

## **Interdisciplinary Capacity Enhancement in Co-Morbid Psychosis – Nicotine Dependence: Studies of Patients Attending the Nova Scotia Early Psychosis Program – Final Report**

### **Applicants:**

**Sherry Stewart, Ph.D.** (Clinical Psychology). Professor, Departments of Psychiatry, Psychology, and Community Health and Epidemiology, Faculties of Medicine and Science, Dalhousie University.

**Sean Barrett, Ph.D.** (Clinical Psychology). Assistant Professor, Department of Psychology, Faculty of Science, Dalhousie University.

**Kim Good, Ph.D.** (Neuroscience). Associate Professor, Department of Psychiatry, Faculty of Medicine, and Assistant Professor, Department of Psychology, Faculty of Science, Dalhousie University.

**Ray Klein, Ph.D.** (Psychology). Professor, Department of Psychology, Faculty of Science, Dalhousie University.

**Ron Leslie, Ph.D.** (Neurobiology). Professor and Head, Department of Anatomy and Neurobiology, and Professor of Psychiatry, Faculty of Medicine, Dalhousie University.

**Heather Milliken, M.D.C.M., FRCPC** (Psychiatry). Associate Professor, Department of Psychiatry, Faculty of Medicine, Dalhousie University; Psychiatrist, Nova Scotia Early Psychosis Program, Capital District Health Authority.

**Alissa Pencer, Ph.D.** (Clinical Psychology). Psychologist, Community Mental Health Services & Adolescent Early Psychosis Program, Izzak Walton Killam (IWK) Health Centre. Adjunct Assistant Professor, Department of Psychology, Dalhousie University.

**David Whitehorn, Ph.D.** (Physiology), R.N., M.Sc. (Nursing). Consultant, Early Psychosis Program, Capital District Health Authority. Lecturer, Department of Psychiatry, Faculty of Medicine, and Adjunct Faculty, School of Nursing, Dalhousie University.

### **Original Purpose of Grant:**

The research described in the original ICE grant proposal was designed to complement a pilot study that was being planned at the time by several members of the ICE grant team (i.e., a genetics project being headed by Dr. Heather Milliken which has since been funded – see Appendix A). The proposed ICE project involved adding a motivational component to this planned study to allow for comparisons of self-reported motives for smoking behaviour: (a) across psychosis patients and matched healthy controls; (b) between psychosis patients presenting with different symptom profiles (e.g., positive vs. negative symptoms); (c) between psychosis patients taking different forms of medication (e.g., traditional neuroleptics vs. newer atypical antipsychotics). Administering these motivational measures within the context of the other planned genetics study also allowed for examination of relations of self-reported smoking motivations to genetic profiles of several candidate genes that are potentially relevant for understanding nicotine dependence – psychosis co-morbidity.

### **Achievements in Relation to the Goals of the ICE Program:**

1. This project facilitated the establishment of a multidisciplinary research team conducting research on a problem of high priority for tobacco control in Canada (i.e., understanding the reasons for the high rates of nicotine dependence in those suffering from psychosis). The team assembled here has conducted innovative interdisciplinary research through the ICE funding that assisted us in securing two additional grants in this area (see Appendix A). The first (genetics project with Dr. Milliken as PI) was the pilot project described in our ICE application to which we intended to attach the ICE project components focused

on smoking motivations. The second successful grant (with Dr. Kim Good as PI) was for the equipment portions of the research we described in the ICE application. With the equipment costs covered, we were able to use more of the ICE funds to cover staffing costs (payment of the graduate and undergraduate research assistants) associated with the project. In total, with the \$5,000.00 awarded through the ICE, we covered payment of these two student research assistants and purchase of a CO monitor.

2. The ICE funding enhanced tobacco control research capacity by engaging students and experienced investigators new to the field. We involved one clinical psychology doctoral student (Heather Fulton; paid stipend), two third-year undergraduate students (Brittany McGillivray, Alison Murton; volunteers), and an undergraduate summer research assistant (Jessica Meisner; summer salary) in the ICE funded projects. All were involved in running Early Psychosis Program participants and healthy controls, recruitment, attendance at regular team meetings, developing clinical interviewing skills, and DNA collection for the genetics portion of the study. Two of these students (Fulton and McGillivray) have also been very active on behalf of the team, in disseminating preliminary results of the ICE project at scientific meetings (see Appendix C). Further, Fulton has since been successful as a co-applicant on a tobacco-related grant (see Appendix B) and has published a tobacco research paper in the top-ranked journal, *Neuropsychopharmacology* (Fulton & Barrett, 2007). The ICE grant also served to bring to the field talented researchers who have not published in the nicotine area previously (i.e., Good, Klein, Milliken, Whitehorn, Pencer, Leslie), but who have much to offer this area of research (i.e., expertise in psychopharmacology, genomic studies, early psychosis symptoms, drug therapy, neurobiology, cognitive psychology). Finally, our team also involved mentoring two new researchers (i.e., Barrett and Pencer) by more experienced investigators. Both have been successful in obtaining funding as PI on tobacco-related grants since beginning their mentorship through the ICE project (see Appendix B).
3. This ICE funded project clearly enhanced tobacco control research capacity in a currently underserved region. Specifically, it facilitated the development of a multidisciplinary research team to address the correlation between schizophrenia and nicotine dependence in Atlantic Canada – a region currently underserved in terms of tobacco control research.
4. Our ICE funding also facilitated improved linkages and collaborations between researchers from different institutions and different disciplines in Atlantic Canada. Specifically, the project involved collaborations between researchers at the Capital District Health Authority (Milliken, Whitehorn), Izzak Walton Killam Hospital (Leslie, Pencer), and Dalhousie University (Stewart, Barrett, Milliken, Whitehorn, Pencer, Klein, Good, Leslie). A broad array of relevant disciplines are also represented in our new team including psychiatry, clinical psychology, psychopharmacology, genomic research, nursing, developmental psychopathology, cognitive psychology, and neuroscience.
5. Our project also served to create improved exchange between researchers and service providers. Members of our team have given talks to the Nova Scotia EPP staff to raise awareness of the importance of this topic. Moreover, the team consists not only of researchers but also of clinicians providing care through the EPP (i.e., Milliken and Whitehorn) which is sure to enhance the likelihood that the research findings will ultimately be translated into improved care for those receiving services through the Program (e.g., improvements to interventions to help these individuals quit smoking or to prevent smoking in those at risk for starting).

## Appendix A

### Related Grants Obtained by the Team since Funding of the ICE Grant

2006-present	Dalhousie Department of Psychiatry Research Fund <u>Genetics, addictions and clinical outcomes in early psychosis: A pilot collaborative study.</u> \$5000	<b>Drs. H. Milliken, S.H. Stewart, M. Alda, R. Leslie, K. Good, D. Whitehorn, &amp; S. Barrett.</b>
2007-present	The Dalhousie Medical Research Foundation-- The Lynn Bourinot Fund in Schizophrenia. Equipment Grant. <u>Co-Morbid Psychosis &amp; Nicotine Dependence: Two Studies of Patients Attending the Nova Scotia Early Psychosis Program</u> \$6000	<b>Drs. K. Good, S.H. Stewart, S. Barrett, R. Klein, R. Leslie, H. Milliken, A. Pencer, &amp; D. Whitehorn</b>

Note: ICE team members' names are highlighted in **bold**.

**PSYCHIATRY RESEARCH FUND  
APPLICATION FORM**

**A. Cover Page**

<b>Principal Investigator:</b>	Heather Milliken
<b>Department and Position:</b>	Associate Professor, Department of Psychiatry
<b><sup>1</sup>Co-investigators/Affiliations:</b>	Sherry Stewart, Martin Alda, Ron Leslie, Kim Good, David Whitehorn, Dalhousie Department of Psychiatry, Sean Barrett, Department of Psychology.
<b>Collaborators/Affiliations:</b>	Dr. R Jooper, McGill University
<b>Eligible Applicant (if not the PI):</b>	
<b>Short Title:</b>	Genetics, addictions and clinical outcomes in early psychosis: a pilot collaborative study.
<b><sup>2</sup>Status of Ethics Review:</b> <i>If obtained, provide a copy of the official approval letter; if to be submitted, indicate to which REB.</i>	Application in process

**Signatures**

**Date**

Principal Investigator	
Eligible Applicant	
Head, Department of Psychiatry	

Applications should be submitted to: **Administrative Coordinator, Research Section**  
Department of Psychiatry  
8<sup>th</sup> Floor AJLB

<sup>1</sup> The PI has overall responsibility for the conduct of the research. Other investigators have a significant intellectual input into (some of) the formulation of the research question, the design of the study, its analysis and interpretation. Collaborators may provide essential services or resources related to the conduct of the research.

<sup>2</sup> All human subject research requires prior ethical approval by a duly constituted Research Ethics Board (i.e., the REBs of the Capital Health District, IWK Health Centre or Dalhousie University. If you believe that this project does not require ethical approval, you must obtain a written statement from one of these REBs to that effect.

## B. Proposed Research

### **Summary** (250 word maximum):

Psychiatric disorders, including those involving psychosis, arise as a complex interaction between genetic and environmental factors. Recent studies have indicated that these disorders are influenced by many “susceptibility” genes, each of which exerts a small overall effect (Kendler, 2005). The influence of any particular susceptibility gene depends upon interactions with other genes and environmental factors. For example, a recent birth cohort study demonstrated that a COMT polymorphism imparts a differential risk of developing psychosis, only in the presence of adolescent cannabis use. Such findings suggest that study of interactions between genetic profiles and substance use will be a powerful approach to understanding diversity amongst patients with psychotic disorders regarding clinical features and outcomes. The present proposal represents an initial effort to examine associations among genetic and substance use profiles in data obtained from the well-characterized patients from the Nova Scotia Early Psychosis Program compared to healthy volunteers. Lifetime and current substance use will be assessed with a battery of self-report tools. Genomic profiles of two highly relevant candidate genes (coding for catechol-O-methyltransferase, or COMT, and for the hepatic cytochrome CYP2A6) will be determined by Dr. R. Joobar. The objectives of this study are (1) to assemble existing expertise and establish a research infrastructure to undertake studies of this nature in the Maritimes (2) to determine and describe genetic, substance addiction and clinical profiles in our sample population and (3) to test initial hypotheses related to the two candidate genes.

2007-present

The Dalhousie Medical Research Foundation-- The Lynn Bourinot  
Fund in Schizophrenia. Equipment Grant.

\$6000 Drs. K. Good, S.H. Stewart, S. Barrett, R. Klein, R. Leslie,  
H. Milliken, A. Pencer, & D. Whitehorn

### **Co-Morbid Psychosis and Nicotine Dependence: Two Studies of Patients Attending the Nova Scotia Early Psychosis Program**

Psychiatric disorders, including those involving psychosis, arise as a complex interaction between genetic and environmental factors. Recent studies have indicated that these disorders are influenced by many susceptibility genes, each of which exerts a small overall effect (Kendler, 2005). The influence of any particular susceptibility gene depends upon interactions with other genes and environmental factors. For example, a recent birth cohort study demonstrated that a COMT polymorphism imparts a differential risk of developing psychosis, only in the presence of adolescent cannabis use. Such findings suggest that study of interactions between genetic profiles and substance use will be a powerful approach to understanding diversity amongst patients with psychotic disorders regarding clinical features and outcomes. The present proposal represents an initial effort to examine associations among genetic and substance use profiles in data obtained from the well-characterized patients from the Nova Scotia Early Psychosis Program compared to healthy volunteers.

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## Appendix B

### Tobacco-Related Grants Obtained by the Two New Investigators on the ICE Team since beginning their Mentoring through the ICE collaboration

2006-present	Canadian Tobacco Control Research Initiative (CTCRI) <u>How do the acute and chronic effects of smoking contribute to the addictive properties of tobacco?</u> \$14,950 <b>Dr. S. Barrett, Dr. S.H. Stewart, Dr. R. Leslie, &amp; D. Steeves</b>
2007-present	Interdisciplinary Capacity Enhancement (I.C.E) Seed Grant, University of Waterloo. <u>Examining links between tobacco use and psychiatric symptoms.</u> \$5000 <b>Dr. S. Barrett, Dr. S.H. Stewart, H. Fulton, Dr. U. Busto, Dr. L. Zawertailo, &amp; Dr. T. George</b>
2008-present	Canadian Tobacco Control Research Initiative (CTCRI) Idea Grant Program <u>Individual differences in the response to nicotine and the non-nicotine components of tobacco smoke.</u> \$49,300 <b>Dr. S. Barrett, Dr. S.H. Stewart, Dr. R. Joobar, Dr. R. M. Klein, &amp; D. Steeves</b>
2006-present	IWK Health Centre <u>Prevalence of substance use and risk profiles in adolescents presenting to a mental health clinic.</u> \$4000 <b>Dr. A. Pencer &amp; Dr. S.H. Stewart</b>

Note: ICE team members' names are highlighted in **bold**. Students trained through the ICE grant are highlighted in *italics*.

## Appendix C

### List of Presentations Resulting from the ICE Grant

*Fulton, H.G., Barrett, S.P., & Stewart, S.H. (2007). Genetics of early psychosis and the influencing effects of adolescent drug use. Presented at the 33rd Annual Department of Psychology In House Conference, Dalhousie University, Halifax, Nova Scotia, May.*

*Fulton, H.G., Barrett, S.P., Stewart, S.H., Good, K., Leslie, R., Pencer, A., Whitehorn, D., & Milliken, H. (2007). An examination of drug use initiation and cessation in first episode psychosis patients. Presented at the 33rd Annual Dalhousie Psychiatry Research Day, Halifax, Nova Scotia, September*

*Fulton, H.G., Barrett, S.P., Stewart, S.H., Good, K., Leslie, R., Pencer, A., Whitehorn, D., & Milliken, H. (2008). Patterns of use, motivations for and acute subjective effects of tobacco use in early psychosis patients. Submitted for presentation at the 69th Annual Convention of the Canadian Psychological Association, Halifax, Nova Scotia, June.*

*MacGillivray, B., Fulton, H.G., Barrett, S.P., Stewart, S.H., Good, K., Leslie, R., Pencer, A., Whitehorn, D., & Milliken, H. (2008). Personality and tobacco use by early psychosis patients and age- and gender- matched controls. Submitted for presentation at the 69th Annual Convention of the Canadian Psychological Association, Halifax, Nova Scotia, June.*

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Fulton, H.G., Barrett, S.P., & Stewart, S.H. (2007). Genetics of early psychosis and the influencing effects of adolescent drug use. Presented at the 33rd Annual Department of Psychology In House Conference, Dalhousie University, Halifax, Nova Scotia, May.

#### Abstract

Many argue that schizophrenia develops through a gene by environment interaction. Interestingly, most individuals with schizophrenia abuse drugs making drug use a possible environmental trigger. More specifically, when individuals with an underlying genetic vulnerability use certain drugs at a critical developmental window, an interaction may occur where they develop the disorder. A recent study by Caspi et al. (2005) implicated a particular genetic polymorphism; individuals who had this polymorphism and used cannabis in adolescence were at five-fold increased risk for the development of schizophrenia. However, the investigators did not control for use of several other substances (e.g., tobacco). Thus, the results may not be specific to cannabis. This study will investigate the role of genes in NS Early Psychosis Program patients and matched control participants, and then relate this information to each individual's substance use history to test the gene x environment interaction theory and its specificity to cannabis.

Fulton, H.G., Barrett, S.P., Stewart, S.H., Good, K., Leslie, R., Pencer, A., Whitehorn, D., & Milliken, H. (2007). An examination of drug use initiation and cessation in first episode psychosis patients. Presented at the 33rd Annual Dalhousie Psychiatry Research Day, Halifax, Nova Scotia, September.

#### Abstract

Almost 80% of individuals with schizophrenia abuse drugs at some point during their lives, compounding problems associated with the disorder (e.g., poorer prognosis). Many hypotheses have been proposed to explain the high rates of substance use among individuals with schizophrenia, yet none has fully accounted for why these individuals continue to use drugs of abuse despite their negative consequences. We compared first episode psychosis patients to healthy control subjects on age of initiation of drugs of abuse, age they reported using a drug most frequently in their life, reasons for using each drug, and reasons for stopping or attempting to stop the use of each drug. Preliminary analyses suggest that patients try alcohol and drugs earlier than controls but use tobacco more frequently later in life. Patients are also more likely to have tried hallucinogenic drugs. Patients appear to use drugs for similar reasons to controls, yet there are some notable differences (e.g., patients are more likely to use substances to relieve symptoms associated with psychosis). A comparable pattern is observed in participants' reasons for stopping or attempting to stop the use of drugs (e.g., patients are more likely to stop using/attempt stopping because they had a bad experience).

Fulton, H.G., Barrett, S.P., Stewart, S.H., Good, K., Leslie, R., Pencer, A., Whitehorn, D., & Milliken, H. (2008). Patterns of use, motivations for and acute subjective effects of tobacco use in early psychosis patients. Submitted for presentation at the 69th Annual Convention of the Canadian Psychological Association, Halifax, Nova Scotia, June.

#### Abstract

Many explanations have been put forth (e.g. the Self Medication Hypothesis) to explain the high rates of tobacco use by patients with psychotic illnesses. Studies examining tobacco use by these individuals, however, have typically only involved chronically ill patients. Consequently, it is unclear whether the high rate of tobacco use by this population is attributable to a desire to self-medicate for the symptoms of their psychotic illness, a desire to manage side effects of their medication, or some other factor. The present study compared tobacco use patterns, motivations for use and subjective effects while using tobacco as reported by early psychosis patients and age- and gender-matched controls. Results suggest that early psychosis patients initially try tobacco at an earlier age than controls, and use it more frequently later in life. Patients also used tobacco on significantly more days in the past month than control subjects. Controls felt “less happy” when using tobacco, while early psychosis patients reported “no change” in their feelings of happiness during use. The present data suggest that such differences in tobacco use are present before patients develop their disorder, and differences in subjective feelings about tobacco use may help explain differing rates of use.

MacGillivray, B., Fulton, H.G., Barrett, S.P., Stewart, S.H., Good, K., Leslie, R., Pencer, A., Whitehorn, D., & Milliken, H. (2008). Personality and tobacco use by early psychosis patients and age- and gender- matched controls. Submitted for presentation at the 69th Annual Convention of the Canadian Psychological Association, Halifax, Nova Scotia, June.

#### Abstract

Psychotic illnesses affect more than one percent of the population and can have profound implications on affected individuals' lives. A high proportion of these individuals also smoke tobacco; a behaviour associated with considerable morbidity (e.g., lung cancer). Previous studies have investigated personality as a possible factor predisposing these individuals to use tobacco, however little research to date has compared personalities of individuals with psychotic illnesses to tobacco-using controls. Further, minimal research has been conducted examining how personality may affect patterns of use and co-use of tobacco with other substances (e.g. using tobacco and alcohol together). The present study will examine patterns of tobacco and other substance use (using the Time Line Follow-back method) in relation to personality (using the Substance Use Risk Profile Scale) in early psychosis patients and age- and gender-matched controls. It is hypothesised that early psychosis patients with an impulsive personality type will be more likely to use tobacco with other substances, and they will do this more frequently than impulsive personality type controls or patients with different personality types. Findings from the present study will help to better understand the high rates of tobacco use in these disorders and identify possible predisposing factors for this behaviour.