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Collaboration to Advance Negative Symptom Assessment in Schizophrenia

Submitted by Melanie Bennett, PhD

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Upcoming Events

Negative symptoms are an important feature of schizophrenia and include: anhedonia (a decrease in experiencing pleasure), asociality (decreased interest and participation in social relationships); avolition (a decrease in goal-directed activity); blunted affect (a decrease in the outward expression of emotion); and alogia (a decrease in the amount of speech). Negative symptoms are major determinants of the social and occupational impairments in schizophrenia, are substantial sources of distress for care-givers, and are predictors of poor long-term outcome. Despite advances in pharmacotherapy for schizophrenia, negative symptoms are only marginally responsive to even the second-generation antipsychotics. The Food and Drug Administration (FDA) has yet to approve any medication with an indication for negative symptoms. As part of efforts to design and test medications to treat negative symptoms,

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Oxytocin and DMXB-A as Possible Treatments in Schizophrenia

Submitted by William Keller, MD and Robert Buchanan, MD

Schizophrenia is a heterogeneous disease with multiple symptom domains. One symptom domain is negative symptoms, as described in the article above. Another symptom domain is cognitive impairment. These symptom domains have a substantial impact on people with schizophrenia because they impair a person's ability to interact with other people and perform daily activities. The current treatments available to address these impairments have limited benefit. We are doing a study that simultaneously tests the effects of two medications on social and cognitive deficits in schizophrenia. One of the medications (oxytocin) has shown

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experts in the field have determined that a new measure of negative symptoms needs to be developed that taps all five negative symptom domains with multiple items. The Negative Symptom Rating Scale (NSRS; NIMH-MATRICS Negative Symptom Workgroup, 2007) has recently been designed by a panel of experts to measure the current level of severity of negative symptoms in patients with schizophrenia and schizoaffective disorder.

Negative symptoms are major determinants of the social and occupational impairments in schizophrenia

The MIRECC has recently begun a program of research focused on testing this new measure of negative symptoms. Last year, MIRECC investigators Melanie Bennett, PhD, and Jack Blanchard, PhD, along with BVA intern Courtney Forbes, MA, received funding to conduct a pilot study of the NSRS. The goals of this project were to collect data on the reliability and psychometric properties of the NSRS, to examine the relationships between negative symptoms as measured by the NSRS and depression, psychosis, and social functioning, to examine the acceptability of the NSRS by people with schizophrenia and schizoaffective disorder, and to make changes in the length of time of administration, the wording of interview items, and general administration procedures as needed. A total of 38 subjects participated in this project and data analysis is underway.

Dr. Blanchard has received a 3-year grant to further examine the NSRS in a larger sample of people with schizophrenia spectrum diagnoses. The project, called "Collaboration to Advance Negative Symptom Assessment in Schizophrenia" (CANSAS), is a multi-site trial with University of Maryland School of Medicine/Baltimore VAMC as the lead site. Other sites include the University of Pennsylvania (Dr. Raquel Gur, site PI), University of California - Berkeley (Dr. Ann Kring, site PI), and University of California, Los Angeles (Dr. Bill Horan, site PI). Approximately 500 individuals with schizophrenia will be studied in order to further develop the NSRS. The goal of the study is to develop the NSRS as the next-generation negative symptom scale to be used in psychopathology research and pharmaceutical trials.

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promise for improving social interaction while the other (DMXB-A) may be of benefit for cognitive impairments.

Oxytocin is critical for the formation of social bonds in mammals. In studies involving rats, the amount of social interaction between rats is improved when they are given oxytocin. Social memories and social learning are affected by oxytocin. In recent studies, oxytocin has been shown to improve facial recognition ability in healthy volunteers and increase the perception of trust in interpersonal situations. Disruption of normal function of the oxytocin system may be a contributing factor to negative symptoms in individuals with schizophrenia. Evaluating oxytocin as a treatment for schizophrenia is important given the limited treatments available for negative symptoms and the morbidity associated with impaired social functioning associated with the negative symptom cluster of schizophrenia.

Improved treatment for negative symptoms and cognition will have a dramatic effect on morbidity associated with schizophrenia

DMXB-A is an alpha 7 nicotinic receptor agonist and is associated with cognition. In previous studies, healthy subjects given DMXB-A have improved performance on tasks that measure cognition such as reaction time, word and picture recognition memory, and word recall. The alpha 7 nicotinic receptor is thought to be important in schizophrenia. In one recent study, DMXB-A was given to people with schizophrenia, who were also non-smokers, and was found to be superior to placebo on neuropsychological measures of attention and memory. In light of the potential utility of this agent for enhancing cognition in schizophrenia, the evaluation of DMXB-A in a sample of both smokers and non-smokers is of critical importance.

The study currently being conducted at the Maryland Psychiatric Research Center (and soon at the Baltimore VAMC) evaluates oxytocin and DMXB-A compared to placebo for the treatment of negative symptoms and cognitive impairments in schizophrenia. People with schizophrenia who participate and meet criteria for the study will be randomly assigned to one of three treatment groups for six weeks. One group will receive oxytocin and a placebo instead of DMXB-A. One group will receive DMXB-A and a placebo instead of oxytocin. The third group will receive two placebos instead of oxytocin or DMXB-A. These medications will be delivered as an adjunctive treatment to their current treatment for schizophrenia. The primary assessments for negative symptoms include the Scale for the Assessment of Negative Symptoms and performance on social role play vignettes. The primary measures of cognitive function will be a composite score from tests measuring attention, processing speed, verbal and visual processing speed,

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working memory and various evoked potential and eye-tracking measures. The proposed hypothesis is that oxytocin will selectively improve the various measures of negative symptoms, while DMXB-A will selectively improve cognitive function.

Improved treatment for negative symptoms and cognition will have a dramatic effect on morbidity associated with schizophrenia. People with schizophrenia will be better able to interact with others and perform their daily activities. DMXB-A and oxytocin are two promising treatments for these indications.

For more information, or to refer a potential participant, please contact Mary Olandu at Baltimore VAMC (410-605-7284, molandu@mprc.umaryland.edu) or Dr. Robert Buchanan at MPRC, (410-402-7876, rwbuchanan@mprc.umaryland.edu).

Recent MIRECC Publications



Goldberg, R., Hackman, A., Medoff, D., Brown, C., Dickerson, F., Fang, L., Kreyenbuhl, J., Dixon, L. (2008). Physical wellness and employment status and adults with serious mental illness. *Community Mental Health Journal*, 44:245-251.

Goldberg, R. & Seth, P. (2008). Hepatitis C services and individuals with serious mental illness. *Community Mental Health Journal*, 44:381-384.

Nidecker, MF., DiClemente, C.C., Bennett, M.E., & Bellack, A.S. (2008). Application of the Transtheoretical Model of Change: Psychometric properties of leading measures in patients with co-occurring drug abuse and severe mental illness. *Addictive Behaviors*, 33, 1021-1030.

DiClemente, C.C., Nidecker, M. & Bellack, A.S. (2008). Motivation and the stages of change among individuals with co-occurring disorders *Journal of Substance Abuse Treatment*, 34, 25-35.

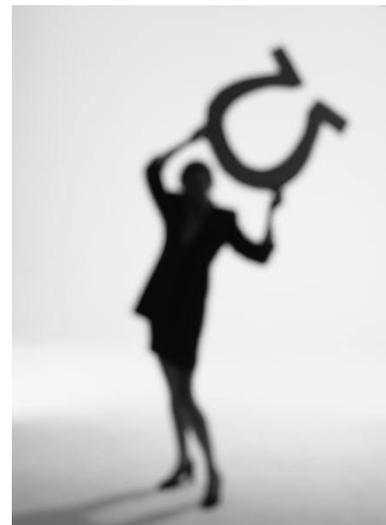
Welcome to New MIRECC Staff



Sophia Autrey, MPH, CLC, joins the MIRECC as the Program Evaluator for the Psychosocial Rehabilitation Training Program. Her degree of Public Health was earned from Morehouse School of Medicine with a concentration in Health Administration and Policy. Prior to joining the MIRECC, she was the Lead Evaluator for the Georgia Division of Public Health, Office of Birth Outcomes. She has also worked with the Centers for Disease Control and Prevention, National Center for Infectious Diseases. Her expertise as an evaluator includes quantitative and qualitative analyses, survey methods, logic modeling and performance management. She will be an essential part of creating an evaluation infrastructure within the MIRECC that compliments performance management strategies.

Good-bye and Good Luck!

Melissa Nidecker, PhD, recently left the MIRECC for a Clinical Psychologist position with the Department of Defense. Dr. Nidecker started her career at UMB in the late '90s as a Research Assistant in the Center for the Behavioral Treatment of Schizophrenia, completed her internship in Clinical Psychology in the VAMHS/UM School of Medicine Consortium, and did a year of post-doctoral work at the MIRECC. We are grateful for her many years of service and wish her much success in her new position.



UPCOMING EVENTS

◆ Monthly SGA Consultation Seminar ◆

First Thursday of every month:

March 5, 2009

April 2, 2009

1:00 - 2:00 PM

MIRECC conference room, BVA (6A-168)

or PPVA VTel conference room, Bldg 364 (C-110)

or call 800-767-1750, code 79846

There has been increasing concern, both within and outside of the VA, about the metabolic side effects of second generation antipsychotic medications (SGAs). VAMHCS clinicians are encouraged to bring their difficult or complicated SGA cases to this seminar for consultation and advice. Anyone can present a case or just ask questions in this informal setting, so please join us as we learn from the consultants and from each other. The consultants are Robert Buchanan, MD, from the MIRECC Psychopharmacology Clinic and Maryland Psychiatric Research Center, and Julie Kreyenbuhl, PhD, PharmD from the MIRECC.

◆ 3rd Annual VA Mental Health conference ◆

"Meeting the Diverse Mental Health Needs of Veterans: Implementing the Uniform Services Handbook"

July 21- 23, 2009

Washington DC metro area

This meeting will allow for information sharing among mental health professionals and administrators on the current state of implementation of the Uniform Mental Health Services Handbook, the utilization of enhancement funding, and research-informed practices, as well as best practices identified by clinicians in the field.

The deadline for oral presentations, workshops, & poster proposals is March 13, 2009.

The number of oral presentations is limited and highly competitive. The number of workshop presentations is also small. A large poster session is being planned. Priority will be given to quality proposals that address implementation of the Uniform Mental Health Services (UMHS) Handbook.

For detailed information about each type of submission, topics of particular interest, or specifics about how to submit a proposal, please contact Jan Kemp, Center of Excellence in Canandaigua, at Jan.kemp@va.gov.

◆ Recovery-Oriented Small Grants Program ◆
Application Deadline: March 1, 2009

The VISN 5 MIRECC offers a small grant mechanism to fund recovery-oriented clinical and educational innovations in response to the VA's Action Agenda to transform VA mental health services to a recovery model. This program especially encourages (but is not limited to) proposals such as: creating, adopting, launching or expanding recovery-oriented clinical or self-help projects, new programs to educate staff, veterans, and/or family members of veterans about mental health recovery models, or specific recovery-oriented services/programs.

For more information or to receive an application, please contact Alicia Lucksted, PhD, MIRECC Recovery Coordinator, at Alicia.Lucksted@va.gov, 410-706-3244.