

[Home](#) > [Research](#) > [News & Stories](#) > [Stroke of Despair](#)

[Research Home](#)

[News & Stories Home](#)

[Research Stories Archives](#)

[Press Release Archives](#)

A Stroke of Despair

By Laura Pratt
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When a person has had a stroke, it is reasonable to assume that her mental state would suffer. But Dr. Krista Lanctôt, a neuroscientist and head of the neuropharmacology research program at Sunnybrook Research Institute, was amazed to learn, in some instances, just how much.

While the annual incidence of stroke is 50,000 per year in Canada, a decline in mortality has led to more stroke survivors. And post-stroke depression (PSD) is revealing itself to be a serious problem, with more than 27% of survivors falling victim to it (that compares to an average of 3% to 9% of the population aged over 65 years who might otherwise be expected to be depressed). The prognosis for these people is not good. PSD is associated with a decline in the ability to perform everyday tasks easily and higher rates of death. What's more, current pharmacotherapy options leave 40% of these depressed patients unresponsive—and their doctors scratching their heads as to the reason why.



Dr. Krista Lanctôt investigates depression among recovering stroke victims. - Photo by Doug Nicholson

"We've never understood why some of these people never recover and then get dementia later," says Lanctôt, who has focused her research on the neuropsychiatric symptoms of mental illness in post-stroke patients. "There's no reason why these people, who are improving physically, shouldn't mentally be OK. And yet they fall into this depression that resists all treatment attempts."

Lanctôt was intrigued by a curious commonality among those who develop depression only in association with a mental illness—the underlying illness was always associated with inflammation. She realized that inflammation would elevate levels of cytokines in their bloodstreams and deplete serotonin. Serotonin is a brain chemical that helps to control a person's mood. And it works in delicate balance with other brain chemicals to keep a person's mental health on an even keel.

What's more, the presence of these higher-than-normal levels of cytokines produces a neurotoxic metabolite that, say the scientists, may be responsible for these patients' lack of response to antidepressants. "They don't respond to treatment as well as they might, because they have the dual problem of loss of serotonin, and production of brain toxic substances," says Lanctôt.

Lanctôt and her team, which comprises an elite multidisciplinary crew of some of the finest experts in this field, is anxious to confirm the connection between the abundance of cytokines, its resulting depression and cognitive loss, and the part this mix has to play in a person's resistance to treatment.

Armed with a two-year grant from the Heart and Stroke Foundation, Lanctôt has undertaken to test her hypothesis on 100 people: 50 with depression and 50 without. To her mind, a combination of antidepressants and a drug that blocks the neurotoxic metabolite that is the

byproduct of the serotonin/cytokine interaction, might spell blessed relief for these suffering souls.

"I am excited," says Lanctôt. "Can you imagine being able to identify this early on and stop it?"

Laura Pratt is a writer with Sunnybrook Research Institute.