



Stress, Neural Systems, and Genetic Code

An Interview with Neuroscientist Judy Cameron

NATIONAL SCIENTIFIC COUNCIL ON THE DEVELOPING CHILD

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For more information on the Council and the science of early childhood, go to www.developingchild.net.

Abstract: Research indicates some early life stresses can have a profound impact, resulting in changes in brain function and behavior, and even differences in the ways some genes express their particular genetic code signature. At various times during early development, different neural systems appear to have an increased sensitivity to stress and can influence long-term social behavior in a number of ways. A stable, nurturing environment is an important element in normalizing the development of a child experiencing stress.



Council Member **Judy Cameron** is Professor of Psychiatry at the University of Pittsburgh, Senior Scientist at the Oregon National Primate Research Center, and Professor of Behavioral Neuroscience, and Obstetrics & Gynecology at Oregon Health and Science University. She also directs training programs in reproductive biology and women's health research at OHSU, and is director of the NIMH Conference Series on Comparative and Primate Research. She is a member of the Research Network on

Early Experience and Brain Development. Her research focuses on the effects of everyday life stresses on long-term health. Three current areas of interest in her laboratory are the effects of genetic factors and early life experiences on anxious and depressive behaviors, identification of factors that lead to stress sensitivity versus stress resilience, and the interactions between metabolic and psychosocial stresses in the development of stress-sensitive disease processes.

Please give us a brief overview of your work.

Our laboratory studies the effects of early life experience on behavior, and the underlying neural systems within a developing brain that might guide that behavior. We also have separate research that identifies stress-sensitive and stress-resilient individuals and looks for differences in brain architecture between the two groups. The central question of this research is: Where does stress sensitivity come from? A third area of study that contributes indirectly to the Council agenda asks the question: What are the genes that are linked to many mental-health disorders in children? We have a large collaborative study under way to help us answer that question.

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Science demonstrates the developing brain is most malleable in the first few years of life. What have you discovered about the way environments and experiences interact with genes?

There is an interaction—visualize a layering—between genetics and life experiences. You start by being born with genes that influence how you react to early life experiences, whether they are stressful life experiences or not. Each time you have a major life experience, that has a significant impact on the brain. It literally changes the way you behave, and that experience also changes genes' expression. In other words,

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an experience won't change what genes you inherited, but it will change which of those genes are being expressed. How genes regulate functions within your body will be changed as a result. A subsequent momentous experience—for example, you lose a parent—will again change your gene expression. Both genetics and life experiences determine outcome in a very interactive way. Science demonstrates clearly that children are shaped by both genes and experiences. So the old question about whether children are shaped by genes or experience should be retired. It's both. And the truth is in the interaction.

What role does gene expression play in development? We know relationships with supportive caregivers offer great benefit to children of all ages, genetic makeup notwithstanding.

Each person is born with an individualized genetic code. For example, your height is going to be predominately determined by your relatives' heights—your mother and father and grandparents. But even if your genes favor tallness, early life experience can cause stunted growth, probably by determining whether the tallness genes are expressed. Genetic code resides in the nucleus of a cell.

To produce an outcome, it must be uncoded and transferred—scientists sometimes use the word “transcribed”—into proteins, and those proteins are sent out of the cell as intercellular messages. Think of it as sending a message, but in code.

To get back to the height example, negative psychological stress can stunt a child's growth—can cause “failure to thrive.” If, however, that child is taken out of the stressful condition, he or she can once again thrive. But even if the stressful situation is reversed, the child's long-term growth is likely not to be as robust as it would be under normal conditions. Other functions of the brain, including those that influence social behavior and the development of psychological problems, like anxiety and depression, are even more susceptible to psychological stress.

How do scientists know this?

Child psychologists and other scientists learn about behavior by carefully studying behavior in various situations. For example, conducting a “playroom test” is one way we assess a young child for anxious behavior. A mother and child enter a playroom with lots of interesting toys; the mother is asked to sit nearby and to neither encourage nor



discourage play. Most young children will sit on their mother's lap for a few minutes and then climb down to investigate the toys. A very anxious child is less exploratory, very worried about leaving the mom, or may leave the mother but return to her repeatedly for comfort.

Of course, much of what we know about associations between early experience, interaction and the developing brain has been learned through animal studies. Using monkeys as our experimental subjects, we have conducted essentially the same playroom tests and achieved similar results. Using such tests allows careful examination into how inherited traits, as well as life experiences, alter the behaviors that are displayed under specific conditions. In other studies using monkeys, one-week-old infant monkeys living in a social group had their mothers removed from the group (a stressful early life experience). We found these young monkeys grow up to be much less interested in social interaction compared to monkeys nurtured by a mother or an adoptive mother. They didn't develop close bonds with other monkeys. Although a normal adult monkey would spend an average of about a quarter of its waking hours in close social interaction, an animal that had experienced maternal separation at one week of age would spend just eight to ten percent of its time in close interaction. In contrast, monkeys experiencing the same early life stress just a few weeks later, at one month of age, grow up to seek increased social interaction with other monkeys, even into adulthood. These monkeys are "clingy" and seek a lot of social attention. Extrapolating from there, think of the implications for a society, a workforce, or a community where children grow up to be less social than normal, or alternatively seeking more social interaction than normal.

Stress can stunt a child's growth—cause a "failure to thrive." Even if the stressful situation is reversed, the child's long-term growth is likely not to be as robust.

Regarding children, then, what can we glean from your work?

Two outcomes have been well documented in children who have experienced early life stresses, especially the early life stress of a broken affiliative bond—such as growing up in orphanages or foster care. Sometimes, these children have an increased desire for socialization, and become profoundly clingy. If they are in school, these children will always want the teacher's attention. Or, conversely, such children can react to early life stress by becoming somewhat dissociated and not very social. Even if adults try to interact with the child, he or she is detached from adults (and from other children), and not likely to do what adults want them to do, or to seek activities that will please adults. Detachment is much less common than increased clinginess, but it is certainly well documented in humans who have had profound early life stress.

What we are seeing in studies using infant monkeys is a confirmation of those two characteristics we see in children who have experienced the early life stress of a broken affiliative bond: detachment, with a decreased desire to socialize; or an increased desire to socialize. Both outcomes are accompanied by various anxious behaviors. Imagine the effect on a community if a sizeable portion of its members are disaffected. Those communities are likely to be unstable, and we all feel the impact.



Science has demonstrated that positive intervention can benefit children of all ages. Does your research suggest an optimum time for intervention?

Yes. We have just finished an intervention experiment where we introduced adoptive mothers to infant monkeys that had been separated from their birth mothers when the infants were a week old. Then, when the young monkeys were different ages (between 1 month of age and 2.5 months of age), we introduced an adoptive parent to the infant to assess what difference that would make in the infant's behavior. We found that if you introduce the adoptive mother after the infant has been separated about three weeks, the new mother quickly forms a bond that reverses much of the anxious or detached behavior we see in separated animals. The young now develop the ability or desire to seek normal social contact.

The goal is to use our growing knowledge to strengthen the foundation on which healthy brains are built.

We also found if you wait until the young monkey is two months of age to introduce an adoptive mother, the adoptive mother will not be able to reverse the damage. Although children's brains continue to develop throughout childhood, and children can benefit from positive interaction through their teen years, our findings underscore the importance of thinking carefully about what happens to young children taken by society from parents for whatever reason—because of parental drug abuse, incarceration, maltreatment, or what have you. If these children could be moved into a more permanent, more nurturing situation right away, they would certainly benefit. The quality and timing of that placement is going to matter a great deal in how lasting are the effects of this stress.

But when we talk about the impact of stress, we have to be very clear about our terms, and how they apply in each situation. We have to remember there are different forms of stress, and very importantly there are individual differences in response to stress. Some severely stressful experiences certainly can lead to undesirable long-term outcomes, especially when there are no supportive relationships to help a child cope. The Council has termed such experiences "toxic stress". Scientists suspect that different neural systems have an increased sensitivity to stress at different times during early development. A stressful experience early in life that is severe enough to be described as "toxic" can affect a child's long-term social behavior in different yet predictable ways. As we learn more about brain architecture and we are better able to recognize which experiences weaken the evolving structure and make individuals more susceptible to the long-term effects of early life stress, we will be able to more adequately counteract those influences through better human interactions, including therapy, applied at the right time. In the final analysis, the goal is to use our growing knowledge to strengthen the foundation on which healthy brains are built and long-term developmental competence is achieved. ●

The interviewer: Dean Stahl is a researcher and writer, and co-author of *Abbreviations Dictionary* (CRC Press), a desktop reference and one of the most extensive English-language collections of abbreviations. Also the author of "Dolphins" (Child's World Inc., 1991), he is a longtime contributor to *Pacific Northwest* magazine. He worked for several years as an editor at *The Seattle Times*.