Beating the Blues

Canadian Biomarker Integration Network in Depression (CAN-BIND)

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CAN-BIND is one of the world's leading depression research networks. The lead researcher of this network, Dr. Sidney H Kennedy, discusses his team's latest project, CAN-BIND, a program that aims to revolutionize the way doctors view depression.

To start out: why depression research? How did you become interested in your area of study?

Depression affects more than 350 million people around the world and yet research to explore the basis of depression and provide adequate treatment services has been dramatically underfunded.

I've always been interested in the relationship between our environment and our genetic makeup and depression is a prime example of genetic risk interacting with multiple adverse life events. In fact, the first research study I ever published showed that people with Bipolar Disorder, at that time, considered to be highly genetically determined, experienced a marked increase in life events before episodes of mania. In many ways, our current research investigates these relationships using more sophisticated tools and approaches.

Depression is a growing issue in many developed countries. As an expert in the field, do you have any insight into why that may be?

Depression is not just a concern for developed countries. In 2010, authors of the Global Burden of Disease Study concluded that depression is the second leading cause of disability worldwide, with growing awareness that presenteeism accounts for even more of the economic burden of depression than absenteeism. Although some would argue that depression is a "disease of modernity or affluence" due to a larger prevalence in high income countries, it remains one of the top 5 leading causes of Disability-Adjusted Life Years (DALYs) in all regions of the world, regardless of GDP per capita, with the exception of Africa where the burden from communicable, maternal, perinatal and nutritional conditions is greater.

At the societal level, some would say the widening gap in income distribution, the breakdown of social cohesion, increasing isolation in many urban centres and the growing competition to secure employment have led to increased rates of depression.

You argue that current depression treatments are inadequate. Could you elaborate on the problems with the way depression is treated today?

Diagnosing a Major Depressive Episode (MDE) is a different process from identifying most medical disorders. For example, a physician is able to detect arthritis by checking for swollen joints, reviewing X-rays and blood levels for the presence of antibodies 'rheumatoid factors' in the case of Rheumatoid Arthritis. In contrast, there are no laboratory tests or brain imaging scans that can confirm a subtype of 'clinical depression': we are still reliant on clinical interview and self-report measures to confirm a diagnosis of depression.

Many genetic, biological and environmental risk factors interact to produce the symptoms of depression. Each person experiencing depression has a unique genetic background, personality and neurobiological makeup as well as distinct early childhood experiences, life events and social support systems. These variables not only trigger the onset of depression, but contribute to the on-going risk for relapse and recurrence. Current treatments which include antidepressant medications, psychotherapies and neurostimulation, work for some individuals but not others. The challenge is to predict treatment outcomes and tailor it according to what works best for the individual.

CAN-BIND will be a major step forward in personalized healthcare. What is the benefit of CAN-BIND? What impact do you expect it to have?

The CAN-BIND research program uses a standardized platform of clinical and biological measures which include measures of brain structure (MRI) and function (fMRI and EEG), genetic and clinical information for each individual. Many previous research studies have focused on one or two of these measures, but since depression may result from an interaction among many factors, the comprehensive and integrated CAN-BIND approach should provide unique patient data. Our core hypothesis is that there are numerous underlying pathways (subtypes) to the final presentation of depression.

We have an unprecedented level of sustained funding over 5 years from the Ontario government, through the Ontario Brain Institute (www.braininstitute.ca). With this funding support, we are able to maintain a high level of scientific rigor and quality control across sites, and carry out critical follow-up studies to validate the findings from initial studies. We have designed several sequential projects that will use the same platform to identify biomarkers using different treatments (pharmacotherapy, psychotherapy, brain stimulation devices), different populations (adult MDD, youth at-risk, geriatric) and different types of mood disorders (unipolar and bipolar).

A Bold New Approach to Treating Depression

Depression is a growing problem throughout the world, and addressing it is one of modern medicine's biggest challenges. Dr. Sidney H Kennedy and his team are taking treatment in a bold new direction.

Depression affects more than 350 million people worldwide, in both developed and developing countries. It's correlated with a host of health problems, ranging from weight gain to cancer. It's also associated with rapidly increasing medical costs in the UK, US, Canada, and a number of other countries.

Why are people so unhappy? Scientists and sociologists have cited numerous and varied reasons for rising depression rates. More aggressive job competition, economic hardship, genetic predisposition, technology-driven social isolation, increased environmental toxins—all of these factors have been implicated in depression. Times are tough. But with increasing awareness of depression and decreasing stigma surrounding it, more and more people are identifying with the symptoms of depression and are looking for help.

Why is depression treatment so ineffective? Dr. Sidney H Kennedy, one of the foremost experts in the field, has an answer.

Even after decades of research, the challenge of finding successful treatment for depression remains the biggest barrier in helping patients. Scientists still aren't sure how different factors interact to cause it. In addition, they are not able to pinpoint the possible biological subtypes and optimal treatments based on those subtypes. What is known about the disorder is its complexity, far more than what has been previously imagined. A range of techniques have been used to address it, including talk therapy, antidepressant medication, and electrical stimulation, among others. But the results across all of these treatments have shown that the success of each type of treatment can vary across the different groups of patients.

Depression is more common than ever, but finding the right treatment for a particular individual can be very challenging. Happiness, it seems, is in short supply these days.

THE COMPLEXITY OF DEPRESSION

Dr. Sidney H Kennedy, one of the foremost experts in the field, has found an answer to the biggest question: Why is depression treatment so challenging? "Diagnosing a Major Depressive Episode (MDE) is a different process from identifying most medical disorders", he says. "For example, a physician is able to detect arthritis by checking for swollen joints, reviewing X-rays. In contrast, there are no laboratory tests or brain imaging scans that can confirm a subtype of 'clinical depression'. We are still reliant on clinical interview and self-report measures to confirm a diagnosis of depression".

And therein, Kennedy argues, lies the big problem. Depression presents itself in many different ways. Some cases are severe, others less so. Depressive bouts may last only weeks or they may last years. Even the symptoms themselves change from person to person, and these variations require different methods of treatment. With such a complicated and varied disorder, analysis of an individual's depression requires much more sensitivity than a clinical interview provides.

"Each person experiencing depression has a unique genetic background, personality, and neurobiological makeup. Add to that the complexity of an individual's distinct early childhood experiences, life events, and social support systems", Kennedy explains. Each depressed person experiences the disorder differently, due to different underlying causes. Because this is the case, no cure-all exists. A single treatment will not work for everyone. What the healthcare community needs is a more individualized approach to combatting depression – one that considers each person's case using a comprehensive set of tests.

CAN-BIND: LOOKING AT THE BIGGER PICTURE

Kennedy and his colleagues have developed such an approach to treatment. After years of planning and research, they have created the Canadian Biomarker Integration Network in Depression (CAN-BIND), a research program that views the treatment of depression in a bold new way. The CAN-BIND program works two ways. First, it will systematically evaluate outcomes using different types of treatments (medication, neurostimulation, psychotherapy). Second, CAN-BIND will collect data on three standardized platforms: 1) symptoms (i.e. hopelessness, sadness, weight gain, etc.), and other factors unique to the individual, such as environmental stress, quality of life, personality, childhood trauma, lifestyle factors, 2) structual and functional neuroimaging and EEG and 3) a comprehensive proteomic and genomic analysis of blood samples.

By analysing so many variables, Kennedy and his colleagues aim to find biomarkers – biological measures like specific proteins, genes, or brain abnormalities – that influence outcome in depression. In addition, Dr. Kennedy and his colleagues have developed complex

mathematical models that can analyse these biomarkers to look for patterns in large populations of depressed individuals. The large-scale approach aims to use CAN-BIND to help researchers in identifying common subgroups of depression. By identifying people who have certain biomarkers, or combinations of biomarkers, Kennedy and his team aim to find what kind of treatment plans typically work for individuals dependent on the depression sub-group they are associated with. On top of specific treatments, the researchers are also looking at different demographics—men and women, young and old—for a more encompassing method.

CAN-BIND's big picture approach doesn't stop there. Its size and scope alone could cause the project's progression to take years before completion. But Kennedy and his colleagues have developed a solution for that issue as well. More than 10 different major Canadian academic centres are working together to make the venture a reality. Each institution is implementing CAN-BIND and sharing its results with all the others.

This collaborative approach is far from the norm. Researchers are infamous for guarding their results and protecting novel findings until they are ready to publish their work. This competitive approach limits sharing of expertise and productivity. CAN-BIND has avoided this problem with the generous financial support of players in both industry and government. The Ontario government has provided an unprecedented five-year funding commitment to this program through the Ontario Brain Institute. Together with significant contributions from Lundbeck, institutions like Pfizer, Bristol-Myers Squibb, and Servier have all come together to support the project.

A project of this scope is a benchmark for the scientific world. In a field that all too often sacrifices progress due to competition with colleagues or lack of funding, CAN-BIND shows that science and business can come together, forming a united push to end one of the most pressing medical concerns of the 21st century.

A HAPPIER FUTURE

According to Kennedy, the preliminary results of the first CAN-BIND projects will be published by the end of 2015. Hopefully with it will also come a flood of new information to further understand depression. The program doesn't end with research, though. CAN-BIND is also developing a worldwide network of healthcare providers that will help spread results, allowing them to be incorporated into treatment practices around the world quickly and effectively.

There's a final benefit. By elucidating the biomarkers of depression, CAN-BIND aims to change the way the world looks at this powerful disorder. Too often, depression is trivialised and stigmatised. Because there are no biological tests for it – unlike for, say, heart disease – depression is frequently seen as mental weakness, or something that can and should be overcome. Kennedy hopes to change that.

"Viewing depression in the same light as other medical conditions", he says, "will help de-stigmatise mental illness and improve treatments through a targeted and personalised medical approach". With decreased stigma and better treatment, CAN-BIND aspires to provide something that sufferers of depression desperately need: hope. By spreading awareness, identifying causes, and personalising treatment, the CAN-BIND project is taking a brave step toward making the world a brighter place.

Researcher Profile

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Dr. Sidney H Kennedy is Professor of Psychiatry at the University of Toronto and a Scientist at Li Ka Shing Knowledge Institute and Toronto Western Research Institute, Toronto, Canada. Dr. Kennedy is the lead investigator for a large depression biomarker initiative. He has published extensively on new drug evaluation, neuroimaging and neurostimulation therapies, personality factors in depression, antidepressant effects on sexual function and treatment guidelines for Major Depressive Disorder and Bipolar Disorder. Dr. Kennedy is the Immediate Past President of the International Society for Affective Disorders, a former President of the Canadian College of Neuropsychopharmacology and the founding chair of the Canadian Network for Mood and Anxiety Treatments (CANMAT). He has published more than 350 peer reviewed publications and 11 books on depression and related topics.

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