



Clinical RESEARCH DEPARTMENT

DR. SIDNEY KENNEDY, DIRECTOR

- 36 Addictions
- 37 Mood and Anxiety
- 38 Personality and Psychopathology
- 40 Psychobiology of Aggression and Antisocial Behaviour across the Lifespan
- 42 Schizophrenia

THE CLINICAL RESEARCH DEPARTMENT (CRD) CONTINUES to support research, treatment and education goals of CAMH through scientific publications, presentations and transfer of knowledge to evidence-based practice and to the community at large. Dr. Larry Grupp is the Clinical Research Liaison Officer, whose mandate is to identify, promote and facilitate research opportunities and collaborations between CAMH staff at all sites and between CAMH and external partners at University Hospitals and other clinical and research institutions.

During 2001/2002, the CRD has initiated and supported a variety of intra- and interdepartmental program initiatives. *Mind Mood and Mental Health*, a publication of the Mood and Anxiety program, focused on diversity and community partners in research. This publication was widely distributed in the greater Toronto area, with over 10,000 copies placed in Shoppers Drug Mart and Guardian Drugs stores, hospital waiting rooms and doctors' offices. *Clinical Guidelines for the Treatment of Depressive Disorders* were published as a collaborative CANMAT/CPA supplement on June 2001.

Through the Family Practice Mood and Anxiety Research Network, we held a conference called Psychiatric Aspects of Sexual Health in Men and Women. This led to several clinical research projects involving testosterone in depressed and non-depressed men and estrogen replacement strategies in post-menopausal depressed women.

The CRD also supported a successful conference on Psychopathy for the Psychobiology of Aggression and Antisocial Behaviour across the Lifespan Section. In addition, a joint Intrapersonal Psychotherapy Program-CRD initiative brought Dr. James McCullough for an extended visit to discuss the Cognitive Behavioral Analysis System of Psychotherapy at CAMH and Mount Sinai Hospital.

Two of the five sections (Addictions and Mood and Anxiety Disorders) underwent external reviews during the summer of 2001. A combined review of both the clinical and research aspect of the Mood and Anxiety Program was completed.

A joint effort of the Addictions and Personality sections of the CRD was successful in obtaining a grant from the Ontario Problem Gaming Foundation to study personality variables in people who gamble. The principal investigators for this grant are Drs. Peter Farvolden and Michael Bagby (Personality and Psychopathology Research Section) and Dr. Tony Toneatto (Addictions Section).

Dr. Saulo Castel obtained a CIHR Fellowship to develop measures of psychopathology in people who have concurrent substance use problems and mental illness.

Dr. Sidney Kennedy resigned from his position as Director of Clinical Research on January 31, 2002, to take up his new position as Psychiatrist in Chief at the University Health Network, University of Toronto. Dr. R. Michael Bagby, who is a Senior Psychologist and Section Head of the Personality and Psychopathology Section, assumed the role as Acting Director of the CRD.





DR. TONY TONEATTO, HEAD

Addictions

CLINICAL RESEARCH DEPARTMENT

The Addictions Section conducts clinical research, both experimental and applied, in all aspects of addiction. In the past year, the section has undergone a formal internal and external review, the results of which will serve to strengthen and guide the development of our work.

Gambling Research

The Gambling Research stream, headed by Dr. Tony Toneatto, is committed to developing empirically supported psychotherapies for problem gambling, exploring the role of pharmacotherapies for problem gambling, and contributing to the knowledge of the cognitive and behavioural phenomenology of gambling. This area of research continues to attract considerable research grant funding and to establish collaborations with several scientists within CAMH and throughout Canada.

Psychopharmacology Research

The Psychopharmacology Research stream (Drs. Bruna Brands, David Marsh, Peter Selby and Beth Sproule) is committed to expanding the range of pharmacological tools to treat substance use disorders. This goal is accomplished by evaluating novel medications, integrating existing medications into treatment settings and approaches, and applying statistical methods to predict treatment outcome. Dr. Sproule is the newest scientist in our section, joining us in January, 2002. Dr. Selby was successful in obtaining funding from Health Canada for a program directed at educating pregnant woman who smoke.

Treatment Outcome Research

The Treatment Outcome Research stream consists of three clinics headed by psychologists; the goal of this group is to address comorbid addiction populations requiring specialized care.

The Anger and Addiction Clinic, headed by Dr. Lorne Korman, provides novel, empirically-supported treatments for clients with concurrent anger, aggression and substance use problems. The Dialectical Behaviour Therapy Clinic (Dr. Shelley McMain) is committed to the specialized treatment of borderline personality disorder (with or without a concurrent addiction) using the principle of dialectical behaviour therapy. The Eating Disorders and Addictions Clinic (Dr. Christine Courbasson) is developing new clinical approaches to treat concurrent eating disorders and substance use disorders. All three clinics also provide consultation and training to other mental health care professionals throughout Canada and beyond.

In addition, a new psychologist, Dr. Rebecca Dempster, has recently been recruited. Dr. McMain received a commitment of funding from the CAMH Foundation for a study treating suicidal behaviour in people who have borderline personality disorder. Recently, Drs. McMain and Korman have completed evaluating the effectiveness of dialectical behaviour therapy for people diagnosed with concurrent borderline personality and substance use disorders. This small sample pilot study has demonstrated significant benefits of DBT compared to treatment as usual for this patient sample. Drs. McMain and Korman have been presenting the results of this research at conferences and workshops throughout Canada and internationally.

Clinical Services Research

The Clinical Services Research stream (Dr. Tony Toneatto) was formed after recommendations from an external review of the existing clinical follow-up services at the Russell Street site. Clinical Services Research conducts rigorous evaluation research, both controlled and naturalistic, of individual addiction treatment programs. The goal is to improve both the content and delivery of clinical treatment and to experimentally evaluate treatment innovations. We are set to begin an evaluation of the Guided Self-Change program, one of the major clinical programs for addictions at CAMH. We hope to evaluate the treatment components to identify predictors of positive outcome and means of improving this treatment. We are collaborating with several other programs to conduct similar evaluations.





Mood and Anxiety
CLINICAL RESEARCH DEPARTMENT

DR. SIDNEY KENNEDY, HEAD

Members of the Mood and Anxiety Program conduct research activities in seven areas across four Clinical Units.

Genetics

In collaboration with Dr. James Kennedy, several investigators have received funding to investigate, and have published on, genetic aspects of depression, OCD and bipolar disorder.

Epidemiology & Health Systems

In collaboration with the Health Systems Research Unit at CAMH, Dr. Sagar Parikh has focused on health care utilization across Ontario. Dr. William Gnam continues his research on the economics of mental health issues with special emphasis on the impact of psychiatric disorders on the workplace and the labour market. Dr. Robert Cooke continues to investigate “Quality of Life” issues across the bipolar and other clinical populations.

Functional Imaging

Several investigators hold CIHR funding for PET studies. Dr. Jeff Meyer has continued to use PET to study the relationship between psychiatric symptoms in depression and abnormalities in serotonin and dopamine receptors. Recently, using a novel serotonin transporter ligand developed by Dr. Alan Wilson at the PET Centre, Dr. Meyer and collaborators have completed studies involving antidepressant effects on the serotonin transporter. Drs. Helen Mayberg, Zindel Segal and Sidney Kennedy are investigating changes in brain metabolism following successful antidepressant medication and cognitive therapy. Drs. Mayberg and Michael Bagby continue to investigate the influence of personality dimensions on brain metabolism.

Psychopharmacology

During the past year a number of investigator-initiated and industry-initiated trials involving Anxiety Disorder, Bipolar Disorder and Major Depressive Disorder have been completed.

Psychological Mechanisms & Treatments

A series of CIHR-funded studies are continuing. Dr. Segal has received funding to evaluate the role of mood-linked cognitive changes in predicting prospective relapse/recurrence following either cognitive therapy or pharmacotherapy for depression. Dr. Segal is also collaborating with colleagues in the UK in an NIMH-funded randomized trial to evaluate a prophylactic intervention designed to reduce this type of mood-linked cognitive processing.

Drs. Mark Lau and Neil Rector are funded to study the roles of cognitive inhibition and rumination in mediating the patient’s ability to benefit from treatment. In addition, Drs. Rector, Peggy Richter, Michael Gemar and Eilenna Denisoff were funded to examine cognitive factors that predict successful treatment

response and relapse potential in OCD. Dr. Martin Katzman continues to draw industry support for researching novel pharmacological interventions for anxiety. Dr. Parikh continues to evaluate cognitive-behaviour therapy and psychoeducation in people with bipolar disorder.



Psychobiological Studies

Dr. Robert Levitan has received ongoing funding from a number of federal and provincial agencies to study cortisol in adult and infant populations. Dr. Roger McIntyre has received funding to study underlying mechanisms of weight gain following treatment with antipsychotic and anticonvulsant agents and is focusing his research activity on the roles of leptin and reproductive hormone changes. Dr. McIntyre is also collaborating with Dr. James Kennedy to identify candidate genes that increase the risk for weight gain.

IPT

Drs. Carolina Cristi and Bagby have received funding from OMHF to investigate patient dimensions as predictors of outcome following several antidepressant treatments. The Clinic continues to develop a database for future IPT and related research.



DR. MICHAEL BAGBY, HEAD

Personality and Psychopathology CLINICAL RESEARCH DEPARTMENT

Research in the Personality and Psychopathology Research Section examines a broad range of topical and methodological themes related to personality and psychopathology. Some of the current projects focus on: identifying alternative structures of personality psychopathology; exploring personality traits as mediating and moderating variables in treatment outcome for several disorders, including depression, anxiety and problem gambling; studying personality as a vulnerability or risk factor for mental disorders; examining the influence of acute distress on personality and its assessment; and investigating the role of neurotransmitter mechanisms in personality. The section also develops tests and instruments to assess personality and related constructs and develops strategies to assess and treat mental disorders using the Internet.

Personality and Cognitive Vulnerability and Problem Gambling

Surprisingly little is known about the personality and cognitive characteristics of people with gambling problems. In an ambitious new program of research, Drs. Michael Bagby and Peter Farvolden hope to identify personality and cognitive factors that distinguish people who remain “social gamblers” from those whose gambling activities escalate into a dysfunction or problem gambling. The long-term goal is to identify “vulnerability” factors and to develop treatments to target these vulnerabilities.

Behavioural Inhibition, Behavioural Activation, Personality and Novelty

Theorists have proposed that two, or perhaps three, basic neural circuits — behavioral activation (BAS), behavioral inhibition (BIS) and flight-fight — mediate all of our different motivations and emotions.

Our researchers are working on a project to examine the relationship between BIS and BAS sensitivity and other major empirical systems of personality and preference for novelty.

Panic Disorder, Agoraphobia, Anxiety Sensitivity and Attachment

According to current explanations of panic disorder and agoraphobia (PD/AG), panic attacks are the result of a “false alarm” combined with an over-attentiveness to internal bodily sensations and/or a tendency to catastrophize. Agoraphobia is seen as a marker for a more severe form of panic disorder.

Some evidence suggests that increased vulnerability to separation distress and/or an “insecure” attachment style may also have an important role in PD/AG. A current project examines the relative importance of individual differences in anxiety sensitivity and attachment security in panic symptoms and panic disorder.



Personality, Positive Mood and Attentional Biases in Depression

Major depressive disorder (MDD) is an extremely prevalent mental health problem with vast socio-emotional and economic costs. High rates of relapse and recurrence create a continuing challenge in the treatment of MDD. This project examines the potential role of “positive” traits, such as behavioural activation sensitivity, extraversion, ability to experience positive mood and “positive” cognitive biases, in predicting response to treatment and relapse in depression.

Childhood Adversity, Adult Attachment Style and Interpersonal Functioning in Depression

This study explores a model that relates negative childhood events and adult attachment style to interpersonal functioning in people who have depression. We hypothesize that different kinds of negative childhood events (abuse versus neglect) will be associated with different adult attachment styles (avoidant versus anxious-ambivalent). In turn, these attachment styles will be associated with different styles of interpersonal functioning in depression, with potentially important implications for treatment.

Application of the Five-Factor Model of Personality to Psychopathology

Ongoing research in this area attempts to determine whether the dimensions of personality represented by the Five-Factor Model of Personality can be applied successfully to a variety of patient samples and used to better understand the relevant neurobiology, psychopharmacology and structure of personality psychopathology.

Relationship between Stability and Change in Personality

This study attempts to find a way to reliably assess personality traits in the context of acute psychiatric illness.

We are exploring the differences between absolute and relative stability of personality traits and issues related to personality stability — ipsative and factorial stability. This project looks at such stability issues in patients with depression, before and after treatment.

Neurotransmitter Mechanisms in Modulating Dimensions of Personality

In two ongoing studies, we are working to understand the relationship between dimensions of personality and specific neurotransmitters (serotonin, dopamine and norepinephrine).

Personality as a Predictor of Recurrent Major Depressive Episodes

Many people successfully treated for depression experience a recurrent episode following several months of remission. We continue a study of the role of personality psychopathology as a contributing factor to depressive illness.

Personality, Limbic-Cortical Function and Vulnerability to Major Depression and Other Imaging Studies

We continue to explore vulnerability to depression. PET scans in patients with depression display specific patterns to induced sad mood; people who have a high score on “neuroticism” are vulnerable to develop depression. Our research examines whether never-depressed “normal” subjects with high neuroticism scores show the same response as people who are depressed or were previously depressed.

Other ongoing PET studies examine specific receptor occupancy and the relation to personality traits thought to be regulated by these specific receptors.

Personality as a Mediator of Treatment Outcome

This ongoing project examines whether different types of personality traits (dependency and self-criticism) moderate and/or mediate treatment outcome differently in three standard and empirically established effective interventions for depression (interpersonal therapy, cognitive-behavioural therapy and pharmacotherapy).





DR. LESLIE ATKINSON, HEAD

Psychobiology of Aggression and Antisocial Behaviour across the Lifespan CLINICAL RESEARCH DEPARTMENT

Aggression and antisocial behaviour pose huge challenges and costs to perpetrator, victim, and society. To address this issue, the Psychobiology of Aggression Clinical Research Section incorporates researchers from the Child Psychiatry and Law and Mental Health Programs, permitting the conduct of this research across the lifespan. Section researchers address issues of etiology and risk (both genetic and environmental), intervention/management and knowledge transfer.

Etiology and Risk

Several investigators are attempting to unravel the etiology of aggressive and antisocial behaviour. Drs. Joe Beitchman and James Kennedy and colleagues are investigating select serotonin system genes and aggressive behaviour. They demonstrated that one form of one of the serotonin system genes was significantly more common in a group of aggressive children than in matched controls.

Approaching genetics from a different perspective, Drs. Karine Cote and Martin Lalumiere are studying the influence of birth order on paraphilias, delinquency, and aggressiveness, among other issues, and the relevance of evolutionary, social, and immunological theories to explain these influences. Their research is based on a sample of individuals adopted at birth.

Adopting an environmental perspective in a quantitative literature review, Dr. Leslie Atkinson and colleagues showed early mother-child attachment relations are consistently but moderately associated with aggression later in childhood. Research also showed that the association between parent-child relations and aggression may be strengthened by the mediating role of emotion regulation (Dr. Fiona Miller) and antisocial cognitions and attitudes (Dr. Atkinson).

Dr. Beitchman and colleagues continue to collect data in a 14-year longitudinal study of children with speech/language disorder. Investigators hope to find how speech/language disorder and other risk factors influence antisocial behaviour and substance use problems in late adolescence/early adulthood. Dr. Tracy Skilling is investigating predictors of life-long antisocial behaviour. Drs. Skilling and Christine Wekerle are studying the overlap between bullying and substance use.

Examining more specific forms of disorder, Dr. Sherri MacKay, Joanna Henderson and colleagues are exploring mental health and specific fire-related risk factors related to juvenile firesetting. Dr. Eva Chow is investigating impulse control disorders such as kleptomania, oniomania, pathological gambling and attention deficit-hyperactivity disorder. Dr. Chow also pursues research in female sex offenders.

Dr. Howard Barbaree is examining the effects of age at release from custody on risk for sexual recidivism in sex offenders.

Intervention/Management

Dr. Miller and colleagues received funding to study the effectiveness of parent skills training and child social skills programs in moderate- and high-risk communities. Dr. Skilling is studying the design and evaluation of treatment outcomes for chronic adolescent offenders. Dr. MacKay, Ms Henderson and colleagues are preparing a randomized clinical trial to evaluate a firesetting intervention for juveniles. Dr. Wekerle is conducting a survey of child welfare adolescents along four constructs: psychiatric diagnoses, risky sexual behaviours, dating violence, alcohol and drug use. Dr. Wekerle is also evaluating a dating violence prevention program included in high school curricula in several high schools across four Canadian provinces.

Dr. David Nussbaum has standardized an instrument to assess fitness to stand trial. Drs. Cote and Barbaree are investigating the epidemiology and psychiatric, criminogenic, and social needs of individuals who are common clients of the mental health and the criminal justice systems in Ontario. Dr. Michael Seto completed a literature review on police and court diversion efforts, treatment needs, treatment, and community risk management for forensic patients. Dr. Barbaree, Dr. Seto, and colleagues are developing a model of risk management that incorporates actuarial risk, institutional treatment, dynamic risk factors, and community supervision in the prediction and prevention of sex offender recidivism.



Knowledge Transfer

Dr. Miller and colleagues received funding to study the effectiveness of evidence-based parent and child treatment programs in moderate- and high-risk communities.

Ms Henderson and colleagues conducted a province-wide study of factors affecting the acceptance and implementation of an arson prevention program for children by mental health and other community professionals. They found that implementation of “best practice” children’s mental health interventions can be enhanced by targeting professionals with particular characteristics, by designing interventions to be perceived as easy-to-use and compatible with existing practice, and by using specific dissemination strategies, including enhanced educational opportunities and ongoing “expert” support. These findings indicate that the research-practice gap can be better understood through scientific examination and that intervention developers and researchers have an important role to play in closing the gap. Dr. MacKay, Ms Henderson and colleagues are preparing a clinician’s manual for treating juvenile firesetting.

Dr. Seto chaired a committee that produced *Practice Standards and Guidelines* for members of the Association for the Treatment of Sexual Abusers.

Dr. Wekerle edited a volume integrating literatures on child maltreatment, school bullying, teen dating violence, date rape, courtship violence, domestic violence and violence among older adults with alcohol and other drug use. The book covers state-of-the-art empirical knowledge, theoretical formulations, model clinical programs, and clinical applications.

Dr. Lalumiere submitted for publication a book on juvenile delinquency.



DR. SHITIJ KAPUR, HEAD

Schizophrenia CLINICAL RESEARCH DEPARTMENT

The Schizophrenia Research Program is dedicated to a greater understanding of the “mechanisms of response” in persons with schizophrenia. We aim to determine how and why people get better and how they can best maintain their recovery. We ask this question across the spectrum of schizophrenia — from first-episode to chronic phases of the illness, across lines of gender, ethnicity and biological types. Our research effort combines contributions from all professional disciplines with the latest neuroimaging, neuropsychological and psychosocial techniques. Understanding the mechanism of schizophrenia gives us new approaches to treatment: reduced doses of antipsychotics, better algorithms for choosing antipsychotics, better augmentation therapies for patients for whom single-treatments don’t work, better group therapies and more effective educational strategies for families and patients.

Five-Year MRI Study Concludes

We recently concluded our five-year longitudinal study of comparative MRI changes in brain structure between people with schizophrenia and normal controls. The results revealed no significant brain structure changes between the groups over the study period. From this, we concluded that functional and cognitive decline in schizophrenia is not related to progressive changes in brain processes.

VCFS as a Clue to Schizophrenia

Velo-cardio-facial syndrome is a mental illness, with a known genetic defect, that presents with schizophrenia-like picture. We continue our projects examining the genetic basis of the illness and establishing how these genetic changes express themselves in psychosis. We have recently initiated a large-scale screening study to detect the incidence of this genetic defect within the Schizophrenia Program client population at CAMH.

Early Intervention in Schizophrenia

A single episode of psychosis can have a significant impact on a person’s life. We are continuing our work to prevent psychotic episodes in people showing early signs of the illness, through low dose drug treatment and supportive therapy.

Psychosocial Interventions to Enhance Outcome

Ongoing studies examine if brief, targeted education for patients and families improves quality of life and treatment adherence and, in turn, if this influences outcome. We continue to develop intervention protocols to enhance motivation. Our ongoing study, comparing psychoeducation and activity-oriented groups, continues.

Resource Use and Satisfaction among First Episode Populations

The First Episode Psychosis Program has joined with three other Ontario first episode programs to track use of available resources over a one-year period. The project will compare user rates and client satisfaction surveys between the centres. The interpretation of the data collected in this project will enable these centres to improve services and create effective new services.

How Often Do We Need to Give Antipsychotics?

Daily medication is a common part of psychiatric illness treatment. However, our brain imaging studies have shown that the effects of antipsychotics last much longer in the brain than in the blood. We have been continuing our pilot study looking into the optimal dosing frequency of antipsychotic medications. Subjects continue to receive their medications every other day for three months, then every three days for three months. At the same time, schizophrenia researchers at the PET Centre are trying to determine the best dosing interval for the new injectable “depot” atypical antipsychotics.

Augmentation Strategies to Clozapine

While clozapine may provide substantially improved treatment of resistant symptoms of schizophrenia, some people feel there is further room for improvement in their treatment. We have begun two new studies using medication augmentation to a clozapine treatment plan. The results of these studies may uncover more effective treatment strategies using available medications.





Magnetic Stimulation to Study Brain Defects in Schizophrenia

We have used magnetic stimulation techniques to explore how the connectivity of the different brain regions may be impaired in schizophrenia. The results show that brain regions in patients with schizophrenia show impairments in inhibiting each other, especially when patients are acutely ill. Based on our findings from these studies, we are now beginning to explore if magnetic stimulation may have a role in treating symptoms of illness.