Alberta Addiction and Mental Health Research Partnership Program

Alberta Centennial Addiction & Mental Health Research Chairs Program

Dr. Jean Addington – Annual Report

June 30th 2009 – Web Version

Dr. Jean Addington

Alberta Centennial Addiction & Mental Health Research Chair
Inaugural Chair in Child and/or Adolescent Mental Health

BACKGROUND

Psychotic disorders, including schizophrenia and affective psychotic disorders are common, affecting about 5% of the general population. Development of these disorders usually results in significant disability. Psychotic disorders rank among the top 10 causes of disability worldwide. Psychosis is "brewing" long before its manifestation as a diagnosable illness and there are identifiable signs and symptoms that precede the development of frank psychotic symptoms. Over the last decade there has been a worldwide movement to develop comprehensive early intervention programs for schizophrenia. However there is now compelling evidence that in the pre-psychotic phase the formation of symptoms and disability changes have already begun.

A major focus of Dr. Addington's work is participating in the NAPLS consortium. NAPLS represents a collaboration of eight clinical research centers based at Emory, Harvard, North Carolina, UCLA, UCSD, Yale, Zucker Hillside Hospital and the University of Calgary. In a prior phase of the consortium, NAPLS 1, these investigators pooled clinical and psychosocial data obtained on a large sample of patients (N=291) who had been identified using a standardized set of operational diagnostic criteria for a "prodromal" risk syndrome. Risk for onset of psychosis in this population was 35% after 2 and 1/2 years of follow-up, with a decelerating rate of conversion over this period. Moreover, prediction algorithms incorporating baseline clinical and psychosocial variables dramatically improved positive predictive power (~80%) compared with the prodromal criteria alone, but achieved only modest sensitivity (~40%).

Dr. Addington along with other collaborator in the NAPLS consortium has recently been funded for a new NAPLS project. The goal in NAPLS 2 is to improve upon these prediction algorithms by incorporating biological measures with clinical measures and to test the possible differential course of change in biological indicators in those who convert to psychosis.

The potential utility of biological indicators in elucidating predictors and mechanisms of psychosis in the prodromal population is thus far based exclusively on analyses of data collected at individual sites with small samples. For example, the UCLA team, working collaboratively with investigators in a prodromal program based in Melbourne, Australia, has recently demonstrated a significantly steeper rate of gray matter reduction in prefrontal cortical regions in prodromal patients who convert to psychosis compared with those who do not over a 1-year follow-up period. This pattern of accelerated change in prefrontal regions is mirrored in a sample of first-episode schizophrenia patients compared with age- and gender-matched healthy controls over a 2-year follow-up period. Together, these data suggest that during the prodromal and early phases of schizophrenia, there is an exaggeration of the regressive neuromaturational processes (programmed cell death, synaptic pruning) normative to late adolescence and early adulthood, changes that may participate in the pathophysiology of psychosis onset. To test this model rigorously, while at the same time accounting for the marked heterogeneity in outcomes among prodromal and early psychosis patients, will require sample sizes many times larger than those available in any single site. In addition, ideally, any

investigation into the course of gray matter reduction in the prodromal phase of psychosis would incorporate information from other assessment modalities (genomics, proteomics) that can reveal molecular mechanisms for the steeper rate of change in the converting group.

These putatively prodromal or clinical high risk subjects are help-seeking individuals who require help for their presenting concerns as well as interventions to delay or prevent the onset of the psychotic illness. Medication trials have suggested positive outcome in terms of reducing current symptoms and possibly delaying onset. Although concerns with side effects of medication and the limited number who are willing to try this treatment make a psychological intervention appealing, the potential value of psychological interventions is bolstered by preliminary evidence supporting the effectiveness of a psychological intervention with this clinical high risk group. A cognitive behavioral approach would also appear to be the psychological treatment of choice in addressing the range of needs of this population. Yet, a comprehensive approach to early intervention requires not only the development of an effective treatment but also establishing that it is being offered to those who need it. This necessitates understanding more fully two relatively neglected areas: the pathways to care and the target population.

The overall objectives of Dr. Addington's research are:

1. to determine the predictors of psychosis
2. understand the mechanisms of conversion to psychosis
3. determine means to identify young people in the earliest stages of psychosis
4. develop effective treatments for the earliest stages of psychosis

DEVELOPMENT OF RESEARCH PROGRAM

Much of the effort in this first year of the Chair program has been to set up a research program that focuses on early psychosis research. The research program is housed in the Heritage Medical Research Building in Calgary. The first few months focused on the completion of renovations to the research space and the setting up space for the research staff, such as organizing phone lines, purchasing and setting up computers. The research program has to exist in conjunction with a, clinical service. Thus, we have combined efforts with the PRIME Clinic which is a specialized clinic for individuals at risk for psychosis that operates under the Early Psychosis Treatment Service at Foothills Hospital. The PRIME Clinic was underutilized. In the fall of 2008 we worked with the PRIME Clinic so that it was operating at capacity, with the intention of having two fully functioning PRIME clinics by the end of 2010. A wide range of materials such as fliers and posters have been designed through the research program for the clinic. In order to expedite referrals into the research study, the research program is helping to manage referrals to the clinic.

The next several months was devoted to hiring and training staff in the clinical, neuropsychological, and electrophysiology assessments necessary for the research program and for conducting assessments for future studies. The research program has recently added two postdoctoral students. It is planned that clinical students from the Clinical Psychology Program at the University of Calgary will join the research program in the fall of 2010.

OVERVIEW OF ONGOING RESEARCH

NAPLS 2

NAPLS 2 is an ongoing 8 site 2-year project called "Predictors and Mechanisms of Conversion to Psychosis" which was funded in September 2008 for 5 years by the National Institute of Mental Health (NIMH). Although this is an 8 site study where each site conducts an identical study, each site is

independently funded. This study will have 720 clinical high risk for psychosis subjects (CHR) and 240 controls with 90 CHR subjects and 30 controls coming from Calgary. In terms of psychosis prediction, we seek to determine whether biological abnormalities preceding psychosis onset contribute to prediction of psychosis independently from that of the best performing clinical algorithms and whether they can be combined with the clinical measures to enhance predictive utility. Clinical areas include psychopathology, neuropsychology, social functioning and social cognition. Biological areas include imaging, electrophysiology, genetics and cortisol. All sites follow identical protocols but each site is the lead in terms of designing and supervising one of the areas under study. Calgary is responsible for the psychopathology, risk factors and social cognition and for the data management. This study began in October 2008 and will end in September 2013.

PREDICT

PREDICT is a recently completed 3 site (Toronto, University of North Carolina, Yale) NIMH 5-year funded study of 260 putatively prodromal individuals and 100 help seeking controls examining predictors of conversion to psychosis.

ADAPT

ADAPT is a recently completed small randomized control trial (RCT) of cognitive behavioral therapy (CBT) versus supportive therapy that was conducted in Toronto.

PSTEP

PSTEP is a small RCT of CBT versus befriending that is currently being completed in Toronto. This study will end in August 2009 at which point the data will be shipped to Calgary so that analysis and publications can begin. Publications from this data will serve to develop treatment projects in Alberta.

DIRECTIONS FOR FURTHER RESEARCH

Further research in the next year will focus on the development of research proposals to address treatment in the pre-psychotic period and testing different methods for screening for early signs of psychosis. These projects will be developed and submitted for funding in the spring of 2010.

KNOWLEDGE TRANSFER ACTIVITIES

Knowledge transfer activities within Alberta have focused on education about early detection in the pre-psychotic period. The purpose is to educate health care providers and families about the research clinics and offer preliminary information about experimental treatments underway for young people who are at risk of developing psychosis. Efforts have consisted of:

1. Developing informational and recruitment focused fliers and posters about early detection and the PRIME Clinic
2. Distribution to every family physician and mental health worker in Southern Alberta information about early detection in the pre-psychotic period; details about the PRIME clinic and details about research projects that will offer additional assessments
3. Presenting at the AMHB Showcase meeting in Banff in 2008
4. Conducting two workshops on early detection that were delivered throughout Alberta on the telehealth network

See Publications section for other presentations and lectures.

COLLABORATIVE ACTIVITIES

Dr. Addington received an appointment in the Clinical program of the Department of Psychology beginning in the 2009-2010 academic year. This should allow for new collaborations in the next academic year.

Dr. Addington is leading Psychosis Research Group in the Department of Psychiatry at the University of Calgary. This group consists of other department members who are also participating in research into psychosis. The purpose of this group is to review common interests and to develop collaborative research projects in order to expand the scope of psychosis and schizophrenia research in the Department of Psychiatry

PAN-ALBERTA COLLABORATION

Pan-Alberta collaboration was initiated with the University of Alberta and will be initiated with the University of Lethbridge in the fall of 2009. Initial discussions at the University of Alberta focused on potential research into genetics of schizophrenia. Such collaborations can be developed over the next year.

PUBLICATIONS (JULY 2008 – JUNE 2009)

JOURNAL ARTICLES

1. **Addington, J**. & Addington, D.E. (2008) Social and Cognitive Functioning in Psychosis, *Schizophrenia Research*, 99, 176-181

2. **Addington. J**., Epstein, I., Reynolds, A., Furimsky, I., Rudy, L., Mancini, B., McMillan, S., Kirsopp, D., & Zipursky, R.B. (2008) Early Detection of Psychosis: Finding those at clinical high risk *Early Intervention in Psychiatry, 2, 147-153*

3. Mizrahi, R., **Addington, J**., Remington, G. & Kapur, S. (2008) Attribution style as a factor in psychosis and symptom resolution. *Schizophrenia Research*, 104, 220-227

4. Compton, M.T., Goulding, S.M., Ramsay, C.E., **Addington, J.,** Corcoran, C. & Walker, E. (2008) Early Detection and Intervention for Psychosis: Perspectives from North America. *Clinical Neuropsychiatry*, 5, 263-272

5. Pencer, A. & **Addington, J**. (2008) Models of substance use in adolescents with and without psychosis. *Journal of the Canadian Academy of Child & Adolescent Psychiatry*, 17, 202-209

6. Hawkins, K.A., Keefe, R.S., Christensen, B.J., **Addington, J.,** et al., (2008) Neuropsychological course in the prodrome and first episode of psychosis: findings from the PRIME North American Double Blind Treatment Study. *Schizophrenia Research, 105*, 1-9

7. **Addington, J.** & Addington, D. (in press) Outcome after discharge from an early psychosis program. *Schizophrenia Research*

8. Corcoran, C., Cornblatt, B, & **Addington J**. (in press) "Won't Leave his Room". DSM-IV-TR Casebook and Treatment Guide for Child Mental Health" Editors: Peter Jensen and Cathryn Galanter. APPA press.

9. **Addington, J.** & Addington, D. (in press) Symptom remission in first episode patients. *Schizophrenia Research*

10. **Addington, J.** & Tran, L. (in press) Using the Brief Core Schema Scales with Individuals at Clinical High Risk of Psychosis. *Behavioral and Cognitive Therapy*

11. Woods, S.W., **Addington, J**., Cadenhead, K., Cannon, T.D., Cornblatt, C., Heinssen, R. Perkins, D.O., Seidman, L.J., Tsuang, M., Walker, E., & McGlashan, T.H. (in press) Prodromal risk syndrome for first psychosis. *Schizophrenia Bulletin*

12. Addington, J. & Mancuso, E., (in press) Cognitive-behavioral therapy for individuals at high risk of developing psychosis. *Journal of Clinical Psychology*

BOOK CHAPTERS

1. Addington, D. & **Addington, J**. (2008) First-Episode Psychosis in K. T. Mueser & D.V. Jeste Clinical Handbook of Schizophrenia. New York: Guilford Press

2. **Addington**, J., Lambert, T. & Burnett, P. (2009) Complete and Incomplete Recovery from First-Episode Psychosis. In Jackson, H.J. & McGorry, P.D. (eds). The Recognition and Management of Early Psychosis: A Preventive Approach.

3. Phillips, L., **Addington**, J. & Morrison, A. (2009) At Risk Mental State: Management In Jackson, H.J. & McGorry, P.D. (eds). The Recognition and Management of Early Psychosis: A Preventive Approach

PUBLISHED ABSTRACTS

1. McGlashan, T.H., **Addington**, J., Cadenhead, K.S., Cannon, T.D., Cornblatt, B., Heinssen, R., Perkins, D.O., Seidman, L.J., Tsuang, M., Walker, E.F., & Woods, S. (2009) A new diagnostic class: the prodromal risk syndrome for psychosis. *Schizophrenia Bulletin*, 35, p 5

2. Menon, M., Anderson, A.k., Schmitz, T.w., Korostil, M., **Addington, J**. & Kapur, S. (2009) Delusions of reference and abnormalities in social cognition. *Schizophrenia Bulletin*, 35, p 176

3. Cornblatt, B., Lenscz, T., **Addington**, **J.,** Cadenhead, K.S., Walker, E.F., Baskir, L., Seidman, L.J., Cannon, T.D., Perkins, D.O., Woods, S., Tsuang, M., McGlashan, T.H., & Heinssen, R (2009) Social and role functioning: Critical outcome domains independent of psychosis. *Schizophrenia Bulletin,* 35, p 319

4. **Addington**, J., Perkins, D.O., Woods, S, Cadenhead, K.S., Cannon, T.D., Cornblatt, B., Seidman, L.J., Walker, E.F., McGlashan, T.H., Tsuang, M., & Heinssen, R. (2009) Functional impairment: the hallmark of risk for psychosis. *Schizophrenia Bulletin*, 35, p 324-5

INVITED PLENARY LECTURES

1. "The Prodrome Concept and Interventions: A focus on CBT" The 3rd Biennial Schizophrenia Treatment: Bridging Science to Clinical Care. The University of Minnesota, Minneapolis, October 6th – 7th 2008.

2. "The Past and Future of Psychosocial Interventions in Early Psychosis" The 6th International Conference for Early Psychosis, Melbourne, Australia, October 2008.

3. "Psychosocial Treatment for those at Clinical High Risk of Psychosis" Schizophrenia Days, Stavanger Norway, November 2008.

4. "Psychosocial Treatment for those at Clinical High Risk of Psychosis" Presented at the Zucker Hillside Hospital, North Shore LIJ, New York, February 25th 2009.

5. "Clinical High Risk for Psychosis: treatment and Outcomes" Presented at Grand Rounds, Department of Psychiatry, University of Alberta, April 29th 2009.

6. "Identifying and Treating Schizophrenia in the Prodromal Phase: Are we ready for clinical practice". Presented at "A bridge over Troubled Water: Early Detection and Intervention in Schizophrenia" University of Haifa, Haifa Israel. June 11th 2009.

7. "Attenuated Psychotic Symptoms: What is the risk?" Presented at the Department of Psychiatry Symposium, Sackler Faculty of Medicine, University of Tel Aviv, Tel Aviv, Israel, June 14th 2009.

FUNDING

Name of Agency:	National Institutes of Health
Date of Award:	2008-2013
Project Title:	Predictors and Mechanism of Conversion to Psychosis
Total Amount:	US$2,107,918
PI:	Addington, J.

Name of Agency:	Canadian Institutes of Health Research
Date of Award:	2009-2010
Project Title:	Using dance to translate research on early psychosis
Total Amount:	$24,000
PI:	Boydell, K.
Co-Investigator(s):	Addington, J., Goering, P., McKay, B., Gladstone, B., Stasiulis, E., Volpe T

Name of Agency:	Canadian Institutes of Health Research
Date of Award:	2008-2011
Project Title:	Stress induced dopamine release in subjects at clinical high risk for psychosis: A [11c]-(+) PHNC PET study
Total Amount:	$418,678
PI:	Wilson, A., Mizrahi, R.
Co-Investigator(s):	Addington, J., Houle, S., Rusjan, P.

ABOUT THE ALBERTA ADDICTION AND MENTAL HEALTH RESEARCH PARTNERSHIP PROGRAM

The *Alberta Addiction and Mental Health Research Partnership Program* is comprised of a broad-based multi-sectoral group, representing service providers, academic researchers, policy-makers and consumer groups, working together to improve the coordination and implementation of practice-based addiction and mental health research in Alberta.

The mission of the Research Partnership Program is to improve addiction and mental health outcomes for Albertans along identified research priority themes, by generating evidence and expediting its transfer into mental health promotion, prevention of addiction and mental illness, and innovative service delivery.

The Research Partnership Program sets out to increase Alberta's excellence and output of addiction and mental health research findings, and to better translate of these findings into practice improvements.