

The state of mental illness

Inflammation and disturbances in body metabolism may cause depression

BY LYNN KEANE

On a random Tuesday in April of 2009 my son, Daniel, took his life. Suddenly, I was thrown into my own grief-driven depression. For the first time in my life I came close to experiencing the misery and nothingness of depression. The horrifying world that my son had inhabited was now in view.

Suicide never leaves behind a simple narrative. Depression and diseases of the brain arise from a complexity of factors, which are often misunderstood. The common thread in suicide however, is an overarching sense of hopelessness and an inability to see past the present moment. In his memoir, *Darkness Visible*, William Styron, writes:

Depression is a disorder of mood; so mysteriously painful and elusive in the way it becomes known to the self. To the mediating intellect, as to verge close to being beyond description. As the shock began to lift and I gradually came to the realization that my son was not coming home, I began my search for answers as to why my 23 year old son would take his life.

Every day it seemed as though I was peeling back another layer of Daniel's other world. I learned that he had felt alone and isolated in his first year away at university and that he had skipped classes and began drinking. He had become reckless and prone to injury. He may have imagined that he'd become a burden to his family. Impulsively turning his anger inward and unburdening himself of the despair.

Thomas Joiner, author of *Why People Die by Suicide*, and a suicide survivor states:

Various kinds of recklessness may predispose



people to suicide precisely because it leaves them open to injury and danger. Repeated injurious experiences, he suggests, "in turn, makes people fearless about a lot of things, including self-injury."

My son was involved in a variety of sports including hockey, basketball and football. He was also an avid long boarder. After his death I found out that he boarded onto street ramps, often getting perilously close to oncoming traffic. On one of those occasions he returned home to his apartment bloodied and bruised from falling hard on the pavement. He adapted to physical injury, just as he'd done with his asthma and life-threatening food allergies as a child. His melancholy was another problem that he alone would sort out.

In the spring of 2010 my search led me to the University Health Network and Dr. Roger S. McIntyre, Professor of Psychiatry and Pharmacology at the University of Toronto and Head of the Mood Disorders Psychopharmacology Unit at the University Health Network. Dr. McIntyre's research in inflammation and its connection to mood disorders

are in part responsible for reshaping the model of treatment for sufferers of depression.

Dr. McIntyre directed me toward academic research being conducted at his centre as well as research at other centers of excellence in neuroscience and mood disorders. These resources served as a foundation for my education into major depression and also assisted me in understanding why my son's life went so terribly wrong.

Recently, I asked Dr. McIntyre to offer his views on the state of mental illness.

Q: As we look to the future are you hopeful that we will one day look at depression and disorders of the brain through 'a broader lens,' as you have noted in the past? And how will that impact those affected?

RM: We are learning that inflammation or disturbances in body metabolism may not just be a consequence of depression but also cause depression. If this is true, which we think it is, there's the potential to fundamentally change the way we treat these disorders. In other words, some people may have depression primarily because of abnormalities in brain chemistry while others may be depressed because their body and brain is in a state of inflammation and/or their brain is unable to use energy appropriately (we refer to that as bioenergetics). If this is true, there may be a future role for using medications that correct abnormal inflammatory processes and bioenergetics (i.e., drugs that are typically used to treat diabetes). We are taking a drug or category of drugs that was originally intended for condition X that we're now considering for condition Y. There are over 27,000 pharmaceutical agents around the world. This library of medicines provides a wonderful opportunity to be considering repurposing medications across different medical and psychiatric conditions.

Q: With regards to depression can you explain 'integrated vulnerability'? And how can we better

understand the complex factors involved in major depression?

RM: Today it is still the case that many people believe you need a reason to be depressed. This is false. This is no more true than you need a reason to have arthritis, diabetes, and heart disease. Now, there's no question that we have identified features that put you at risk of, for example, diabetes and heart disease, e.g. smoking, poor diet. However, the reality is that half of people that die of heart disease, don't have any of the foregoing risk factors for heart disease. Bringing this back to psychiatry, many people have had many stressful things happen to them and don't become depressed, while others do. What this tells us is that our vulnerability to medical and psychiatric illness is the result of a complex interaction between our environment and our genetic predisposition. In many cases, our genetic predisposition is so robust, we will become depressed no matter what we do.

Q: Is the presence of a physical health condition a risk factor for suicidal behaviour, even in the absence of a mental disorder?

RM: Yes. We believe that the conspirators that link diabetes and obesity to depression are, again, related to inflammation and bioenergetics. In other words, diabetes and obesity results in "your brain being on fire" and as well, it is unable to use energy normally. It needs to be highlighted that one does not need diabetes and obesity in order for inflammation and bioenergetics to be abnormal in the brain.

Q: As survivors of suicide we are heartbroken and frustrated at not knowing 'why' our family member completed suicide. By focusing research on the (biological, epigenetic and chronic health conditions, as example) will earlier diagnosis and treatment follow?

understanding

RM: I absolutely believe this is critical. The reality is that most individuals who commit suicide have a mental illness. What we've also learned is that in most cases the mental illness has not either been identified and/or correctly diagnosed, and/or has not been sufficiently treated. There are several lines of scientific evidence that indicate very clearly that when mental illness is diagnosed and appropriately treated the rates of self-harm and completed suicide decrease. What is, however, particularly tragic is that some people, even when they receive the best of care, still die of suicide, reminding us that suicide is a behaviour that never has a single and simple explanation.

Q: Dr. McIntyre, you have spoken before about the 'future vistas' in terms of understanding mental illness. Can you elaborate?

RM: The major future vista as we see it right now is to further refine our knowledge. We also can envisage a time where instead of treating mood (and other mental) disorders, we're going to prevent mood disorders. I would also see the future as including objective tests to assist us in making the correct diagnosis, differentiating the different psychiatric conditions, prognosticating the person's future illness trajectory and as well, guiding clinicians as to what treatments to use and not to use. The future for psychiatry is exciting and will be rich with new opportunity. Notwithstanding, let's not lose sight of the fact that the majority of people with mental illness are not receiving the existing treatments appropriately. Just like other chronic illnesses, e.g. heart disease and diabetes, we need to take an integrated approach when the best outcomes are achieved when we combine education with appropriate medicines, appropriate community supports, counselling and therapy where needed, and longitudinal care delivered in a timely, coordinated, comprehensive, and coherent way.

Q: Are you seeing a move away from the stigma and shame that is associated with these illnesses?

RM: I absolutely do. Other areas of medicine that have benefitted from a reduction in stigma include, but are not limited to, cancer and HIV. It is noteworthy that many public figures have announced that they are suffering from mental illness and are receiving treatment. In light of the fact that one in four people suffer from mental illness at some time in their life, everybody knows somebody that has been affected by one of these conditions.

Q: What are the current treatment modalities for severely depressed, suicidal individuals?

RM: The treatment of people with depression and thoughts of suicide is generally no different than treating someone who is not expressing suicidal ideation, as suicidal ideation is part of the illness. It would be expected of course that in people who are actively planning suicide and are determined to be at very high risk, treatments would be different insofar as there would be an urgent need for acute care, psychosocial supports, and in many cases hospitalization, which is more commonly involuntary.

Q: Do you see the role of the big pharmaceutical companies changing to better address the needs of patients?

RM: During the next five-10 years, pharmaceutical companies may play less of a role in helping deal with the needs of our patients. In fact, there has been a retreat of sorts by many companies away from psychiatry and they have divested their activity into other medical disorders. There are several reasons for this. First, the cost of drug discovery is extraordinary in psychiatry and the likelihood of finding a successful treatment is very low. This makes it unattractive to companies to have a return on their

investment. Secondly, the regulatory and reimbursement environment has changed, wherein it is increasingly difficult for companies to have their products either receive timely evaluation and/or coverage. The trend towards increasing generic medication is highly concerning from the point of view that generic companies do not invest any resources into the research and development of novel treatments for mental illness, nor do they contribute to the education of stakeholders on these conditions. Indeed, we welcome cheaper medications offered by generic companies, but we also need to find a social contract with pharmaceutical companies that rewards innovation and investment in research, and at the same time, allows medications to be available to those who need them in a cost effective fashion. Historically, psychiatry has been underfunded by government research agencies; this needs to change if in fact the burden of mental illness is going to be reduced in the general population. On a related, but separate note, given the fact that mental illness is the number one reason individuals are unable to fulfill their role in the workforce and as a result are receiving disability benefits, I would like to see the corporate world partner with academia, advocacy, and other stakeholders to reduce the scourge of mental illness on the workforce.

Q: Can you explain a combined approach to treatment? How important is it in the long-term mental health of the patient?

RM: Just like treating any chronic disease, e.g. heart disease, diabetes, individuals require biological treatments, physical treatments, and psychological treatments. This is the approach every line of evidence tells us integrated management is really the best way to bring about the best outcome. In other words, treating mental illness is not about taking a pill. We have to bring all of our resources together

and synergize the various treatment modalities.

Q: Can you explain biosignature of these conditions?

RM: What we do in psychiatry is we give people a diagnosis based on what we observe. This is no different than visiting a dermatologist and having he or she make a diagnosis based on the colour of your rash. This clearly has to change. A biosignature refers to a combination of biological features that tell us about the underlying disease and what stage it's at. It can highly inform not only disease prognostication but also treatment selection. One of the best examples you may have heard of, is the identification of the HER protein. Women who have been diagnosed with breast cancer may have their tumour profiled to determine whether it has the HER protein. If it does, that will determine the type of treatment she might receive. That is just one small example, but what we need to do is get into the biology of these conditions to find out what that profile actually is. Currently in psychiatry, we don't have any mechanism to inform what the right treatment is for an individual. As a result, we rely on trial and error, which is not satisfactory to anybody.

Q: You have talked about the 'invisible impairment' for the sufferer. With so many dimensions to depression how do we as family members and the larger community support those suffering?

RM: The key issue is advocacy and being in the public domain. This was the same issue cancer and HIV suffered from 20 years ago and now it seems as though every week I'm hearing about new exciting programs raising resources for these conditions. A good lesson for us all.

Q: A study led by researchers at the University of Montreal states "that a blow or bruising to the frontal

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lobes could cause severe damage, even trauma if it affected the cognitive part of the brain responsible for decision-making and organizational responses." Can you help us to understand this important area of the brain that is also responsible for controlling moods and behaviour?

RM: The brain should be conceptualized in some ways like a map. There are main interstates, there are state highways, and there are municipal roadways. These roadways overlap, yet are each originating and ending up in different places. Some are taking on higher volume of traffic than others, and although they have overlapping purposes they may be very different. We know that some regions of the brain are responsible for learning and memory, others for emotion, and others for what we call social cognition (that is learning social cues and responding to them appropriately), etc. As expected these areas all communicate to each other.

Q: Many post mortem studies connect brain injury and suicide, particularly in young males. Can you elaborate on how the brain function changes with injury? And what impact this altered functioning has on a person?

RM: The link between brain injury and suicide is highly complicated and poorly understood. One leading hypothesis is that the brain injury could affect the person's ability to inhibit impulses and as a result, someone may unfortunately follow through on acts of self-harm.

Q: What can you say to underscore the need for further awareness and education in relation to depression; disorders of the brain?

RM: I think we need to communicate that suicide is a very complicated, devastating and complex behaviour. You can only identify someone who is at

high risk. The most robust intervention we can offer is the prevention and treatment of depression, and other mental illnesses.

Keep in mind that most suicide completion is impulsive, and is impossible to predict. Many studies have shown this, which reminds us of how important it is to do whatever we can to reduce risk. Reducing the risk means doing the best we can to prevent and treat depression, when it occurs. Even if we do that, 100 per cent perfectly, we still cannot guarantee we will be successful in preventing suicide. It's important also that asking people about whether they're suicidal doesn't "put the thought in their head." That's never happened. In fact, every line of evidence tells us that patients are relieved when they're asked about this issue. So it's not something we should be fearful of. It is also important to be aware of the fact that there is no single cause to suicide. Although it is tempting to simplify human behaviour, no person has ever taken their life because of a single reason. Moreover, there rarely is a single intervention that can remedy someone's wish to kill themselves. We need to understand suicide as a complicated behaviour that is often preventable, but not always.

The most exciting message is that we have reasons to believe that we are improving our understanding of how the brain operates, which will position us to really better understand how to treat and prevent mental illness. It's also important to highlight that we are also in a position now to develop very new models of thinking about what's causing, and what's consequential to these illnesses. As you can see, the future is extremely bright. ■

Lynn Keane is a suicide prevention advocate and writer. Her memoir, Give Sorrow Words, will be published in 2014. Watch for it in the Bookshelf section of Moods magazine.