

Understanding the Root Cause of Anxiety and Depression

Mental illnesses such as anxiety disorders, depression, bipolar disorder, and schizophrenia are extremely common, can be very disabling, and negatively impact physical health. Anxiety disorders are the most common mental illnesses and are frequently accompanied by depression and substance abuse. In addition to creating immeasurable suffering and dysfunction, the worst outcome of mental illness, suicide, is increasing and is among the leading causes of death in adolescents. Each year over 30,000 lives are lost to suicide in the United States, and worldwide suicide is the leading cause of violent deaths. It is estimated that in any 12 months 26% of the population suffers from a diagnosable mental illness. Forty-six percent of the American population will suffer from a mental illness at some point during their life. A study by the World Health Organization shows that of all the medical illnesses, mental illness and substance abuse are the most costly to society and the most disabling. Most mental illnesses have their beginnings during childhood and the earliest presentation of these problems frequently is increased levels of anxiety. Abnormal levels of childhood anxiety can greatly increase the risk for adolescent and adult mental illness.

Based on work performed at the University of Wisconsin with young rhesus monkeys born into UW-Madison's primate research colonies, we now know that brain alterations are at the root of early abnormal anxiety. This work not only demonstrates the specific parts of the brain that have altered function <http://www.news.wisc.edu/15363>, but also shows that this altered brain function that is important for anxiety can be inherited <http://www.med.wisc.edu/28620> & <http://www.med.wisc.edu/39097>. Based on an understanding of these brain abnormalities, current studies are aimed at uncovering the factors that will help correct a child's early predisposition to develop abnormal anxiety and other mental illnesses.

While some of our current treatments for illnesses like anxiety disorders and depression are effective, many patients do not get better and face life-long suffering. We are a long way from a cure. To develop treatments that will be more effective it is necessary to understand the root cause of these illnesses. The importance of studying young rhesus monkeys lies in the potential to develop new effective interventions for children with extreme and abnormal anxiety. Similar to the human brain, the monkey brain has a complex prefrontal cortex that continues to develop well into early adulthood. The prefrontal cortex is one of the most critical sites malfunctioning in anxiety disorders and other psychiatric illnesses. Using the rhesus monkey allows researchers to be confident that the knowledge that is acquired is directly relevant to understanding the causes of human suffering. This knowledge provides the best chance to identify new and more effective ways, informed by scientific evidence, to treat the fundamental causes of abnormal anxiety and other psychiatric disorders.

Anxiety disorders and other psychiatric illnesses are in part inherited but are also very much determined by environmental events. It is now widely accepted that early stressful environments ranging from severe abuse and neglect to more moderate levels of adversity, including parental stress and absentee parenting, are the most relevant environmental risk factors for the later development of anxiety and other psychiatric illnesses. Unfortunately, this type of childhood adversity is endemic in our society. These early adverse circumstances, even when moderate, can change the trajectory of a

developing child's brain such that it becomes wired in a way that leads less fortunate individuals down a path of anxiety, depression and other forms of psychopathology. Recent University of Wisconsin research demonstrates how early family stress can influence children's development by making children more sensitive to stress and more likely to develop psychopathology later in life. For example, moderate levels of family stress occurring during the first year of life result in increased stress hormones at 4 years of age, more psychological problems when entering school, and in girls alterations in brain function as adolescents <http://www.news.wisc.edu/21255>. However, the means by which early adversity actually influences the brain is unknown and such an understanding is key to developing new ideas about early intervention.

Discovering new interventions aimed at preventing the long term consequences of early adversity in children is critical and requires a basic understanding of the influences of a suboptimal upbringing on the primate brain. The goal of the new studies in young monkeys is to understand how moderate levels of early adversity influence the brain systems that lead to a greater likelihood of becoming anxious. This will lead to insights into the brain molecules that link adverse experience to brain changes and will provide new treatment targets. In one experiment, young monkeys will initially be raised in a nursery by humans and when able to feed themselves will live with their peers. This well-established rearing approach is used in laboratories and zoos all over the world to mitigate the consequences of spontaneously occurring maternal rejection. Importantly, this type of upbringing does not produce the level of traumatic isolation and abuse that many children experience, but it does model a fairly common level of moderate early-life stress among children. Some critics have compared the treatment of these monkeys to the maternal deprivation experiments from the 1950s. However, many of those experiments used stressors considerably more severe than those currently being used. Those famous studies by Dr. Harry Harlow and others yielded groundbreaking insights into mother-child bonding that changed the way young children are cared for in many settings including neonatal intensive care. As important as those early studies were, the new research seeks to answer different questions than those originally asked by Harlow. Recent advances in neuroscience, brain imaging, and molecular neurobiology allow for the first time, the ability to understand how the brain adapts to adversity. An understanding of how inherited genetic predispositions interact with adversity-related molecular changes has the promise to lead to new ideas about treatments aimed at countering the effects of early adversity on childhood development.

UW research has helped point to the importance of early childhood interventions to save children from developing anxiety, depression and the drug and alcohol abuse that can arise as an attempt at self-medication. Anxiety and depression can be crippling, and this important research provides a real chance to better understand and alleviate human suffering, which is the ultimate goal of this work. The goal of these studies is to find interventions that prevent or reverse the long-term brain and psychological consequences of early adversity in human children.