



MEETING REPORT

Pharmacological Optimization of Performance

a workshop sponsored by
Division of Neuropsychiatry
Walter Reed Army Institute of Research
Washington, DC 20307-5100

A 2-day workshop on "Pharmacological Optimization of Performance" was held on 20-21 September, 1984 in Silver Spring, Maryland. Organized by CPT John Leu and sponsored by the WRAIR Division of Neuropsychiatry, the subject of the workshop was pharmacologic interventions to maintain or improve performance under conditions which normally result in serious performance decrements. The emphasis was on reducing the rate of degradation rather than improving rested optimal performance.

The workshop was organized around four topic areas, reflecting major aspects of performance subject to degradation during military operations. These were: (1) Sleep and Circadian Rhythms, (2) Memory and Cognitive Functioning, (3) Strength and Fatigue, and (4) Fear and Anxiety. A half-day session was devoted to each of the four topic areas with two invited speakers for each topic serving to set the stage for a subsequent discussion period. The agenda allowed ample time for a free-ranging discussion involving speakers from each of the topic areas as well as others in attendance at the workshop.

Workshop Goals

1. Define the problem areas.
2. Discuss criteria for evaluating potential treatments.
3. Evaluate pharmacological treatments currently available for their ability to maintain or improve performance under normally degrading conditions.
4. Evaluate scientific trends to identify those areas which appear to be most promising for further research efforts.

Sleep and Circadian Rhythms

The first morning session, chaired by Dr. Fred Hegge, began with introductory comments by COL C. Fred Tyner, Director of the WRAIR Division of Neuropsychiatry. Dr. James Krueger of the University of Chicago presented the first paper on "Neuromodulators and the Control of Sleep". Dr. Thomas Roth of the Henry Ford Hospital, Detroit Michigan next spoke on "Pharmacological Issues of Rhythm Related Sleep Disturbances".

Memory and Cognitive Functioning

The afternoon session chaired by CPT Vince O'Donnell began with Dr. Elkan Gamzu of Hoffman La-Roche speaking on "A Search for Compounds to Improve Learning and Memory". Dr. James McGaugh of the University of California, Irvine then spoke on "Modulation of Learning and Memory Storage with Drugs and Hormones".

Strength and Fatigue

The workshop resumed on the second day with a session on strength and fatigue. Chaired by LTC Gregory Belenky, the session began with Dr. John Faulkner of the University of Michigan speaking on "Maximum Physical Performance Capacity: The Limitation of Skeletal Muscle Fatigue and Injury". The session continued with a talk on "Non-thermodynamic Principles of Brain Biological Energy and Fatigue" by Dr. Arnold Mandell of the University of California, San Diego.

Fear and Anxiety

The final afternoon session, chaired by CPT Jeff Witkin, concerned the areas of fear and anxiety. The first speaker in this session was Dr. Phil Skolnick of NIH on the topic of "Anxiogenic Actions of Benzodiazepine Receptor Antagonists". The final speaker of the workshop was Dr. Duncan Taylor of Bristol-Meyers who spoke on "Nonbenzodiazepines in the Management of Fear and Anxiety".

20 September 1984

PHARMACOLOGICAL OPTIMIZATION OF PERFORMANCE
Workshop and Seminar Series

MAILING LIST OF SPEAKERS:

Sleep & Circadian Rhythms

James Krueger, PhD, Professor of Physiology, Department of Physiology and Biophysics, University of Health Sciences/ The Chicago Medical School, 3333 Green Bay Road, North Chicago, Illinois, 60064.

Thomas Roth, PhD, Director, Sleep Center, Henry Ford Hospital, Detroit, Michigan, 48202.

Clinical Professor of Psychiatry, Department of Psychiatry, University of Michigan

Memory & Cognitive Functioning

Elkan Gamzu, PhD, Research Group Chief, Department of Pharmacology, Hoffmann-La Roche Co., Nutley, New Jersey, 07110.

James McGaugh, PhD, Director, Center for the Neurobiology of Learning and Memory, University of California, Irvine, 92717.

Strength & Fatigue

John Faulkner, PhD, Professor of Physiology, Department of Physiology, University of Michigan, 48109.

Arnold Mandell, MD, Professor of Psychiatry, Department of Psychiatry, University of California, San Diego, La Jolla, California, 92093.

Fear & Anxiety

Phil Skolnick, PhD, Chief, Section on Neurobiology, NIH, 9000 Rockville Pike, Bethesda, Maryland, 20205.

Duncan Taylor, PhD, Senior Research Scientist, Pre-Clinical CNS Research Group, Bristol-Meyers Co., Evansville, Indiana, 47721.

Two primary questions will be addressed in each case:

What is the state of the art in treatment of dysfunction in these areas?

What areas of further research might be most productive in developing new or better treatments for these problems?

It is hoped that this will be an interactive session where not only the speakers but all in attendance will freely discuss the issues raised. To encourage a free ranging discussion the workshop will be limited to 56 persons, including the speakers, so please call if you must decline your invitation. Those persons planning to attend are encouraged, if at all possible, to attend the entire workshop.

Workshop coordinator and point of contact is CPT John R. Leu, Division of Neuropsychiatry, SGRD-UWI-B, Walter Reed Army Institute of Research, Washington, DC 20307-5100, (202)576-3008/2483.

Conclusions and Recommendations

- I. Sleep and Circadian Rhythms:
 - A. Triazolam, a benzodiazepine compound, should be considered as a short-acting sleeping pill, especially for use in situations requiring circadian shifts (e.g. R D F).
 - B. Benzodiazepine antagonists such as R 015-1788 should be considered for possible application as a counter-agent for "sleep inertia" induced by natural or benzodiazepine induced naps.
 - C. Time released preparations could be devised which would provide an initial release of the sleep inducing compound followed, at an appropriate time, by an antagonist.
 - D. Methylphenidate Hydrochloride (RITALIN) should be considered as a CNS stimulant with fewer undesirable side effects than amphetamines.
 - E. Differences between sleep induction, sleep prolongation, and sleep enhancement should be studied. Many sleep inducing compounds either have unknown affects on sleep quality or are known to degrade the quality and effectiveness of sleep.
 - F. Effectiveness of naps should be studied: This should included the timing, duration, and types of performance affected.
- II. Memory and Cognitive Functioning:
 - A. Naturally occurring hormones, including ACTH, epinephrine, and endorphins, play an important role in memory acquisition, consolidation and retrieval.
 - B. Training should be under conditions of physiological and emotional arousal similar to those under which the tasks are likely to be performed.
 - C. Consideration must be given to performance variables: These include: attention and perception, motivation, degree and type of required response, and task complexity. Both the magnitude and direction of drug effects in animals depend on these variables as well as dose level.
 - D. No currently known pharmacologic compounds appear to be useful in improving functioning in rested, normal individuals. There are however a number of agents which have been shown to improve functioning in aged or dysfunctional individuals; their effectiveness in improving degraded performance in normals has not been systematically studied.
- III. Strength and Fatigue:
 - A. Exercise prescriptions: Train for the task; If the goal is to be able to march long distances in boots with pack, train by doing that, not jogging in sweats and running shoes. This not only trains the specific muscle motor units involved but also improves the cortical motor and cerebellar modulation of movement.
 - B. Effects of various methylxanthines on fatigue should be studied systematically.
 - C. Research should be encouraged to determine what it is about exercise that increases strength and causes beneficial muscle hypertrophy. Possible applications could lead to physiological treatments to maintain or improve strength and prevent muscle atrophy.
 - D. Studies should address the question of increasing the duration of acceptable levels of performance, as opposed to improving short-term optimal levels.
- IV. Fear and Anxiety:
 - A. Distinctions between "fear" and "anxiety" should be studied with a goal to determining underlying physiological differences between the two states.
 - B. Buspirone or related compounds should be studied as a potential "anxiety" reducing compounds.
 - C. Short acting benzodiazepines might be considered for forward treatment of battle-stress casualties; perhaps serving the dual function of reducing anxiety and providing needed restful sleep.
 - D. Propanolol or related compounds might be considered for use during some training situations (such as markmanship).
- V. Consultants:

Strongly recommend that Dr. Elkan Gamzu of Hoffmann-LaRoche and Dr. John Faulkner of the University of Michigan be retained as consultants or considered for research funding.