Biopsychology

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Overview

Using behavioral, cognitive, and physiological techniques, the Biopsychology Department investigates brain-behavior relationships and the neurobiological and cognitive mechanisms underlying neuropsychiatric disorders. Research involves basic and preclinical studies, development and application of laboratory-based assessment, and clinical trials. The department comprises four units - Clinical Chronobiology, Psychophysiology, Temporal Cognition, and Somatosensory and Pain, as well as a training component focusing on under-represented minorities.

Current Research

Clinical Chronobiology Program

Drs. Michael and Jiuan Su Terman completed an NIMH-supported six-year study of three nonpharmaceutical treatments for seasonal affective disorder (SAD) – dawn simulation and high-density negative air ionization delivered during sleep, and post-awakening bright light therapy. The findings, published in *American Journal of Psychiatry*, indicated that all three interventions exceeded the placebo rate to low-density ions. The Termans also completed an FDA Phase I trial of a new low-dose (0.2 mg) formulation of controlled-release melatonin, designed to facilitate phase-advance shifts of the internal circadian pacemaker system without causing a direct soporific effect. Dr. Macchi completed an NINDS-supported jet lag study of light-induced circadian rhythm phase advances in preparation for travel from New York to Paris. The results were positive but

not impressive, likely due to the phase-advancing effect of natural light exposure upon arrival at the destination. Neither melatonin nor light treatment trials for jet lag adjustment have thus far proved significantly advantageous for travel across six time zones.

Psychophysiology Laboratory
Drs. Bruder, Tenke and Kayser, in collaboration with the Depression Evaluation Service (DES), continued their NIMH-funded studies of right-left brain function in depressive disorders. Most recently, they replicated prior findings suggesting the potential of electrophysiologic (EEG) measures of regional hemispheric asymmetry as predictors of therapeutic response to an SSRI antidepressant and found that these EEG predictors are reliable and stable following treatment. As part of Dr. Myrna Weissman's longitudinal, high risk study of depression, offspring with both parents having a major depression showed the same pattern of EEG alpha asymmetry seen in adolescents and adults having a depressive disorder. This supports the hypothesis that the EEG alpha asymmetry represents a trait marker of vulnerability for a familial form of depression. A study with Dr. Taylor of the DES found evidence that neuropsychological tests of psychomotor speed are also predictive of clinical response to an SSRI antidepressant. A slowing of cognitive processing may identify a subgroup of depressed patients having a dopaminergic deficit that is unresponsive to serotonin reuptake blockers.

Drs. Bruder, Tenke and Kayser, along with members of the Schizophrenia Research Unit and the Lieber Center, continued their NIMH-funded studies of brain event-related potentials and cognitive function in schizophrenia. Their latest findings provide evidence that verbal working memory deficits in schizophrenia involve a disturbance of frontal and parietotemporal processes mediating the encoding of working memory representations. A study of the genetics of working memory in a large sample of 400 healthy adults found that catechol-O-methyltransferase (COMT), a candidate gene for schizophrenia, was associated with performance on working memory tests that require higher-order mental manipulation, but not on tests that measure simple storage of information. Drs. Kayser and Tenke continued their work developing advanced techniques for processing electrophysiologic data, which are being applied in ongoing studies of schizophrenia and depression. They published a series of articles introducing new methods for measuring cortical brain potentials and their underlying generator patterns.

Temporal Cognition Unit
Dr. Malapani continues her studies of functional and neural mechanisms of time perception and temporal memory in humans as well as animals. The human research focuses on abnormalities of the time sense in patients with degenerative diseases, especially of the basal ganglia, e.g., Parkinson's disease (PD) and Huntington's disease (HD). This research seeks to both understand the basic neural mechanisms of timing and to use cognitive processing as a means of early detection and diagnosis. In collaboration with Dr. John Rinzel (New York University) and Eric Brown (post-doc) and with NSF support, Dr. Malapani has begun modeling the separable encoding and retrieval distortions in PD. Dr. Malapani and Dr. Towey pursued a new research direction this last year, studying putative deficits in temporal cognition among patients with schizophrenia (SZ). Preliminary results show that compared to normal controls (n=20) time estimates

by patients (n=29) when reproducing three target durations were, on average, equivalent in terms of time reproduction accuracy, but patients were significantly more variable than controls. Consistent with prior reports, time estimation and attentional time-sharing of SZ patients differed most from controls at the shortest time duration.

Dr. Malapani followed up her prior work with Deep Brain Stimulation in collaboration with David Hardesty, a neurologist and research fellow at PI, by incorporating timing tasks in a protocol studying PD patients with subthalamic stimulation. This study extends prior work, which showed partial recovery of timing deficits with subthalamic stimulation. Dr. Peter Balsam is now sharing in the supervision of the animal research in the lab, which is currently focused on understanding how time is learned and used to guide behavior. One current aim of this work is to help clarify the role of dopaminergic systems in timing behavior. In this NIMH and NIDA supported work, the roles of dopamine in the learning and retrieval of temporal information are being explored. In collaboration with the laboratories of Dr. Eric Kandel (Columbia), Dr. XiaoXi Zhang (University of Chicago) and Dr. Marcelo Rubenstein (University of Buenos Aires), various strains of mice with altered dopaminergic function are being studied in this ongoing research.

Dr. Michael Drew, a post-doctoral fellow who is co-sponsored by Drs. Malapani and Rene Hen, is exploring the functional significance of neurogenesis in the adult mouse brain. He has made excellent progress in characterizing the cognitive/behavioral functions that are and are not influenced by the presence of new hippocampal neurons. In recent years, the members of the temporal cognition lab have added new lines of human research aimed, in part, at translating basic science into practical application. For example, Dr. Malapani's work on the retrieval distortion associated with PD led to a new line of experiments exploring the role of distinct kinds of feedback in correcting those deficits. This research has also led to a new study that looks at the effects of dopaminergic drugs on timing distortions seen with aging, which is being conducted in collaboration with Drs. Yaakov Stern and Brian Rakitin (Sergievsky Center, Department of Neurology and Cognitive Neuroscience). Using the same timing tasks with young children, college students and healthy seniors, Dr. James Towey has begun to study how the temporal learning and memory changes across the lifespan. In a DARPA funded project in collaboration with Dr. Holly Lisanby, Dr. Balsam is studying the effects of anticipating transcranial magnetic stimulation. Additionally, Drs. Malapani and Balsam have begun to collaborate with Drs. Carl Hart and Sandra Comer (Columbia University) concerning how drugs of abuse and anticipation of these drugs affects temporal information processing.

Somatosensory and Pain Unit

Dr. Clark and his associates continued to study the dimensions underlying painful and emotional experiences. The concurrent construct validity of the 101-item Multidimensional Affect and Pain Survey (MAPS) was demonstrated in cancer patients by relating it to standard pain questionnaires. The MAPS gathers the same information as standard questionnaires, but takes much less time and is the only questionnaire objectively constructed using cluster analysis. A Chinese language version of MAPS was validated by factor analysis of responses by patients experiencing post-operative pain. A

short 30 item MAPS questionnaire was objectively developed by *item analysis* and Cronbach's alpha. They also studied gender differences in pain responses to calibrated noxious stimuli using the statistical or medical-decision making procedure. There were little or no sex differences in neurosensory sensitivity; however, the psychological parameter, report bias, was lower in women, i.e., women were less stoical. This demonstrates that studies that report women are physiologically more sensitive to noxious stimuli are incorrect because they use outmoded measures of pain. Another study demonstrated that the various strategies that individuals use to ameliorate their pain depend upon their belief in the source of pain control. Individuals who believe that they are personally responsible for managing their pain make attempts to ignore their pain, individuals who believe that fate controls their pain often fall into depression, and individuals who believe in powerful others as a source of pain control ameliorate their pain by consulting physicians. Studies with the Appropriate Pain Behavior Questionnaire revealed that Japanese men are much less willing than American men to express pain-related behavior (e.g., grimacing, complaining) in public; however a much smaller difference was found between the women of the two countries. A study conducted with Drs. Mohr (Neurology) and Wharton (Psychiatry) revealed that patients with subcortical stroke (Wallenberg Syndrome) who exhibited facial bilateral asymmetry in sensory sensitivity to calibrated stimuli were much more likely to suffer depression and post-stroke central pain than stroke patients with symmetrical sensitivity.

Education and Training

In a reach-out to the general public, Michael Terman collaborated with Swiss architect Philippe Rahm in a series of exhibitions of light and negative air ion exposure at the Swiss Cultural Center, Paris; Kunsthaus Graz, Austria; and the MAK Center's Schindler House, Los Angeles. Dr. Terman maintains frequent Web and press coverage, with recent articles on MSN.com, About.com, ScienceCentral.com, and numerous health and employee assistance magazines. With Thomas White, M.D., NYS Office of Mental Health, and Janet B.W. Williams, D.S.W., NYSPI Biometrics Research, Dr. Terman launched on an online version of the Hamilton Depression Scale on the nonprofit website of the Center for Environmental Therapeutics, www.cet.org, designed both for patient self-assessment and outpatient clinical monitoring.

Dr. James Towey continues to direct a unique training program for minority undergraduate students. Most are pre-baccalaureate NRSA fellows who received support from NIMH's Career Opportunities in Research (COR) Training Program. The main objective is to increase the diversity of doctoral-level researchers in mental health fields. Mentors for research training at Psychiatric Institute include Drs. Peter Balsam, Hector Bird, Adam Bisaga, Gerard Bruder, Madelyn Gould, Christina Hoven, Sarah Lisanby, Bruce Luber, Chara Malapani, John Martin, Michael Myers, Harry Shair and Rikki Waterhouse. Last year, NIMH granted a highly competitive renewal for this training grant, *COR Training of Mercy Scholars at Psychiatric Institute.*

Clinical Services

The Center for Light Treatment and Biological Rhythms at New York-Presbyterian Hospital, directed by the Termans, serves a broad national and international patient base with supervision of light treatment both as monotherapy and in conjunction with

medication "treatment as usual." The Psychophysiology Laboratory records clinical EEGs for inpatient and outpatient services at Psychiatric Institute.

Awards and Honors

Dr. Michael Terman received the inaugural Elliot D. Weitzman Award from the Sleep Research Society for a pharmacokinetic evaluation of his new low-dose melatonin formulation. Dr. Gerard Bruder was appointed to the editorial board of the International Journal of Psychophysiology.

Highlights

Drs. Michael and Jiuan Su Terman, in collaboration with Gregory M. Sullivan, M.D., established the first U.S. hospital-based outpatient and inpatient program for light therapy of major depressive disorder, bipolar depression and circadian sleep phase disorders.

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