

27

with me +
Jones

Brave Pill

I. Anxiety and Fear

A. General Considerations

B. Psychology

C. Physiology

D. Pharmacology

1. Benzodiazepines

a. general effects

b. mechanisms

2. Non-benzodiazepines

a. general effects

b. mechanisms

II. Pharmacological Treatment/Prevention

A. General Considerations

B. Tolerance

C. Dependence

D. Drug Interactions

E. Potential Antagonists

III. Other Methods of Treatment/Prevention

IV. Conclusions and Recommendations

Dir WPAIR

Dir Div NP

1 March 1984

We have established in Div NP a Psychopharmacology Study Group to assess both theoretical and practical aspects of the pharmacologic alteration of human behavior in military contexts. The group will consider three general topics:

- A. Performance Enhancement: use of chemicals to improve the performance of normal individuals by increasing capacity or by delaying the onset of degradation under stress.
- B. Casualty Management: use of chemicals in the casualty management process.
- C. Threat Assessment/Defense: offensive use of behavior-altering chemicals.

The group will seek data from open scientific and clinical publications, drug companies, the sports medicine community, other military services and federal agencies, intelligence sources, and elsewhere. The group's goal will be to gather and analyze data, and generate informed speculation, for a variety of purposes.

Membership:

CPT Vincent O'Donnell, MSC, Chmn	Dept Behav. Biology
LTC Gregory Belenky, MC	Dept Behav. Biology
Dr. Frederick Hegge	Dept. Behav. Biology
Dr. Jean-Kant	Dept Med. Neurosci.
CPT John Lev, MSC	Dept Med. Neurosci.
Dr. Frank Tortello	Dept. Med. Neurosci.
CPT Jeffrey Witkin, MSC	Dept. Med. Neurosci.

These individuals have experience and interest in experimental and applied psychopharmacology, brain mechanisms, military field research and operations, and human use issues.

The work will initially incur only modest expense and will be supported by existing Div NP funds (MRDC Research Area III). Additional support may be sought subsequently, however; the most likely near-term use for such funds being to expand the literature collection process.

This effort has potentially significant relations with the MRDC chemical defense program: A) the offensive use of behavior-altering chemicals is a direct CW issue, although not one currently receiving much attention. B) The MRDC has chartered a tri-service joint working group (Dr. F.W. Hegge, chmn.) to design screening procedures for evaluating the impact of CW prophylactic/pre-treatment drugs on military performance; this group's screening plan would be an excellent conceptual scheme to aid the collection and evaluation of information.

MINUTES

PSYCHOPHARMACOLOGY STUDY GROUP

2 MARCH 1984

1. The Psychopharmacology Study Group met at 1030 on 2 March 1984 in the Behavioral Biology Conference Room, Bldg. 189, Forest Glenn Annex.

2. Present at the meeting were:

CPT Vince O'Donnell, Chairman	Dept. Behav. Biology
LTC Gregg Belenky	Dept. Behav. Biology
Mr. Gary Harding	Dept. Behav. Biology
Dr. Frederick Hegge	Dept. Behav. Biology
COL Frank Jones	Dept. Milit. Psychiatry
Dr. Jean Kant	Dept. Med. Neurosci.
CPT John Leu	Dept. Med. Neurosci.
MAJ Rick Manning	Div. of NP
Dr. Frank Tortella	Dept. Med. Neurosci.
COL Fred Tyner	Div. of NP
CPT Jeffrey Witkin	Dept. Med. Neurosci.

3. COL Tyner discussed the reasons for forming the committee, which include the gathering and dissemination of information relevant to the use of chemicals for performance enhancement, drug treatment of psychiatric casualties, and the threat of psychoactive chemicals being used against U.S. troops. Implicit in the concept of performance enhancement is the prevention of performance degradation.

COL Tyner also requested that group members review his draft DF to Director, WRAIR regarding the group, and to provide him with any suggestions on its content.

4. A brief discussion was held regarding the organization and function of the study group. It was agreed that membership would be open to interested parties and that minutes would be prepared by the chairman for the internal use of the group.

5. The group discussed topics for future meetings. A high priority for initial activities was placed on the familiarization of group members with sources of relevant information. Such sources include the intelligence community, COL Camp of Military Psychiatry on combat casualty management in Viet Nam, MAJ Terry Fullerton of Military Psychiatry on Sports Medicine, other Armed Services investigators, the WRAIR Foreign Area Activities Officer, and WRAIR library personnel. Dr. Kant stated that studies have been undertaken in England on pharmacological enhancement of performance especially with regard to benzodiazepines and caffeine.

6. With regard to the dissemination of available information, the group discussed the possibility of publishing an overview on the general area or select topics. LTC Belenky mentioned his interest in the use of L-DOPA as a candidate for a performance enhancing drug; MAJ Manning indicated that the committee might concern itself with issues of performance assessment as well as developing a list of candidate drugs.

7. CPT O'Donnell requested that members circulate material of interest among the committee. COL Jones indicated that he would provide a recent article that he has written on performance enhancing drugs.

8. Members of the group will meet with representatives of AFMID on Monday, 5

DRAFT MINUTES

PSYCHOPHARMACOLOGY STUDY GROUP

9 MARCH 1984

1. The Psychopharmacology Study Group met at 1330 on 9 March 1984 in the Behavioral Biology Conference Room, Bldg. 189, Forest Glenn Annex.

2. Present at the meeting were:

CPT Vince O'Donnell, Chairman	Dept. Behav. Biology
LTC Gregg Belenky	Dept. Behav. Biology
CPT Ned Bernton	Dept. Med. Neurosci.
Dr. Frederick Hegge	Dept. Behav. Biology
COL Frank Jones	Dept. Milit. Psychiatry
Dr. Jean Kant	Dept. Med. Neurosci.
CPT John Leu	Dept. Med. Neurosci.
MAJ Rick Manning	Div. of NP
Dr. David Thorne	Dept. Behav. Biology
Dr. Frank Tortella	Dept. Med. Neurosci.
COL Fred Tyner	Div. of NP
Mr. Peyton Williams	Headquarters, WRAIR
CPT Jeffrey Witkin	Dept. Med. Neurosci.

3. The minutes of the previous meeting were read and approved with a minor change.

4. Mr. Peyton Williams presented a description of areas in which he can provide assistance on matters relevant to the study group. He is able to provide access to a wide variety of materials, e.g. trip reports, classified documents, MRDC HQ reports, and reports from the intelligence community.

5. Dr. Frederick Hegge discussed the role of the Military Performance Working Group of the USAMRDC Research Area V. That group is developing testing procedures to determine the behavioral effects of chemical treatment and pretreatment drugs. Evaluation of such behavioral effects will be conducted using information from Phase I clinical testing, from studies with neuropsychological and performance assessment batteries, and ultimately from field studies using military system simulators.

Dr. Hegge noted that there are currently at least 32 military systems within the Army alone judged to have high priority for the determination of chemical defense drug impact. With an initial estimate of about 16 drugs to be evaluated for potential chemical defense use, it becomes clear that individual testing of each candidate drug at multiple dose levels under a variety of operational conditions on all important military systems is not feasible. By constructing a chain of successive validations extending from a performance assessment battery to actual military operations, a valid, reliable, and economical test system will ultimately be available.

Dr. Hegge noted that the peripherally acting anticholinesterase pyridostigmine is the leading candidate for a pre-exposure drug, and that atropine and 2-PAM chloride will probably be used for calibration of test batteries.

6. CPT O'Donnell presented a discussion of several computerized data bases relevant to the work of the group. The Chemical Agent Retrieval System (CARS) is operated on contract from the Institute of Chemical Defense. It is particularly oriented toward literature on offensive chemical agents and covers technical reports as well as literature from professional journals. Dr. Brennie Hackley of ICD is the point of contact for individuals wishing to use the system (301-671-2455).

A second system is the Chemical Defense Data Base (CDDDB) managed from Wright-Patterson Air Force Base. This system contains relatively few articles from professional journals; most of its references are technical reports. Point of contact for access to this system is Mrs. Karen Unfried (513-255-2870 or Autovon 785-2870).

CPT O'Donnell discussed the Chem Neuropsych Biblio system which he is currently compiling. The system is a collection of references in the general topic area of neurochemistry and behavior. References may be selected using logical combinations of assigned keywords. The references have been formatted for use with a CPM software program and are stored on small floppy discs for use with CPM base microcomputers. The first full version of the system will contain approximately 2500 references and is scheduled to be released on 1 Aug 1984. A pilot version will be ready for release within the next several weeks; that version will contain approximately 800 references. Those interested in receiving the pilot version should contact CPT O'Donnell.

The representative of the WRAIR library scheduled for a presentation was unable to attend. CPT O'Donnell indicated that he had received a brochure on the data bases accessible through the WRAIR library and that copies of that brochure could be obtained from library personnel.

7. LTC Belenky discussed the existence of \$32,000 in ILIR funds assigned to the Dept. of Med. Neurosciences for the study of performance enhancement and fatigue.

8. The group discussed the question of what its goals and functions should be. A list of 15 possible functions was compiled. Members were requested to review this list and to be prepared to narrow it down at the next meeting.

9. Dr. Kant raised the question of how often the group would meet. Discussion of the question produced the opinion that fairly frequent meetings would be necessary until specific committee goals had been established, and that after that point less frequent meetings accompanied by individual and subcommittee projects would probably be the rule.

10. It was agreed that the group would next meet on 20 March 1983 at 1330 in the Behavioral Biology Conference Room.

11. The meeting adjourned at 1535.

DISPOSITION FORM

For use of this form, see AR 340-15; the proponent agency is TAGO.

REFERENCE OR OFFICE SYMBOL

SUBJECT

SGRD-UWI-B

Psychopharmacology Study Group: Directions

TO

FROM

DATE

CMT 1

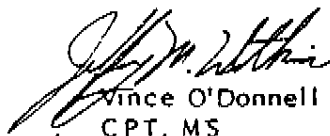
WRAIR Psychopharmacology
Study Group

Vince O'Donnell
CPT, MS

12 MAR 84
vd/427-5521

1. Please consider the following suggested directions for future activities of the Study Group:
 - a. Individual efforts for specific topics
 - b. Educational meetings
 - c. Publication of documents/reviews
 - d. Promote research
 - e. Recommend directions
 - f. Monitor literature and developments and intelligence
 - g. Evaluate intelligence
 - h. Clinical recommendations on combat medicine
 - i. Evaluate 'state of the art' on drugs and attitudes toward use
 - j. Outside speakers brought in
 - k. Broaden approach of group (eg. training, direct other groups)
 - l. Evaluate overall drug philosophy
 - m. Recommend methodologies
 - n. Examine physiology of performance degradation (eg. fatigue, stress)

2. These suggestions (also deletions and/or additions) will be open for discussion in our next meeting of 20 MAR 84 in order to establish a focused direction for the group.


Vince O'Donnell
CPT, MS
for Chairman

PSYCHOPHARMACOLOGY STUDY GROUP

20 MARCH 1984

1. The Psychopharmacology Study Group met at 1330 on 20 March 1984 in the Behavioral Biology Conference Room, Bldg. 189, Forest Glenn Annex.

2. Present at the meeting were:

CPT Vince O'Donnell, Chairman	Dept. Behav. Biology
LTC Gregg Belenky	Dept. Behav. Biology
Dr. Frederick Hegge	Dept. Behav. Biology
COL Frank Jones	Dept. Milit. Psychiatry
Dr. Jean Kant	Dept. Med. Neurosci.
CPT John Leu	Dept. Med. Neurosci.
MAJ Rick Manning	Div. of NP
Dr. Frank Tortella	Dept. Med. Neurosci.
COL Fred Tyner	Div. of NP
CPT Jeffrey Witkin	Dept. Med. Neurosci.

3. COL Tyner presented a condensation of the list of potential group goals and functions discussed at the previous meeting. This condensation was:

I. EDUCATE

- Lit reviews
- Speakers
- Documents written

II. SUPPORT RESEARCH

- In-house
- Funding to other agencies
- RFQ's/RFP's

III. EVALUATE INTELLIGENCE

- As requested
- Our initiative

The group agreed that this condensation of the previously developed function list was an appropriate starting point for further discussion of the group's role.

4. In discussing COL Tyner's list of group functions, it was suggested that all of the specific functions listed except 'as-requested' evaluation of intelligence and guest speakers might flow naturally from the group's preparation of a document or several documents. COL Tyner noted the need to bear in mind that documents should be prepared for a specific target audience. The target audience would govern the length, scope, and format of the documents.

CPT O'Donnell requested that group members prepare a summary of the contents of documents which they believe the group should write. Such a summary could be in the form of a "table of contents" or even a description of specific topics that individual group members are interested in addressing. COL Tyner stated that these summaries should also contain recommendations on the format and intended audience of the documents. CPT O'Donnell requested that group members prepare these summaries and distribute them to all other group members within the next two weeks to facilitate discussion of the documents at the next meeting.

5. LTC Belenky questioned whether the group should expand its focus to include other aspects of military performance such as training, diet, sleep discipline etc. After discussion, it was determined that psychopharmacology alone presented a formidable scope of material for the committee to deal with and that enlargement of the committee's focus beyond that area would be impractical at present. It was stressed however that the committee will have to deal continually with other topic areas in addressing psychopharmacologic issues.

6. CPT Witkin indicated his belief that the group needed to get a clear idea of what other organizations were doing in this area so that we would not needlessly duplicate ongoing work. In response, Dr. Hegge indicated that his Joint Working Group (JWG) differed from the Study Group in several areas besides its concentration on the area of chemical defense. He noted that the JWG does not recommend the use of particular drugs and that its function is restricted to the development of a tool, i.e., a behavioral assessment system.

CPT Witkin indicated that the Psychopharmacology Study Group would do well to coordinate with other ongoing research efforts in the future, especially those in other services.

7. Dr. Tortella emphasized the need for the group members to actively provide for the group's education. He noted that the group's function would cover a wide variety of areas including military applications, and that most group members would be familiar only with restricted parts of the group's overall effort. Recognizing the need for continued education of the group, it was decided to provide regular presentations from experts within and outside of the group. CPT Leu will arrange for such presentations beginning in May. CPT Leu requested that group members provide him with input as to topic areas and specific speakers that would be appropriate.

8. The next meeting of the group was set for 1330 on 17 April 1984 in the Dept. of Behavioral Biology Conference Room. At that meeting the group will define the documents it will produce and establish the priority for the production of these documents.

9. The meeting adjourned at 1500.

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6 MARCH 1984

TO: PSYCHOPHARMACOLOGY STUDY GROUP

FROM: CHAIRMAN, PSYCHOPHARMACOLOGY STUDY GROUP

1. Please review the attached draft of minutes from the meeting of 2 March 1984 and bring suggested changes to the next meeting.

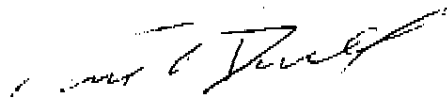
2. Also attached is an agenda for our next meeting. Feel free to contact me for inclusion of other items.

3. I would like to introduce a few concepts for future discussions. First, the group may well find itself viewed as an information resource by a variety of agencies. Would it be worthwhile for members to take on specific areas of interest which they would endeavor to monitor? While this might be merely an extension of their current interest, it would, at worst, enable the group to have a realistic impression of what its limitations are. At best, it would provide a well delineated list of topics that the group could expect to provide information on.

Second, two personal biases of mine are that you do not muck about with CNS neurochemistry without causing wide ranging behavioral effects, only some of which are desirable (see the attached article by Lennard et. al.), and that various "undesirable" behavioral constructs like fatigue and forgetting represent integral subsystems of the organism which have evolved because they are of some value. From the latter, it follows that when we attempt to change a behavioral construct, in alleviating fatigue for example, we may be introducing wide ranging changes in the organism's behavioral systems.

I am suggesting that if one accepts these biases, it follows that a vital function for the committee would be to clarify the total spectrum of effects arising from use of psychochemical agents. Such a clarification is necessary for the combat commander to make a rational decision regarding the use of such agents. Indeed, the realization that psychoactive drugs are not "magic bullets" needs to be brought about at many levels. On the other hand, the decision to push a product without a consideration of its negative effects creates the potential for serious problems down the road, the history of drug development being replete with examples.

I present these ideas merely as springboards for discussion and hope they will induce some spirited debate at future meetings.


Vince O'Donnell
DPT, PhD
Research Psychologist

17 APRIL 1984

1. The Psychopharmacology Study Group met at 1330 on 17 April 1984 in the Behavioral Biology Conference Room.

2. Present at the meeting were:

CPT Vince O'Donnell, Chairman	Dept. Behav. Biology
LTC G. L. Belenky	Dept. Behav. Biology
Dr. Frederick Hegge	Dept. Behav. Biology
COL Frank Jones	Dept. Milit. Psychiatry
Dr. Jean Kant	Dept. Med. Neurosci.
CPT John Leu	Dept. Med. Neurosci.
Dr. Frank Tortella	Dept. Med. Neurosci.
COL Fred Tyner	Div. of NP
CPT Jeffrey Witkin	Dept. Med. Neurosci.

3. The minutes of the previous two meetings were approved as written.

4. CPT Leu reported on his efforts to arrange for presentations by guest speakers. On 21 June, Dr. Ethan R. Nadel will present on the topic, "What Limits Physical Exercise?". Dr. Raymond Bartus will give a talk in September on the pharmacological enhancement of memory. Consideration is being given to inviting Drs. Wilsie Webb, Oakley Ray, and James M. Kruger to speak on sleep research. Speakers will also be invited for the topic of psychopharmacology and fear. CPT Leu would welcome input on desirable speakers for that topic.

5. In accordance with suggestions by Drs. Kant and Witkin, members are requested to circulate materials of interest, especially notices of relevant professional conferences. CPT O'Donnell will maintain a file of trip reports and other documents relevant to the work of the committee which are not typically collected in a single repository. Members having such documents are requested to forward a copy to CPT O'Donnell.

6. It was agreed that committee members will endeavor to develop a degree of expertise on particular topic areas. These topic areas and the committee members responsible for each are listed below:

EMOTIONS (anxiety, fear, aggression, bravery etc.)

COL Jones
CPT Witkin

COGNITION

CPT Leu
CPT O'Donnell

SLEEP/WAKE

Dr. Hegge
Dr. Tortella
COL Tyner

ENDURANCE/STRENGTH

LTC Belenky
Dr. Kant

7. It was agreed that the committee's initial document will be geared toward a TRADOC/line officer audience and will be organized according to the areas of concentration listed in paragraph 6 above. The individuals listed under each area, along with other interested parties, will produce an outline of the material they consider suitable for their portion of the document. Outlines will be reviewed at the next meeting of the committee. COL Tyner and CPT D'Donnell will also provide an outline for an introductory section of the document.

8. COL Tyner noted the possibility for future administrative support for the committee being provided through a contract.

9. The next meeting of the committee will be held on 12 June 1984 at 1330 in the Behavioral Biology Conference Room.

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DRAFT MINUTES
PSYCHOPHARMACOLOGY STUDY GROUP

12 JUNE 1984

1. The Psychopharmacology Study Group met at 1345 on 12 June 1984 in the Behavioral Biology Conference Room.

2. Present at the meeting were:

CPT Vince O'Donnell, Chairman	Dept. Behav. Biology
LTC G. L. Belenky	Dept. Behav. Biology
CDL Frank Jones	Dept. Milit. Psychiatry
Dr. Jean Kant	Dept. Med. Neurosci.
MAJ (R) Rick Manning	Div. of NP
Dr. Frank Tortella	Dept. Med. Neurosci.
CPT Jeffrey Witkin	Dept. Med. Neurosci.

3. The minutes of the previous meeting were approved as written.

4. The committee reviewed a videotape of research on an opioid-like hibernation induction trigger. This videotape had been sent to MRDC as a research preproposal and was forwarded to the committee for evaluation. It was noted that the tape did not propose any further work, but merely reviewed some studies in one laboratory. Dr. Tortella discussed some work on the hibernation induction trigger that has been performed by other researchers. The committee recommended that an actual written pre-proposal containing an outline of proposed work be prepared for further evaluation. CPT O'Donnell noted that accompanying documents from MRDC might restrict the committee's recommendation to either support for the preparation of a full proposal or rejection of the preproposal. The committee agreed that if only these two options for recommendation were available, that a recommendation for preparation of a full proposal would be appropriate.

5. The committee discussed several aspects of the preparation of the document on drugs for performance enhancement and casualty care management. The following points were agreed upon:

a. The four chapter titles previously discussed would be used, although some acknowledgement of their oversimplified nature might be appropriate in the text.