Clinical Research Department

DIRECTOR: R. Michael Bagby

The Clinical Research Department continues to support clinical research activities by producing publications, making presentations to the community and academic audiences, funding specific research proposals and providing start-up funds to "clinician-scientists" located in various clinical and research sections at CAMH.

During 2002/2003, the department funded studies by Dr. Carolina Cristi (Interpersonal Therapy Clinic, Mood and Anxiety Disorders Program), Dr. Christine Wekerle (Child Psychiatry) and Dr. Peter Farvolden (Personality and Psychopathology Research Section). Dr. Beth Sproule has received continued research "start-up" funds.

Ms Justine Joseph, a student in the Mood and Anxiety Disorders Program, also received funding, to examine race-related stressors, non-race-related stressors and the relation of these stressors to depression in Canadians of African descent.

Drs. Tony Toneatto and Bruna Brands received travel funds to attend international and national conferences on addiction. Dr. Brands has also received "bridge funding" for her work in a variety of areas related to addiction.

We collaborated with the Law and Mental Health and Child Psychiatry programs to support a conference at CAMH on risk assessment across the

lifespan, addressing the probability of antisocial behaviour and violence across the lifespan. Dr. Nasreen Khatri, a post-doctoral fellow funded by the Canadian Institute of Health Research, also received support from our department to advance her training in the area of depression and women.

Following previous investment in "between-program initiatives," Drs. Peter Farvolden, R. Michael Bagby and Tony Toneatto received renewed funding from the Ontario Problem Gaming Foundation to study personality variables in people who gamble.

The Personality and Psychopathology Research Section underwent an external review during the Fall of 2002. The review was conducted by Dr. Joel Paris, from the Department of Psychiatry at McGill University, and Dr. Paul T. Costa, Jr., from the National Institute of Health (USA). This review produced uniformly positive appraisal, citing our section as one of the top personality disorder programs on the international stage and arguing for its expansion.

Dr. L. Trevor Young was appointed Acting Head of the Mood and Anxiety Research Section. Dr. R. Michael Bagby, who was the Acting Director of the department, was appointed Director in 2002.

Addictions

SECTION HEAD: Dr. Tony Toneatto

THE ADDICTION SECTION CONDUCTS CLINICAL research, experimental and applied, in all aspects of addiction. Drs. Bruna Brands, Beth Sproule and Tony Toneatto are the Section's scientists. Our research activities focus on four areas: gambling, psychopharmacology, treatment outcomes and clinical services.

Gambling Research

In our gambling research (Dr. Tony Toneatto), we aim to develop effective treatments for pathological gambling.

Within the past year, we have completed two studies, one on the effectiveness of naltrexone for people with concurrent alcohol and gambling problems, and a second comparing several brief cognitive-behavioural treatments. We are now in the follow-up stages with both studies.

During the next year, we will conduct two treatment studies. The first will evaluate manual-assisted tele-counselling for gambling problems. The second, in collaboration with Dr. Nigel Turner and Mr. Warren Spence, will evaluate the effectiveness of acupuncture as a treatment for problem gambling.

Dr. Toneatto is also studying thinking processes in people who have gambling problems; results show a high correlation between irrational beliefs (such as thinking that efforts to regain gambling losses are justified) and the development of problem gambling.

Psychopharmacology Research

Our psychopharmacology research (Drs. Bruna Brands, Beth Sproule, Peter Selby, David Marsh) focuses on the care of opioid addiction.

Drs. Brands and Marsh have co-authored *Best Practices in the Design and Delivery of Methadone Maintenance Treatment Programs*. This publication offers information that can help opioid-treatment programs become more effective and encourage the establishment of new programs.

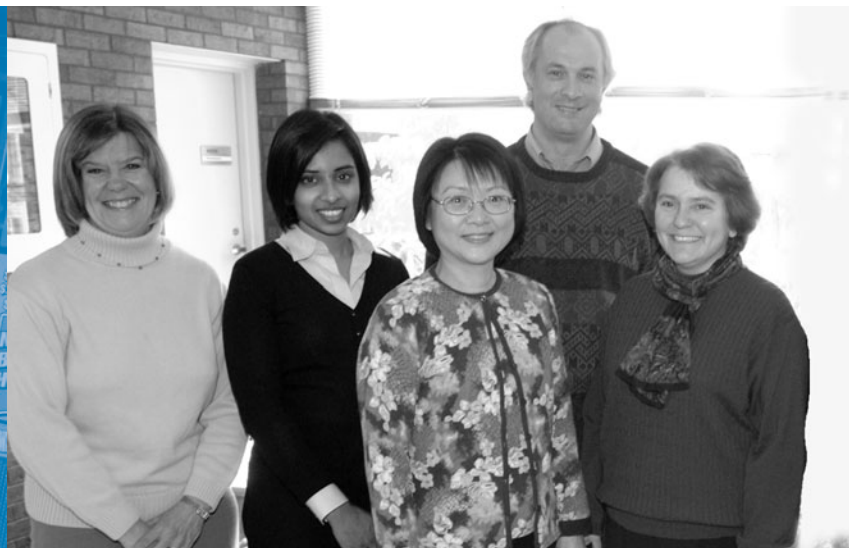
Dr. Brands (with Drs. Joan Blake, Beth Sproule, Douglas Gourlay and Usoa Busto) is studying the expansion of methadone maintenance treatment (MMT) availability to patients with dependence on opioids other than heroin, to increase access to treatment that previously would have been unobtainable.

Dr. Brands is also studying the effectiveness of treatment programs specifically designed for adolescents who are dependent on heroin, among whom multiple drug use is common. We found that, among adolescents who use heroin, the mean age of first use was 15 years. In this population we also saw an association between heroin use and significant comorbidity, including mental health issues and physical health risks.

Dr. Sproule is developing a novel approach to statistical analysis, using "fuzzy logic" to evaluate the relationships between patient characteristics and medication outcomes. We are conducting an ongoing and extensive evaluation of this approach, including comparisons to other methodologies.

In another study, Dr. Sproule has compared the attitudes and professional interactions of community pharmacists toward patients taking mental health–related medications and those taking cardiovascular medications. Despite the generally positive attitudes expressed by community pharmacists, we found that pharmacists interacted less with, and offered fewer professional activities to, patients using mental health medications. This pattern needs to be improved; more interaction could optimize the prevention, detection and management of drug-related problems in these patients.

In collaboration with colleagues in the Clinical Neuroscience Section, Dr. Sproule is also evaluating the effects of hypnotic medications in older adults.



Treatment Outcome Research

Treatment outcome research consists of three clinics, headed by psychologists who are developing empirically based treatments for addictive disorders.

Dr. Shelley McMain, head of the Dialectical Behaviour Therapy Unit, is conducting a five-year, CIHR-funded study evaluating the clinical and cost effectiveness of dialectical behaviour therapy (DBT) for people who have borderline personality disorder, including many who have concurrent substance use problems.

The Anger and Addiction Clinic, headed by Dr. Lorne Korman, is evaluating an integrated treatment for people who have concurrent anger, substance use and gambling problems. The researchers are testing a DBT-based treatment that targets emotion dysregulation, thought to underlie both anger and addiction problems.

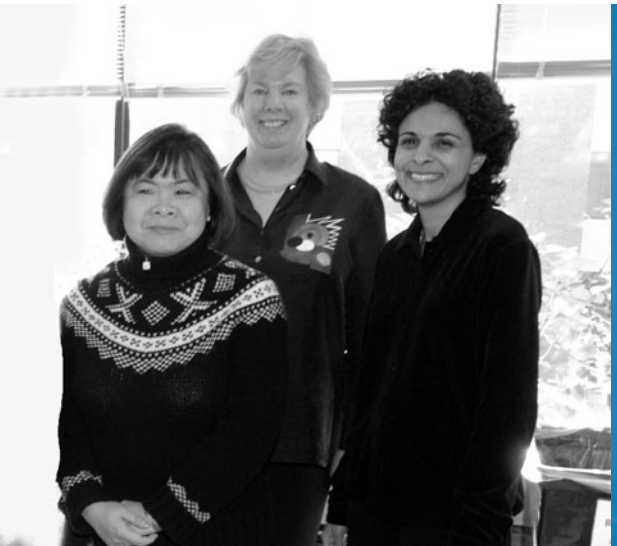
The Eating Disorders and Addiction Clinic, headed by Dr. Christine Courbasson, has developed (with Lauren Dixon) a manualized treatment, rooted in DBT, that targets the emotion regulation problems that are common to both eating disorders and problem substance use. This treatment is the first to tailor DBT to treat concurrent eating and substance use problems simultaneously.

Clinical Service Research

Our clinical services research area conducts effectiveness and process research in collaboration with CAMH addiction programs and services.

We are about to complete a study evaluating the outcome and process of brief treatment for addictions. This study will identify the key treatment interventions that produce therapeutic benefit.

Other projects in progress include studies evaluating the delivery of treatments for problem gambling, addiction in youth and addiction in women.



Mood and Anxiety

SECTION HEAD: Dr. L. Trevor Young

MEMBERS OF THE MOOD AND ANXIETY DISORDERS Program continue to undertake multidimensional research in mood and anxiety disorders. Our work has ranged from studying molecular mechanisms to developing and evaluating new treatments, such as therapies based on meditation. In addition to population-based research methods, we use basic science methodologies, brain imaging techniques, family studies and clinical trials.

Mood Disorders

Dr. Robert Levitan has identified a particular subgroup of women who have chronic depression and who also have a cluster of symptoms such as obesity and attention problems; these women may have an abnormal variance of a dopamine receptor gene.

Dr. Jeffrey Meyer found increased prefrontal serotonin receptor binding potential in people who were depressed and who also showed negativistic thinking. These results may be related to the findings, by other groups, of increased serotonin receptor bindings, in the same brain region, in people who completed suicide.

At the laboratory level, Dr. Jun-Feng Wang used DNA arrays to find new patterns of gene expression after administering drugs such as lithium and antidepressants to cultured brain cells.

Dr. Jerry Warsh has identified specific signal transduction abnormalities related to calcium, using blood cells from people with bipolar disorder.

Dr. Sagar Parikh has started a Canada-wide study of the effectiveness of psychoeducation and cognitive therapy for people with bipolar disorder.

Investigations, led by Drs. R. Michael Bagby and Helen Mayberg, continue to compare 1. brain functioning of people with depression and 2. brain functioning of people whose personality types are thought to make them vulnerable to depression, but who have never developed a depressive episode. Results indicate that the brain functioning in never-depressed, but vulnerable, people was similar to that of people who had previously had a depressive episode.

Dr. Bagby is also examining how changes in personality during treatment may predict outcome in different types of psychotherapies.

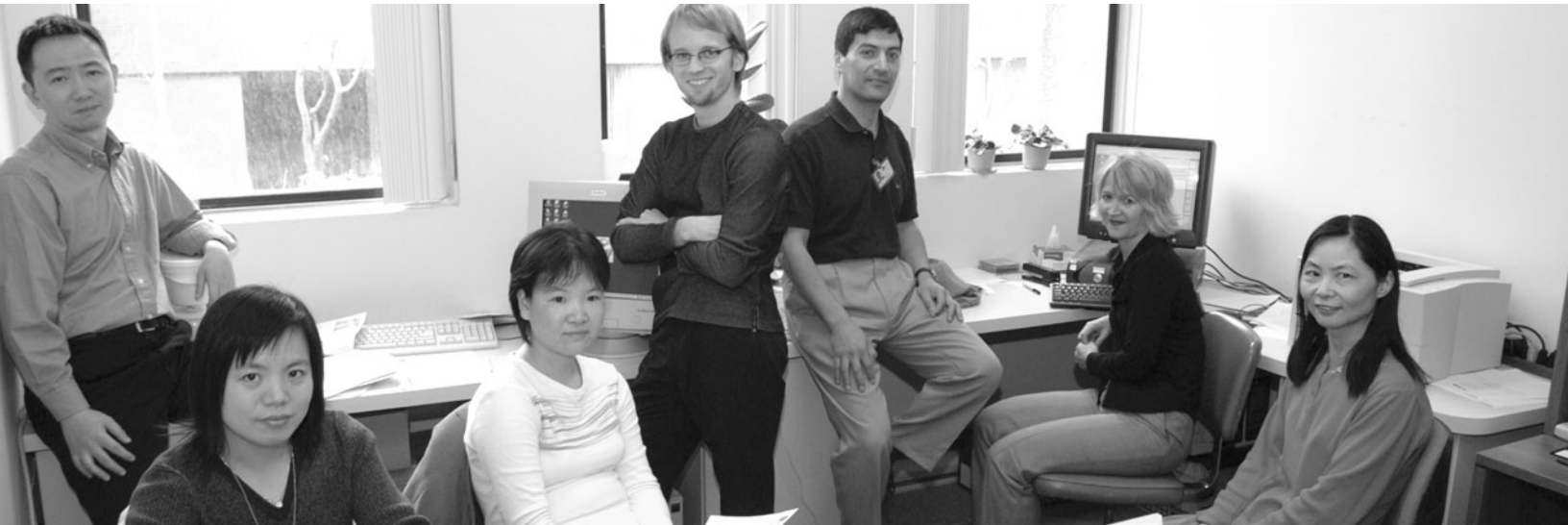
In the Cognitive Behaviour Therapy Unit, Dr. Zindel Segal and Dr. Mayberg collaborated on a study comparing cognitive therapy to antidepressant medication. Using PET scans, they found patterns of changes in brain metabolism in patients who responded to cognitive therapy; these patterns differed from those of people who responded to antidepressant treatment.

Dr. Mark Lau has shown interesting differences in vulnerability to depression using psychological tests in people with depression. His team also continues their internationally recognized trials comparing the effectiveness of cognitive therapy and medications for relapse prevention.

Anxiety Disorders

In the Anxiety Disorders Clinic, the OCD group has been very busy developing a new brief cognitive therapy treatment for people who have concurrent obsessive-compulsive disorder (OCD) and depression, and testing the efficacy of cognitive therapy for medication-refractory OCD.

In collaboration with Dr. Jim Kennedy, Dr. Richter's group have also replicated their earlier finding about the possible role of a serotonin receptor gene in OCD, which conceivably may lead to improved diagnosis and treatment in the future.



Personality and Psychopathology

SECTION HEAD: Dr. R. Michael Bagby

RESEARCH IN THE PERSONALITY AND PSYCHOPATHOLOGY

Research Section examines a broad range of themes related to personality and psychopathology. We also develop tests and instruments to assess personality and related constructs, and develop strategies to assess and treat mental disorders using the Internet.

Our current projects explore: alternative structures of personality psychopathology; the effects of personality traits in treatment outcomes for disorders such as depression, anxiety and problem gambling; the influence of personality on the development of mental disorders; the influence of acute distress on personality and its assessment; and the role of neurotransmitter mechanisms in personality.

Personality and Cognitive Vulnerability and Problem Gambling

Surprisingly little is known about the personality and cognitive characteristics of people with gambling problems. Drs. R. Michael Bagby and Peter Farvolden are attempting 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.

Results to date suggest that, in contrast to people with gambling problems who seek treatment, people with gambling problems who do not seek treatment and social gamblers are not characterized by high levels of psychopathology or alterations in cognitive functioning. This finding challenges conventional thinking about problem gambling.

Behavioural Inhibition, Behavioural Activation, Personality and Novelty

Based mainly on research on how animals learn, Gray's influential motivational model (1994) proposes biological systems that mediate all of our different motivations and emotions: the behavioural inhibition system (BIS), the behavioural activation system (BAS) and the flight-fight system. Gray's BIS and BAS offer promise for explaining a variety of normal and psychopathological behaviour.

We are developing novel paradigms to study the relations between BIS and BAS sensitivity, other systems of personality and preference for novelty. We are tentatively exploring connections to psychopathology by examining these relationships in different patient groups.

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. Although there is considerable support for the current explanations of PD/AG, there is also some evidence that increased vulnerability to separation distress and/or an "insecure" attachment style may also have an important role in PD/AG.

Results to date suggest that neuroticism and attachment style predict anxiety sensitivity, which in turn predicts severity and intensity of panic symptoms. These results suggest some benefit from using personality and attachment dimensions to better understand the onset and maintenance of PD/AG.

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. A continuing challenge in the treatment of MDD is the high rates of relapse and recurrence.

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.

Results to date suggest that response to a positive mood induction may help predict treatment response.

Internet Assessment and Treatment

Considerable data suggest that the Internet can be a powerful tool for delivering collaborative assessment and treatment.

We have recently presented data supporting the potential utility of a Web-based tool for assessing depression and anxiety disorders in primary care. In addition, we have presented data supporting the reach, patterns of use and potential efficacy of a free Web-based smoking cessation program.

Application of the Five-Factor Model of Personality to Psychopathology

Recognition of the limitations associated with the categorical approach to personality psychopathology has led to the development of several new dimensional models of personality psychopathology.

Our ongoing research attempts to find if 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.

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

This project attempts to unify two parallel lines of research examining vulnerability to depression. One line shows that PET scans in patients with depression display specific patterns to induced sad mood; the other shows that individuals 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. These results have recently been published in *Neuroimage*.

Personality as a Mediator of Treatment Outcome

This ongoing project, now in its third year, 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). Previous studies have shown that all these treatments are about equally effective, but no study has systematically examined whether targeting depressive symptoms related to personality traits mediates outcome differently.

Personality, Life Stress and Recurrent Major Depression

More than half of all people with major depression will have multiple recurrent episodes throughout their lives; the impact is often devastating. Recurrence of depression is also an ongoing burden on the public health system. For these reasons, we are trying to understand the mechanism that perpetuates the recurrence of depression.

Several risk factors for recurrent depression include childhood adversity, personality style and poor social support. But what is the mechanism that underlies the relationship between these risk factors and recurrence?

In collaboration with Dr. Kate Harkness (Queen's University), Dr. Bagby is conducting research to see if people who have both depression and a history of childhood adversity, disrupted personality and poor interpersonal functioning are generating stressful events that precipitate new episodes of depression. If this is found to be true, treatments that target stress generation may ultimately help prevent depression from becoming a lifelong disorder.

Drs. Harkness and Bagby have recently received an operating grant from the Ontario Mental Health Foundation to examine this causal model of depression recurrence, with clear targets for treatment and prevention.

Psychobiology of Aggression and Antisocial Behaviour across the Lifespan

SECTION HEAD: Dr. Leslie Atkinson

AGGRESSION AND ANTISOCIAL BEHAVIOUR POSE tremendous risks to individuals, families and society. The Psychobiology of Aggression and Antisocial Behaviour across the Lifespan Section incorporates researchers from the Law and Mental Health and Child, Youth and Family Programs, facilitating lifespan research. In the past year, we have conducted research into risk, intervention/management and knowledge transfer.

Infant Stress

Dr. Leslie Atkinson and others are investigating genetic and environmental influences on infants' response to stress. This group is examining normal infants at 12 to 18 months of age to determine their response to mild stressful events, such as maternal separation.

Chemical analysis of the saliva of the children will determine the levels of important stress hormones in these children. Investigators in the Neuroscience Research Department will then be able to investigate a variety of factors in the hormones and blood samples of these children that may contribute to our understanding of how humans develop both adaptive and maladaptive responses to stress. In addition, these stress hormones are involved in a variety of other behaviours throughout the lifespan, including aggression.

Risk Factors for Aggressive and Antisocial Behaviour

Drs. Joe Beitchman and James Kennedy and colleagues have been focusing on the role of select serotonin genes and family and personality factors in aggression.

This year, they found that one form of serotonin transporter gene was less common in aggressive children than in non-aggressive children. A second variant of this gene was not significantly linked with aggression, but was linked to a diagnosis of ADHD. These findings could have implications, in future, for assessing risk of aggression and implementing early intervention strategies.

Dr. Martin Lalumiere and colleagues showed that, among sex offenders, number of older brothers is positively related to a greater interest in coercive and violent sexuality. Number of older sisters, or younger brothers or sisters, is unrelated to sexual interest. Dr. Lalumiere and colleagues speculate that the link involves maternal immunoreactivity to something involved in sexual differentiation of the brain.These findings may eventually contribute to early identification of risk and intervention strategies.

Dr. Fiona Miller and colleagues studied the risks of childhood disturbance associated with low socioeconomic status (SES) and harsh, inconsistent parenting practices. They found that, although the absolute risk of children developing disorders associated with low SES and harsh parenting is low, the relative risk is high.

For example, relative to his or her mid-SES peers, a child eight or nine years old from a low-SES family is five times more likely to develop conduct disorder, while a child eight or nine years old who experiences harsh parenting is four times more likely to show symptoms of conduct disorder.

Dr. Christine Wekerle is surveying teenagers who have been maltreated by their caregivers; question topics include health risk behaviours (problem substance use, dating violence, risky sexual practices, mental health problems) and resiliency factors (school achievement, leisure activity). The primary hypothesis of the study is that maltreated youth have a high prevalence of risk behaviours and a greater number of overlapping problems.

The survey will also measure mediators (e.g., cognitive expectancies, motives for risky sexual practices), enhancing the study's potential for identifying targets for intervention.

In another study, of reported child abuse, Dr. Wekerle is studying the association of caregiver substance use and maltreatment. Dr. Wekerle found that parents with substance use

problems are more likely than parents without substance use problems to neglect and emotionally abuse their children and less likely to sexually abuse them. No relation was found between substance abuse and physical abuse.

In a third survey, Dr. Wekerle and colleagues identified a small group of adolescent males whose behaviour was broadly antisocial, whose activities included, for example, gambling, weapons possession, stealing, frequent physical violence and bullying. These youths had more difficult backgrounds, a higher rate of depression, more frequent suicidal ideation and reported more problem substance use than other youths.

These findings highlight the unmet mental health needs of antisocial male youth and the challenges to getting help for substance use problems.

Dr. Michael Seto and colleagues compared young people who had been charged with a juvenile sex offence with young people who had been charged with other, non-sexual, juvenile offences. They found a meaningful distinction between juvenile sex offenders who have few conduct problems but engage in sexual misconduct and those who engage in non-sexual forms of criminal behaviour. These findings will help target and focus interventions to better treat the sexual aspects of juvenile delinquency.

Dr. Seto reviewed the literature on pornography's effects on attitudes, aggression in the laboratory and sexual arousal. He concluded that there is an interaction between individual characteristics and the effects of pornography exposure. These findings have relevance to an ongoing debate about the impact of pornography—again, that the impact of pornography depends on the individual involved with it. Students within the section have also been active. Ms Karen Milligan, under the supervision of Dr. Leslie Atkinson, explored how attachment security and maternal sensitivity relate to children's aggressive behaviour. Studying typically developing best-friend pairs, Ms Milligan found that children who were less securely attached exhibited higher levels of aggression.

In a second study of children with Down syndrome, Ms Milligan found that the effect of child intellectual level on aggressive behaviour is moderated by maternal sensitivity. This finding is important, because it had previously been assumed that aggression in this population was entirely due to intellectual factors, which are difficult to change. Interventions focused on the mother-child relationship may reduce later incidents of aggression between the child and his or her peers.

Mr. Calvin Langton (now Dr. Langton), under the supervision of Dr. Howard Barbaree, completed a doctoral dissertation contrasting approaches to risk assessment and violence prediction among adult offenders.

The findings confirmed the validity of actuarial devices but also suggested that structured clinical approaches hold promise. Additional findings indicated that information about offenders' completion of and response to institutional treatment improves the accuracy of sexual recidivism predictions. Drs. Langton and Barbaree are now studying which treatment components are most important for this purpose.

Mr. Mark Watson, Mr. Mark Levi, Ms Carey Sturgeon and Ms Sandy Greenberg, under the supervision of Dr. David Nussbaum, successfully applied a neurobiological model to the prediction of violence and also demonstrated the need to carefully match predictive instrumentation to the population being studied (e.g., different predictors may be necessary when studying people who carry out planned acts of aggression as opposed to people who aggress in reaction to some stressor).

Aggressive and Antisocial Behaviour Interventions and Management

Dr. Wekerle studied the effectiveness of a dating violence prevention and dating health promotion program for

Investigating a variety of factors in the hormones and blood samples of children may contribute to our understanding of how humans develop both adaptive and maladaptive responses to stress.

youth who have experienced childhood maltreatment. The program reduced incidents of physical and emotional abuse in dating and symptoms of emotional distress. Dr. Wekerle and colleagues are extending their studies to incorporate an intervention for substance use problems into the program.

Dr. Joe Ducharme and student Ms Kimberly Harris are evaluating innovative interventions to improve child compliance with teacher requests and on-task behaviour. The interventions, referred to as errorless remediation, are based on the sophisticated use of learning strategies. In this type of intervention, maladaptive responses are treated like errors, and the environment is rearranged to ensure that low levels of these errors occur. Gradually, conditions associated with problem behaviour are introduced at a rate that ensures that these behaviours remain at low levels. This approach has produced gains in compliance, on-task behaviour and peer relationships.

Conducting the largest quantitative review of studies evaluating sex offender treatment outcome published to date, Dr. Seto and colleagues found that treated sex offenders repeated their crimes significantly less often than non-treated sex offenders.

Knowledge Transfer

Ms Joanna Henderson (now Dr. Henderson), under the supervision of Dr. Sherri MacKay, conducted a provincial study of factors affecting the adoption and use of TAPP-C, a community-based children's mental health program for juvenile firesetting. This study revealed that adopter, innovation, dissemination and organizational characteristics are all important in understanding knowledge-transfer from academic settings to community-based settings.

In addition, analyses to examine the relative importance of each group of variables revealed that different variables are particularly important at different stages of program dissemination. For example, innovation characteristics were important in the adoption process, but not at the utilization stage. This study provides preliminary data that will help close the research-practice gap in children's mental health.

A dating violence prevention and dating health promotion program, for youth who have experienced childhood maltreatment, reduced incidents of physical and emotional abuse in dating and symptoms of emotional distress.

Schizophrenia

SECTION HEAD: Dr. Shitij Kapur

THE SCHIZOPHRENIA RESEARCH PROGRAM IS dedicated to understanding the causes and mechanisms of recovery of schizophrenia, with the hope of improving the lives of people and families affected by the illness. In pursuit of this goal, our methods range from molecular studies to community-based research.

Genes and Schizophrenia: Animal Models of Schizophrenia
Dr. Albert Wong and colleagues are using animal models to identify candidate genes for schizophrenia. The team has discovered that two genes, 14-3-3eta and syntaxin1a, are associated with schizophrenia (*Molecular Psychiatry*, 2003). Now, we ask the question of how these genes lead to schizophrenia; studies are under way to test how these genes affect the release of brain chemicals and are involved in brain development.

Genetic Subtypes of Schizophrenia
Drs. Anne Bassett and Eva Chow lead the Clinical Genetics Research Program team, focusing their research on genetic subtypes of schizophrenia. Drs. Bassett and Chow have been instrumental in showing that 22qDS (deletion syndrome of 22q) represents an identifiable genetic subtype of schizophrenia.

With support from the W. Garfield Weston Foundation, our team is following over 70 adults with 22qDS to determine the developmental, psychiatric and medical features, as well as the molecular genetic make-up, of this complex subtype. We have also started a study of children and adolescents with 22qDS, who have a high risk of developing schizophrenia. (Supported by NARSAD and Bill Jeffries Schizophrenia Endowment Fund).

Dr. Chow reported in 2002 (*Biological Psychiatry* 51: 208– 215, 2002) that brain structure in 22qDS-schizophrenia resembles that of other forms of schizophrenia; this is leading us to study whether brain structural features may predict who will develop schizophrenia in young people with 22qDS.

Tackling Schizophrenia Before It Begins
Drs. Robert Zipursky, Irvin Epstein and colleagues have been leading the Prevention through Risk Identification, Management & Education (PRIME) research clinic in early detection strategies and treatment, using psychological tests and brain imaging. These approaches are already showing promise (*Biological Psychiatry*, Woods et al, 2003).

Recently, the team of Drs. Jean Addington, Zipursky, Epstein and colleagues has begun a five-year project, in collaboration with the Universities of North Carolina and Yale, to improve early identification of people who are likely to develop schizophrenia. Early and accurate identification of risk for schizophrenic psychosis may be the field's best hope for developing more effective treatment strategies, including secondary prevention of this typically devastating disorder. (Funded by NIMH).

Drugs and Therapy Go Hand-in-Hand
For many years, we have known that antipsychotic drugs work on the dopamine neurotransmitter. However, we do not understand how drug action on this neurotransmitter takes away the delusions and hallucinations that are a symptom of psychosis.

Dr. Shitij Kapur and colleagues have proposed a new theory to link dopamine to psychosis and to antipsychotic treatment (*American Journal of Psychiatry*, 2003). According to this theory, drugs provide a background of dampened salience of symptoms; this background makes it easier for the person to give up his or her delusions and hallucinations. Our theory predicts how drugs and therapy may actually work hand in hand. Studies are now under way to test this new theory.

Cognitive Behavioural Treatments: A Focus on Functional Recovery

While antipsychotic treatment takes away symptoms of schizophrenia, not everyone returns to their original level of functioning. Recently, the field of schizophrenia research and treatment has not focused on individual psychotherapies, but the last few years have seen a growing interest in this area.

Dr. Jean Addington, a leader in psychological interventions for psychosis, is currently leading the development of new types of psychotherapies for people who are in the early stages of schizophrenia, and is examining if these therapies lead to improvement in functional outcome (funded by the NIH, USA).

Understanding and Managing Side-Effects

Drugs have side-effects. This cannot be avoided. In the Schizophrenia Research Program, we strive to understand antipsychotic side-effects, to help people manage them.

Dr. Tony Cohn, in association with Dr. Gary Remington, runs a research-treatment clinic focusing on weight gain and diabetes problems for people taking antipsychotics. This clinic has led to several new discoveries.

We find that the medication-induced weight gain observed in young people experiencing a first episode of psychosis is substantially higher than previously reported (presented by Dr. Cohn at the International Congress on Schizophrenia Research, 2003).

In people who have experienced chronic psychosis over many years, we found a two- to three-fold increase in rates of type 2 diabetes, abdominal obesity and a syndrome of insulin resistance and abnormalities in cholesterol and glucose metabolism, both in hospitalized and community patients with schizophrenia. (Presented by Dr. Cohn at the International Congress on Schizophrenia Research, 2003).

These factors, combined with the very high rates of cigarette smoking (70 to 80 per cent) in this population, suggest a markedly increased risk for coronary heart disease.

In screening for diabetes among this same group of people with chronic psychosis, we have found that the recommended fasting glucose procedure is only 20 per cent reliable in detecting undiagnosed diabetes and five per cent reliable for determining if persons are at risk for diabetes, compared with a different screen test, the glucose challenge.

This has led us to develop new guidelines for testing for diabetes and risk for diabetes in people with schizophrenia.

Beyond Drugs and Psychotherapy: Magnetic Stimulation as a Treatment

Drs. Jeff Daskalakis and Bruce Christensen have been conducting studies using a new research technique called transcranial magnetic stimulation (TMS). Our studies have shown, for the first time, that people having an active psychotic episode of schizophrenia show abnormal inhibition of neuronal activity of the front part of the brain (*Archives of General Psychiatry,* 2003).

These studies show the path to possible new treatments. We are now working to see if magnetic stimulation can be used to treat these inhibition deficits and lessen hallucinations for people with schizophrenia that does not respond to conventional treatments.

Neuropsychology: Exploring How the Brain Works

Working in the Neuropsychology Lab, Dr. Christensen and colleagues focus on the cognitive and neurobiological effects of schizophrenia. One of the challenges in this area has been to understand the wide variety of cognitive changes associated with this illness in terms of a unified reason.

We have proposed that schizophrenia-related cognitive impairment may be associated with one of two major developmental brain pathways: the pathway that controls goal-directed activity.

As part of our ongoing work in this area, we have completed a study using a visual discrimination paradigm and a visually guided reach paradigm, both of which support this hypothesis—both of these studies have been presented at international conferences and we are currently preparing manuscripts for each.

We are also interested in understanding the prominent memory deficit that is associated with schizophrenia; for example, in people with schizophrenia who do not use memory strategies to improve recall, such as mentally grouping items that belong to the same category (e.g., apple, pear and banana are all fruits).

In a recent study, we have shown that, although patients are able to learn category strategies, having the skill does not improve their recall. This type of problem has been termed a "utilization deficit" and may reflect how general intellectual deficits interfere with using new skills. Our findings also suggest the need for repeated practice in skills training for people with schizophrenia.