced in response to many forms of stress, and likewise helps the brain and body cope effectively with adverse situations. Sustained or frequent activation of the hormonal systems that respond to stress can have serious developmental consequences, some of which may last well past the time of stress exposure. Children who grow up in conditions of economic hardship often exhibit elevated stress hormone levels. Young children who are neglected or abused have abnormal patterns of cortisol production that can last even after the child has been moved to a safe and loving home.

Adverse child events (ACE) early infant experiences (e.g., neglectful maternal care) and serious disruptions of the prenatal environment (e.g., drug and alcohol exposure) can lead to short-term neurobehavioral and neuro hormonal changes in offspring that may have long-term adverse effects on memory, learning, and behavior throughout life.

Children who experienced severe neglect early in life while in institutional settings often have decreased electrical activity in their brains, decreased brain metabolism, and poorer connections between areas of the brain that are key to integrating complex information. These children also may continue to have abnormal patterns of adrenaline activity years after being adopted from institutional settings. Additionally, malnutrition (a form of severe neglect), can impair both brain development (e.g., slowing the growth of neurons, axons, and synapses) and function (e.g., neurotransmitter syntheses, and the maintenance of brain tissue).

In summary several systems—social/behavioral, neuroendocrine, and even genetic—are all influenced by early experiences and interact with each other as a child grows and develops. Even though structural and functional impact can occur especially when the development of brain is in progress the relationship is not absolute since resilience and other protective factors can prevent damage or the damage may be reversible through timely measures.



7 months old damage after birth asphyxia



3 years old cerebral palsy



7 years old autism

Key references

1. Excessive Stress Disrupts the Architecture of the Developing Brain: Working Paper 3. Updated Edition. <http://www.developingchild.harvard.edu> © 2005, 2009, 2014, National Scientific Council on the Dev.
2. McGowan PO, Sasaki A, D'Alessio AC, et al. Epigenetic regulation of the glucocorticoid receptor in human brain associates with childhood abuse. *Nat Neurosci*. 2009;12(3):342–348. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2944040/pdf/nihms233892.pdf>. Accessed May 29, 2014 Effect of genes
3. Center on the Developing Child at Harvard University. How early experiences alter gene expression and shape development. http://developingchild.harvard.edu/index.php/resources/multimedia/interactive_features/gene-expression. Accessed May 29, 2014
4. Jack P. Shonkoff, MD, Andrew S. Garner, MD, PhD, TECHNICAL REPORT The Lifelong Effects of Early Childhood Adversity and Toxic Stress American Academy of Paediatrics www.pediatrics.org/cgi/doi/10.1542/peds.2011-2663 doi:10.1542/peds.2011-2663 PEDIATRICS downloaded August 2016.
5. Understanding the effects of maltreatment on brain development. Child Welfare Information Gateway. <https://www.childwelfare.gov/pubs/issue-briefs/brain-development.April.2015>

6. [Andrea Horvath Marques](#)^{1,2,*}, [Thomas G. O'Connor](#)³, [Christine Roth](#)^{4,5}, [Ezra Susser](#)^{1,6,7} and [Anne-Lise Bjørke-Monsen](#)⁸ The influence of maternal prenatal and early childhood nutrition and maternal prenatal stress on offspring immune system development and neurodevelopmental disorder *Frontiers in Neuroscience* 2013:7,120.
7. Papagani SA, Benetti S, et al Effects of stressful life events on human brain structure: A longitudinal voxel-based morphometry study. *Stress* 14: 227-232, 201
8. Dannlowski et al. (2012). Limbic Scars: Long-Term Consequences of Childhood Maltreatment Revealed by Functional and Structural Magnetic Resonance Imaging. *Biological Psychiatry*, 71(4), 286-293. (Limbic system problems)
9. McCrory, E., De Brito, S. A., & Viding, E.(2011). [The impact of childhood maltreatment: A review of neurobiological and genetic factors](#). *Frontiers in Psychiatry*. 2:48. Epub 2011 Jul 28.
10. Effect of cortisol and hormones 4. McEwen, B. S. (2008). Central effects of stress hormones in health and disease: Understanding the protective and damaging effects of stress and stress mediators. *European Journal of Pharmacology*, 583(2-3), 174-185.
11. National Scientific Council on the Developing Child. (2010). Early Experiences Can Alter Gene Expression and Affect Long-Term Development: Working Paper 10. <http://www.developingchild.harvard.edu>
12. Mehta, M. A., Golembo, N. I., Nosarti, C., Colvert, E., Mota, A., Williams, S. C., Rutter, M., & Sonuga-Barke, E. J. (2009). [Amygdala, hippocampal and corpus callosum size following severe early institutional deprivation: The English and Romanian Adoptees study pilot](#). *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, 50, 943-951.
13. Shonkoff, J. P., & Levitt, P. (2010). Neuroscience and the future of early childhood policy: Moving from why to what and how. *Neuron*, 67, 689-691.
14. Hillary A. Franke, Review Toxic stress:Effects, prevention and treatment *Children* 2014, 1, 390-402; doi:10.3390/children1030390
15. Christian, CW; Block, R; Committee on Child Abuse and, Neglect; American Academy of, Pediatrics (May 2009). "Abusive head trauma in infants and children." *Pediatrics*. 123 (5): 1409–11. doi:10.1542/peds.2009-0408. PMID 19403508

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