Course Overview. Fear and anxiety are normally adaptive motive/emotional states that increase the survival capability and reproductive advantage of complex species. This defensive system functions to organize and constrain behavior in a way that reduces the risk of predation or tissue damage under conditions where the organism's survival (or social status) is immediately threatened. For most species, fear is associated with an extreme emergency in which bodily resources are reallocated to deal with the immediate threat, many times at the expense of other needs and systems. The reaction involves a complex integrated interaction among endocrine and nervous systems and is characterized by exceptionally high energy utilization. Severe stress pathology can result when this normally short-term reaction is prolonged. The problem of anxiety disorders in humans may be exacerbated by our ability to activate this phylogenetically old defensive system with symbolic threats that are far removed from the struggle for survival. Under extreme conditions, the unpleasantness associated with a state of anxiety can lead to the far more serious condition of major depression.

Research on anxiety and affective disorders dramatically expanded over the past decade. There is now an extensive literature on conditioning mechanisms, ontogenetics, pharmacology, neuroanatomy, endocrinology, and genetics of normal and abnormal fear processes. Analysis of these basic research topics has led to significant advances in the classification, diagnosis, behavioral and pharmacological treatment, and the conceptualization of anxiety and related disorders in humans. Psychology 112B is intended as an advanced introductory survey of recent basic and applied research on fear processes.

The course is a mix of standard-lecture and seminar formats. Lectures are divided into two sections. The first five weeks will be spent surveying several research problems related to the study and treatment of anxiety disorders. This introductory material will give us all a common background to deal in detail with a specific research problem during the second five weeks of the course. The focus topic for this quarter is traumatic stress and the transition between anxious and depressive states in the "learned helplessness" animal model of depression and anxiety disorders. Research in this paradigm will be covered in detail to underscore principles outlined during the first five weeks. This section of the course also is intended as an illustration of how complex problems can be structured into a tractable format. Towards the end of the course, we will begin dealing with issues that potentially have direct and substantial implications for the treatment of human anxiety disorders. The seminar aspects of the course and your contribution are described on page 3.
LECTURE TOPICS

Week 1:
1) Organizational Meeting
2) Anxiety and Affective Disorders: Symptoms and Classification

Week 2:
1) Behavioral Mechanisms in Fear: Avoidance, the Common Feature in Anxiety Disorders
2) Behavioral Mechanisms in Fear: Arousal Processes & Application to Agoraphobia

Week 3:
1) Neurobiology of Fear: SNS Activation & Visceral Cuing
2) Neurobiology of Fear: HPAC Regulation of the Central Stress Response

Week 4:
1) Neurobiology of Fear: Central Mechanisms
2) Neurobiology of Fear: Pharmacology of Anxiolytic and Anxiogenic Drugs

Week 5:
1) Treatment: Behavioral Therapy
2) Comorbidity of Anxiety & Depression

Week 6:
1) Anxiety & Helplessness: Historical Perspective
2) Structuring a Problem: Modulator Analysis

Week 7:
1) Modulation of Fear & Traumatic Stress: Extrinsic Variables
2) "

Week 8:
1) Modulation of Fear & Traumatic Stress: Intrinsic variables
2) "

Week 9:
1) Consequences of Chronic Fear: Behavioral Analysis
2) "

Week 10:
1) Neural Consequences of Chronic Fear
2) Brain Energy Failure & Adenosine Regulation
I. STUDENT CONTRIBUTION
This course is designed to give students an opportunity to contribute to the analytical (problem-solving) component of the scientific process. A number of topics that either are or may be related to anxiety and affective disorders are identified on pages 4 and 5. Under each heading is a list of limited problems or areas of expertise in which reasonable knowledge can be acquired in a limited time frame. Students will join a "study group" that gains knowledge in one of these general problem areas; individuals within each group are expected to become the "resident expert" on the current literature in one of the subheadings.

In the second half of the course we will begin dealing with issues for which there is no standard answer and little prior empirical or theoretical analysis. These problems are complex and undoubtedly will require combined knowledge and expertise from several areas of psychology, neurobiology, and medicine for complete understanding and analysis. At this point, you and your study group will be called upon to contribute your specific expertise to the problem at hand.

II. GRADING

A. Midterm (30%)
   Take-home, written midterm

B. Article Summaries (25%)
   1) Each student is required to provide a summary and commentary of 5 of the 10 assigned readings

C. Chapter in Final Report (35%)
   1) Each Study Group will submit a final report on their problem area. Each student will contribute a chapter on their specific area of expertise to that report. Each chapter should be approximately 15, double-spaced pages. The first two-thirds of the paper should consist of a summary of current knowledge in your specific area of expertise. One third is your analysis and application to the topic of choice

D. Class Participation (10%)
STUDY GROUP & PAPER TOPICS

I. Specificity of Fears in Anxiety Disorders
   A. Are traditional explanations for the acquisition of fears adequate?
   B. Reinstatement and Reconstituting of fears by incidental stimuli.
   C. The origin of Phobias
   D. Flashbacks: Where do they come from?
   E. Traumatic Stress and Processing in the mammalian hippocampus
   F. Treatment Issues

II. Drug Treatment for Anxiety Disorders
   A. History of Drug Treatments
   B. Benzodiazepines: Relative Effectiveness for Different Disorders
   C. Benzodiazepines: Mechanism of Action
   D. Natural Benzodiazepines
   E. Drug versus Behavioral Therapy

III. Endocrine Regulation of the Neural Stress Response
   A. Overview of SAM and HPAC responses to stress
   B. Brain Distribution and Function of Glucocorticoid Receptor Subtypes
   C. Effect of GRα Receptor Activation in Hippocampus/Frontal Cortex
   D. Dexamethasone Suppression Test (DST): Relation to Anxiety and Depression
   E. DST: Potential Mechanisms

IV. Neurodegeneration in Stress, Anxiety, & Depression.
   A. Plasticity and degeneration in hippocampal, prefrontal, and striatal neurons
   B. The Excitotoxic Cascade
   C. Why do Glucocorticoids enhance Neurodegeneration?
   D. Super-oxide radicals
   E. Neuroprotective Mechanisms: Brain Acetylcholine Function and Regulation
   F. Neuroprotective Mechanisms: Adenosine Signaling
   G. Neuroprotective Mechanisms: ATP-sensitive K+ channels

V. Psychological Mechanisms in Depression
   A. Freud
   B. Seligman: Helplessness
   C. Seligman: Optimism
   D. Personality Factors in Depression
   E. Major Illness (Injury) and Depression
   F. Comorbid Anxiety and Depression

VI. Neuroendocrine Mechanisms in Depression
A. Monoamine/(catecholamine) theory of depression
B. Brain Neurodegeneration
C. Metabolism: Thyroid Dysregulation
D. Metabolism: Adenosine Signaling and Conservation-Withdrawal
E. Plasticity: Neurotrophins
F. Plasticity: Glucocorticoid receptors

VII. Sickness Behavior and Major Depression
A. Similarities between sickness behavior and major depression
B. Incidence of major depression in critical-care patient
C. Cytokine Signaling: How is peripheral infection expressed in the brain?
D. The role of Interleukin-1β in inducing sickness behavior
E. The role of Interleukin-1β in major depression
E. Purine-cytokine interactions in major depression.

VIII. Stress Resilience
a) Mechanisms of stress resilience
b) Post-stress glucose
c) Neuropeptide Y and DHEA