

Clinical Psychopharmacology

Alexander H. Glassman, M.D., Chief of Psychiatric Research

B. Timothy Walsh, MD, Psychiatrist II

Steven P. Roose, MD, Psychiatrist Research II

Lirio S. Covey, Ph.D., Research Scientist V

Michael J. Devlin, MD, Psychiatrist II

Evelyn Attia, M.D., Psychiatrist II, Associate Professor of Clinical Psychiatry

Diane Klein, M.D., Assistant Professor of Clinical Psychiatry

Lisa Kotler, M.D., Assistant Professor of Clinical Psychiatry

Laurel Meyer, M.D., Assistant Professor of Clinical Psychiatry

Ellen Zimmerli, PhD., Assistant Clinical Professor

Juli A. Goldfein, Ph.D., Instructor of Clinical Psychology

Pamela Raizman, Ph.D., Instructor of Clinical Psychology

Janet Schebendach, R.D., Project Coordinator

Joanna Steinglass, M.D., Instructor of Clinical Psychiatry,

Allegra Broft, M.D., Instructor of Clinical Psychiatry,

Ana Diaz-Zubieta, Ph.D., Instructor of Clinical Psychiatry

Joel Sneed, Ph.D, Post-Doc Research Fellow

Bret Rutherford, M.D. Post-Doc Research Fellow

Gregory Pelton, Research Psychiatrist, Professor of Clinical Psychiatry and Neurology

Robert Berman, M.D., Post-Doc Research Fellow

Overview

Our research efforts have focused on depression, reward systems and their comorbidity. Areas of interest include: biological characteristics and treatment modalities in patients with late-life depression; the relationship of depression to the development of cardiac mortality/morbidity; pharmacological and psychological treatment of eating disorders; psychological concomitants of and risk factors for eating disorders; and smoking dependence, with special interest in the relationship between nicotine addiction and depression, as well as the prevention of smoking relapse.

Current Research

Alexander Glassman, in association with the Department of Medicine and School of Public Health are completing a five-year follow-up of those patients who participated in the study of an SSRI vs. placebo in major depression following myocardial infarction. The initial results of this study republished in JAMA in 2002. Although there was a trend for a reduction in life-threatening events the number of such events that occurred in six months was limited. With five years of follow-up over 25% of the sample will have died. This study involves examining potential predictors of death. Drs. Gregory Pelton, Dev Devanand and Steven Roose began the first study of whether the combination antidepressants and cognitive enhancers will decrease the rate of conversion of depressed patients with cognitive impairment to dementia.

The Smoking Cessation Clinic is participating in an investigation of the efficacy and safety of methylphenidate (Concerta) as an adjunctive smoking cessation medication for adult smokers with Attention Deficit and Hyperactivity Disorder.

In the past year, we have continued our work aimed at examining psychobiological concomitants of bulimia nervosa: eating behavior, stomach functioning, and levels of CCK, a hormone that is released into the blood after eating to signal "fullness." We showed that patients with BN appeared to have diminished sensitivity to gastric distension.. In the past year we also published results suggesting that lack of early medication response predicted an ultimate failure to respond. We continue a collaborative, translational research grant among groups studying various aspects of eating regulation: researchers studying drug abuse/dependence (Dr. Foltin), researchers studying peripheral controls of appetite and satiety in animals (Drs. Schwartz, and Smith), and CNS reward mechanisms involved in eating in animals (Dr. Hoebel).

We completed largest study of medication in the treatment of this potentially devastating illness, aimed at examining the role of fluoxetine in the prevention of relapse. We have also recently completed a controlled evaluation of atypical antipsychotic medication in this disorder, and are preparing for a double blind trial of olanzapine for the outpatient treatment of AN. We have completed and published a study documenting that women with AN who have recently normalized their weight have an abnormal distribution of body fat, and a tendency to collect weight centrally (i.e. abdomen). One study aims to image via PET activity of the serotonin transporter in women recovered from anorexia nervosa. We published our controlled treatment study to determine the relative and additive efficacy of two contrasting treatments for women and men with Binge Eating Disorder who participate in standard group behavioral weight-control treatment: individual CBT and antidepressant medication. We were able to report that adjunctive individual CBT resulted in significant additional binge reduction in obese binge eaters receiving standard behavioral weight control treatment, and that fluoxetine treatment was associated with greater reduction in depressive symptoms. We completed participation in a multicenter study of the efficacy of topiramate in treating binge eating disorder. We are continuing to conduct laboratory studies of eating behavior in obese women with and without binge eating disorder. Finally, we have begun to study the relationship between eating disorders, such as binge eating and night eating, and outcome in patients who have gastric bypass surgery for obesity.

Education and Training

The unit staff is active in a broad range of training programs. The educational objectives for all residents are to learn how to recognize and treat major eating disorders. We have two current research fellows, and our most recent fellowship graduate received a 5-year, NIMH Career Development Award to study excitatory controls of eating in eating disorders.

Clinical Services

All participants receive standard smoking cessation treatment (nicotine patch and counseling) and are randomly assigned to receive Concerta or placebo for 11 weeks in double-blind manner.

Awards/Honors

Dr. James Knowles along with Dr. Glassman has received a grant award for a project titled Genetic Risk Factors for Nicotine Addition.

Diane Klein received a CNS Spectrums Original Research Article of the Year Award.

Dr. Joel Sneed received a K award to study diagnostic criteria for vascular depression.

Laurel Mayer, M.D. was named an Irving Scholar for June 2005-June 2008, and will carry the title of Herbert Irving Assistant Professor of Psychiatry.

Alexander Glassman, M.D, received the NARSAD Distinguished Investigators Award in 2005.

B. Timothy Walsh, M.D. received the Assn of American Publishers, best book in clinical medicine, *Treating and Preventing Adolescent Mental Health Disorders*. Oxford, New York. 2005

B. Timothy Walsh, M.D. was named as a member to the Committee on Psychosocial effects of Deployment Related Stress, Institute of Medicine, National Academy of Science, 2005 - 2006.

Publications

Covey LS, Fried J, Glassman AH, Woodring S, Masmela J, LoDuca C.: Race as a predictor of abstinence in response to combination bupropion, nicotine patch and counseling treatment. Conference Abstracts on Exploring Models to Eliminate Cancer Disparities Among African American & Latino Populations”, American Cancer Society, Atlanta GA, April 21-22, 2005.

Glassman AH.: Treating depression after a heart attack; influencing death? *Frontiers in Medicine*, p. 305. Abstracts of 158th Annual Meeting of the American Psychiatric Association, Atlanta, GA May 21-26, 2005.

Serebruany VL, Suckow RF, Cooper TB, O'Connor CM, Malinin AI, Krishnan KR, VanZyl LT, Lekht V, Glassman AH, Sertraline Antidepressant Heart Attack Randomized Trial: Relationship between release of platelet/endothelial biomarkers and plasma levels of sertraline and n-desmethylsertraline in acute coronary syndrome patients receiving ssri treatment for depression. *Am J Psychiatry*, 2005 Jun;162(6):1165-70.

Glassman A. Schizophrenia, antipsychotic drugs, and cardiovascular disease. *J Clin Psychiatry* 2005; 66 (suppl 6).

Glassman AH.: Does treating post-mi-depression reduce medical mortality? *Arch Gen Psychiatry*, 2005;62:711-712.

Jiang W, Glassman A, Krishnan R, O'Connor CM, Califf RM. Depression and ischemic

heart disease: what have we learned so far and what must we do in the future? *Am Heart J.* 2005 July;150(1):54-78.

Evans DL, Charney DS, Lewis L, et al. Mood disorders in the medically ill: scientific review and recommendations. *Biol Psychiatry.* 2005 Aug 1; 58(3):175-89.

Covey LS, Glassman AH, Laje R, Woodring S, LoDuca C, Masmela J. Psychological and personality differences among smokers with recurrent versus single type of major depression. Proceedings of the 12th Annual Meeting of the Society for Research on Nicotine and Tobacco. Feb. 15-18. 2006, Orlando, FL.

Covey LS, Botello-Harbaum M, Glassman AH, Woodring S, LoDuca C, Fried J. Race differences in short-term smoking cessation and relapse. Proceedings of the 12th Annual Meeting of the Society for Research on Nicotine and Tobacco. Feb. 15-18. 2006, Orlando, FL.

Covey LS, Glassman AH, Jiang H, Woodring S, LoDuca C, Masmela J, Berman J. Will maintenance Psychotherapy reduce relapse to smoking? Proceedings of the 12th Annual Meeting of the Society for Research on Nicotine and Tobacco. Feb. 15-18. 2006, Orlando, FL.

Glassman AH, Bigger JT, Gaffney M, Shapiro PA, Swenson R. Onset of major depression associated with acute coronary syndromes. Relationship of onset, major depressive disorder history, and episode severity to sertraline benefit. *Arch Gen Psychiatry,* 2006 Mar;63:283-288.

Devlin MJ, Goldfein JA, Petkova E, Jiang H, Raizman PS, Wolk S, Mayer L, Carino J, Bellace D, Kamenetz C, Dobrow I, Walsh BT. Cognitive behavioral therapy and fluoxetine as adjuncts to group behavioral therapy for binge eating disorder. *Obes Res.* 2005 Jun;13(6):1077-88.

Golden NH, Iglesias EA, Jacobson MS, Carey D, Meyer W, Schebendach J, Hertz S, Shenker IR. Alendronate for the treatment of osteopenia in anorexia nervosa: a randomized, double-blind, placebo-controlled trial. *J Clin Endocrinol Metab.* 2005 Jun;90(6):3179-85. Epub 2005 Mar 22.

Klein DA, Schebendach JS, Devlin MJ, Smith GP, Walsh BT. Intake, sweetness and liking during modified sham feeding of sucrose solutions. *Physiol Behav.* 2006 Mar 30;87(3):602-6. Epub 2006 Jan 24.

Mayer L, Walsh BT, Pierson RN Jr, Heymsfield SB, Gallagher D, Wang J, Parides MK, Leibel RL, Warren MP, Killory E, Glasofer D. Body fat redistribution after weight gain in women with anorexia nervosa. *Am J Clin Nutr.* 2005 Jun;81(6):1286-91.

Rosenbaum M, Goldsmith R, Bloomfield D, Magnano A, Weimer L, Heymsfield S, Gallagher D, Mayer L, Murphy E, Leibel RL. Low-dose leptin reverses skeletal muscle,

autonomic, and neuroendocrine adaptations to maintenance of reduced weight. *J Clin Invest.* 2005 Dec;115(12):3579-86.

Sysko R, Walsh BT, Schebendach J, Wilson GT. Eating behavior among women with anorexia nervosa. *Am J Clin Nutr.* 2005 Aug;82(2):296-301.

Walsh BT, Sysko R. Placebo control groups in trials of major depressive disorder among older patients. *J Clin Psychopharmacol.* 2005 Aug;25(4 Suppl 1):S29-33. Review.

Walsh BT, Sysko R, Parides MK. Early response to desipramine among women with bulimia nervosa. *Int J Eat Disord.* 2006 Jan;39(1):72-5.

Zimmerli EJ, Walsh BT, Guss JL, Devlin MJ, Kissileff HR. Gastric compliance in bulimia nervosa. *Physiol Behav.* 2006 Feb 28;87(2):441-6. Epub 2005 Dec 22.

Covey, LS, Bomback A, Yen YG. History of depression and smoking cessation: A rejoinder. *Nicotine and Tobacco Research*, 8 (2):315-319.

Berlin, I, Covey LS, Jiang H, Hamer D. Lack of effect of DRD2 polymorphism for smoking cessation. *Nicotine and Tobacco Research*, 2005, 7:725-728.