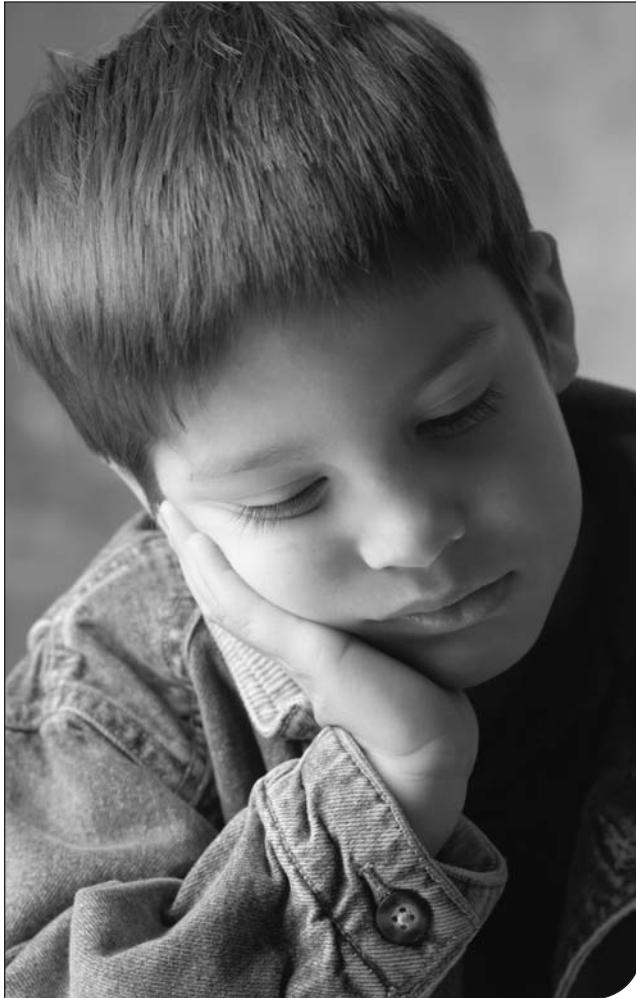


THE GENETICS BEHIND STRESS AND DEPRESSION



We already know that in vulnerable children, certain types of stress, particularly chronic stress, can trigger anxiety and depression. But what makes some children vulnerable and not others?

That question may be too large to answer with one simple study, so an international team of researchers is breaking it down to look at each component separately. The Canadian constituent of the team, led by Dr. Cathy Barr from the Toronto Western Research Institute and the Hospital for Sick Children, is focusing on genetic vulnerability.

Barr and her colleagues examined the genetic makeup of 382 nuclear families in Hungary, in which at least one member was diagnosed with a mood disorder that started before the age of 14. "This is very early onset," says Barr. "The

idea behind that was to get children who are at more risk genetically because when it onsets earlier, it's thought to be more heritable." They targeted a gene known as AVPR1b because it controls the release of a stress hormone known as vasopressin, which in turn plays a role in the regulation of the hypothalamic-pituitary-adrenal (HPA) axis, a hormonal system, that performs a key function in the stress response. Disturbances in hormonal systems involved in the HPA axis have previously been implicated in mood disorders.

Indeed, the researchers did find a link between minor variations in the AVPR1b gene and the risk for development of mood disor-

ders that begin in childhood, particularly among females. "What our study shows is that this gene—AVPR1b—is contributing to childhood-onset depression," says Dr. Barr.

While the research needs to be repeated in other populations to confirm that these findings are not unique to Hungarians, it does have some intriguing implications. First of all, says Dr. Barr, it contributes to the evidence linking stress with mood disorders in children, thus highlighting the need to teach children, from an early age, how to cope with stress. "It puts emphasis again on reducing stress and understanding how stress creates risk in children," says Barr. "We already know that the response to stress is important in regulating mood and the risk for depression. It emphasizes that we need to help children modulate their stress response and learn coping behaviour."

The findings also suggest that the AVPR1b gene may be a good starting point when selecting targets for new antidepressant medications—ones that, unlike many of those on the market today, are safe and effective in children.

Dr. Stan Kutcher, an expert in adolescent mental health from Dalhousie University, who was not involved in this research, says that this study "takes us a step further to understanding the complexities between the influence of environment and the expression of psychiatric disorders. It has identified a potential mechanism for helping us understand how the stress response might lead to depression in some people but not all." What remains uncertain, he says, is whether this mechanism functions outside a stress response. That is, will children with variations in the AVPR1b gene that make them vulnerable develop mood disorders even if they are not faced with significant stress? No one knows yet.

Dr. Barr's team is continuing to study families in Hungary affected by early-onset mood disorders. They have now examined about 700 families. "What we don't know yet is why the gene is different in those with depression," says Barr. "That's the next step in their research, to understand: what's the genetic variation with this gene that causes it to be dysregulated in people with depression?" 🐼

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Ref: Dempster EL, Burcescu I, Wigg K, Kiss E, Baji I, Gadoros J, Tamas Z, Kennedy JL, Vetro A, Kovacs M, Barr CL, International Consortium for Childhood-Onset Mood Disorders. Evidence of an association between the vasopressin V1b receptor gene (AVPR1b) and childhood-onset mood disorders. *Archives of General Psychiatry* 2007;64(10):1189-1195.