



**A Comparison of Sleep Scored
From Electroencephalography
to Sleep Scored by Wrist Actigraphy**

By

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and

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Biomedical Applications Research Division

September 1993

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Fort Rucker, Alabama 36362-5292**

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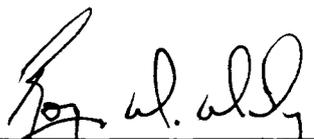
Human subjects participated in these studies after giving their free and informed voluntary consent. Investigators adhered to AR 70-25 and USAMRDC Reg 70-25 on Use of Volunteers in Research.

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Introduction

During military operations, it has been found that soldiers often are required to work for long periods of time without rest. The lack of sleep experienced by soldiers degrades their ability to perform their duties efficiently, correctly, and, in some cases, safely. In order to assist commanders in determining how much rest soldiers receive, various methods of monitoring activity have been used. One unobtrusive method is to use wrist activity monitors (WAMs) to determine how long soldiers are required to work with little or no sleep. Although the WAMs appear to be able to accurately assess both work and sleep, the monitors currently being used by the Army have not been compared to EEG records where one can readily determine when a person is asleep and when he is awake. Before one can satisfactorily use the WAMs in the field for sleep assessments, a reliability study is necessary to determine if the monitors accurately discriminate awake from asleep activity.

The usual method of discriminating an awake state from an asleep state is by an electroencephalograph (EEG). This method involves attaching at least eight electrodes to the head with collodion and recording the electrical signals from the brain through amplifiers using a physiograph which produces a paper record of the data. A paper record of 8 hours of sleep is approximately 900 pages. In order to analyze these data, each of these 30-second pages are scored for stage of sleep--either awake, stage 1, stage 2, slow wave sleep (stages 3 and 4), or rapid eye movement (REM) sleep. Unfortunately, the use of EEG is both time consuming and expensive for the researcher and intrusive for the person being monitored. In addition, it is almost impossible to use with soldiers in a field environment because of the equipment required. Therefore, in order to assess rest and activity of people in a field environment, an alternative method to standard sleep recordings is needed.

A few researchers have compared EEG recordings with various types of wrist activity monitors and have determined there is a high correlation between the two measures. Mullaney, Kripke, and Messin (1980) collected EEGs and activity data from 102 subjects--63 nonpatients and 39 patients. The results of their recordings indicated sleep/wake estimations from EEGs and WAMs were in agreement in 94.5 percent of the 1-minute epochs. Their correlations for EEG sleep measures and actigraph measures were 0.90 for the time subjects were in bed, 0.89 for the time the subjects were asleep, 0.70 for awake time after sleep onset, and 0.25 for the number of midsleep awakenings. Usually the actigraph overestimated sleep time and missed several awakenings during the night. However, the actigraph measures were considered a good overall measure of sleep when the cost in time and simplicity were

compared to the effort and complexity required to obtain an EEG record of sleep.

Borbely (1986) also compared wrist activity to an EEG record to determine how well sleep could be estimated with the WAMs. He concluded that the WAM was a good noninvasive way to monitor sleep over a long period of time; however, the measure only approximates the amount of sleep time and cannot be used to determine the quality of sleep.

In summary, there appears to be a high correlation between EEG and actigraph measures. Thus, the potential for obtaining reasonable estimates of the amount of sleep based on wrist activity data is good. However, the method of scoring sleep from the WAM data remains varied.

In the earlier studies, most of the WAM data were scored based on a "best guess" to determine awake from sleep activity (Kripke et al., 1978; Mullaney, Kripke, and Messin, 1980; Borbely, 1986). Later, researchers developed automatic scoring systems for wrist activity data which relied less on subjective interpretations of the data. These scoring algorithms, discussed by Hauri and Wisbey (1992), initially use a computer to score sleep based on number of actigraph counts per epoch, but then require human judgement to derive the final determination of sleep vs awake. For example, one scoring algorithm developed by Webster and colleagues (1982) consists of the following: 1) after at least 4 minutes of data are scored as awake, the first 1 minute of data that looks like sleep is rescored as awake; 2) after at least 10 minutes of data are scored as awake, the first 3 minutes that look like sleep are rescored as awake; 3) after at least 15 minutes of data are scored as awake, the first 4 minutes of data that look like sleep are rescored as awake; 4) 6 minutes or less of data scored as sleep that are surrounded by at least 10 minutes, both before and after, of epochs scored awake are rescored awake; 5) 10 minutes or less that would be scored as sleep surrounded by at least 20 minutes, both before and after, of epochs scored as awake are rescored as awake. This is probably the most complex scoring method in use. Another scoring system, written into a computer program called Sleepest, has three options: 1) score each epoch as either awake or asleep regardless of what precedes or follows it; 2) score each epoch as either awake or asleep, but after at least 4 minutes of data scored awake, the first 1 minute of data that looks like sleep is rescored as awake; and 3) the same as the preceding method with the inclusion of the criteria that after at least 10 minutes of data scored as awake, the first 3 minutes that look like sleep are rescored as awake.

Sadeh and colleagues (1989) used a scoring method which involved examination of the number of zero threshold crossings in

each 1-minute epoch to determine awake and asleep. A discriminant analysis was used to validate this scoring procedure. Their results indicated a high degree of reliability in using wrist activity data to determine wake from sleep, even in clinical populations.

One of the wrist monitors currently in use by the Army has an automatic scoring program based on number of counts calculated per epoch (usually 30 seconds) which is similar to the first option described in the program Sleepst discussed above. After the results are calculated, the researcher reviews the scored data and subjectively corrects any obvious misscorings. For example, when the wrist monitor is taken off for the person to shower, the automatic scoring program scores this period as asleep since there are no movements. In this case, the researcher rescores the data as awake. This scoring method seems to work well; however, validation work is required to substantiate the existence of a reliable relationship between actigraph measures and EEG measures of sleep based on this scoring system.

Method

Subjects

Six subjects were recruited from the employees at the U.S. Army Aeromedical Research Laboratory. The data reported here were collected as part of a study to determine the ability of two different sleeping pills to aid daytime sleep. Each subject was informed about the purpose and the procedures of the study at the outset. The subject was told that participation was voluntary and that he/she could withdraw at any time without penalty. Any hazards associated with any of the procedures were explained fully to the subject both verbally and in writing, and after the consent form was signed (See Appendix A), the subject officially was admitted.

Apparatus

Grass* silver silver/chloride electrodes were used to record electrical activity from the brain (EEG), muscles (EMG), and eyes (EOG). The signals were recorded by a Nihon Koden* model EEG-4321P polygraph. EEGs were recorded from standard sites C₃, C₄, O₁, and O₂ referenced to the contralateral mastoids using Grass* E5SH silver cup electrodes. The high pass filter was set at 1 Hz and the low pass filter was set at 35 Hz. EOG was recorded from the outer canthus of each eye. The high pass filter was set at 0.3 Hz and the low pass filter was set at 10 Hz. Submental EMG

* See Appendix B for manufacturers' list.

was recorded with a high pass filter of 10 Hz and a low pass filter of 120 Hz. The 60 Hz notch filter was not used except when absolutely necessary. The paper speed was set at 10 mm per second. Collected data were recorded on standard paper traces for later analysis. (See Figure 1.)

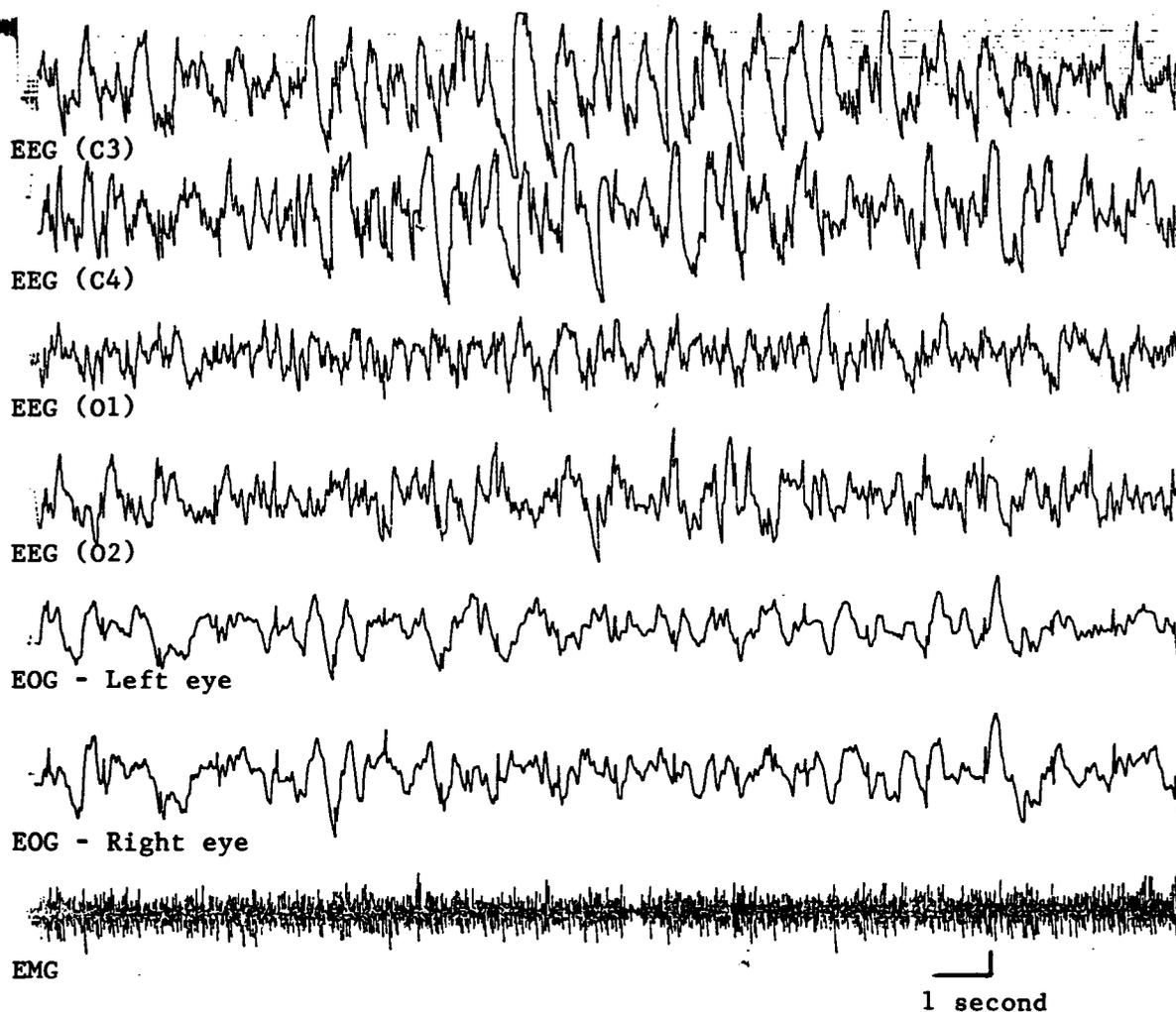


Figure 1. A sample of EEG sleep data.

The wrist activity monitor (WAM) used in this study was specifically designed by Precision Control Design* (PCD) for field studies in order to measure the activity level of soldiers during continuous operations. (See Figure 2.) The exact design and specifications are explained by Redmond and Hegge (1985). The monitor weighs 3.5 oz and is affixed by two Velcro® straps to the nondominant wrist. The monitor records movements of the arm by a piezo-electric bender element. A low power computer chip records the number of activity counts per epoch and stores the data into a 16K resident memory. The data were transferred to a computer through an RS-232 link for future analysis. (See Figure 3.)

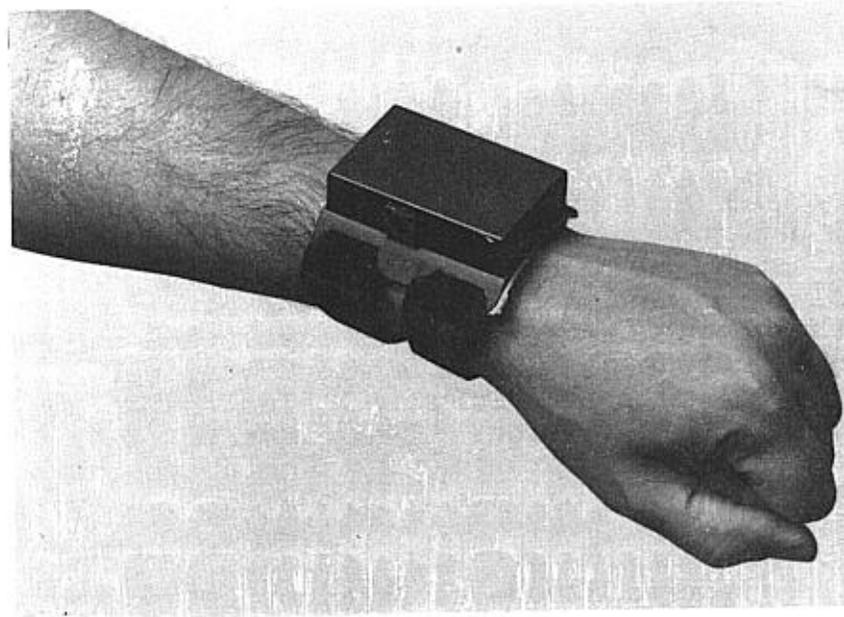


Figure 2. The wrist activity monitor (WAM).

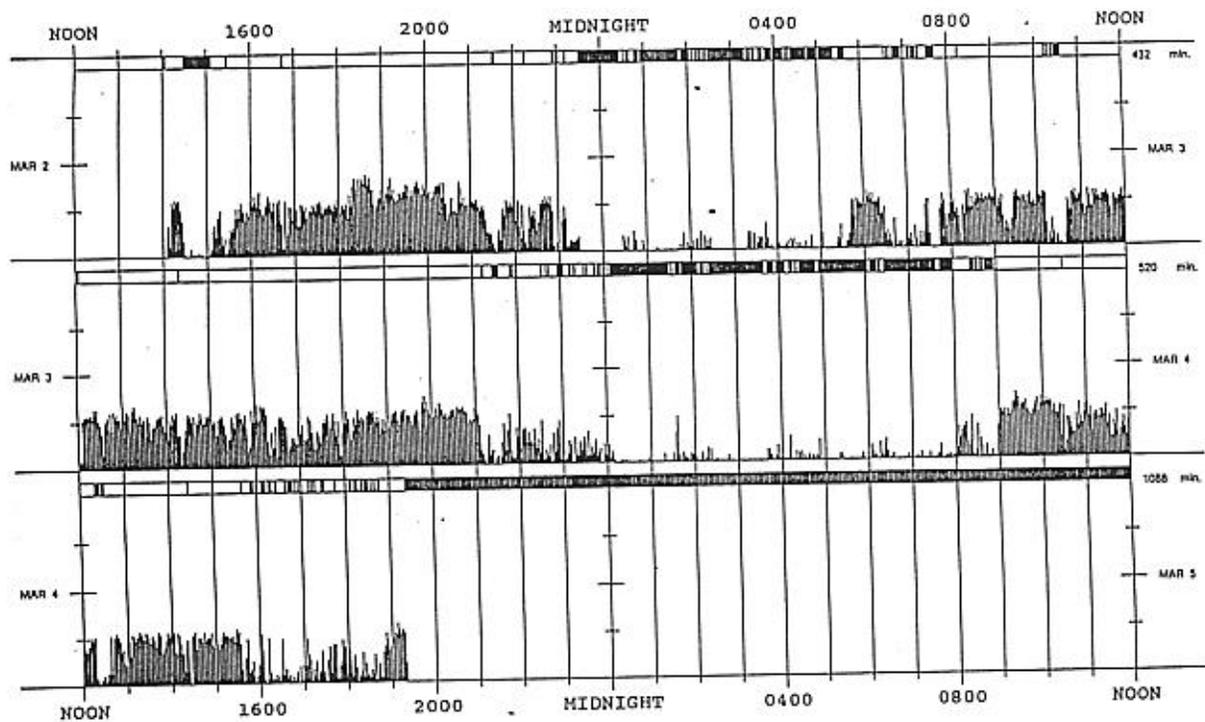


Figure 3. Graphed activity data from the WAM.

Procedure

Subjects came to the laboratory at 0730 for electrode application. They were seated in a chair while the technicians measured for the electrode placements. EEG electrodes were placed at C₃, C₄, O₁, and O₂, according to the International 10-20 System. Acetone was used to reduce the impedance of the placement sites to below 10,000 Ohms, as recommended by Rechtschaffen and Kales (1968). Collodion was used to ensure the electrodes remained in place for the length of the study (2 days), and each electrode was filled with electrode gel. Active electrodes were referenced to the contralateral mastoid. Submental electromyography (EMG) was used to record muscle tension. Eye movements (EOG) were recorded from electrodes placed approximately 1 cm above the outer canthus of the left eye and approximately 1 cm below the outer canthus of the right eye.

Once the electrodes were satisfactorily applied, the wrist activity monitor was strapped to the subject's nondominant wrist. The clock on the WAM and the clock on the polygraph were synchronized to within 2 seconds in order to match the time base as much as possible using a separate clock for each device. The subject then was escorted to a private bedroom in the Laboratory and permitted to sleep. Lights out was at 0830. After at least 1.5 hours of sleep, the subject was awakened and performed cognitive tasks at a computer terminal for 30 minutes. Afterward, he/she returned to bed until he/she was awakened at 1700. If the subject woke up before 1700 and could not return to sleep, he/she was allowed to end the sleep period. Data were recorded for 2 consecutive days. The electrodes were removed each evening before the subject left the Laboratory, and the WAM was removed the afternoon following the second day of recording.

Data analysis

Each 30-second epoch of each polysomnograph was scored by three trained sleep scorers following the guidelines set forth by Rechtschaffen and Kales (1968). The wrist activity data were scored by computer program which yielded activity counts per 30-second epoch. Data from the EEG and the WAMs were calculated across the entire sleep period. These data then were subjected to a discriminant analysis to classify the wrist activity data into awake and asleep categories based on the already scored EEG data, which was used to indicate whether the subject was either awake (epochs scored as awake or movement time) or asleep (stages 1, 2, 3, 4, and REM sleep). Based on the epochs of activity data classified as either awake or asleep from the discriminant analysis, a cutoff score based on the number of counts per 30-second epoch was determined and used in a scoring algorithm to then rescore the wrist activity data as either awake or asleep.

The number of minutes awake, number of minutes asleep, sleep onset time, number of minutes awake after sleep onset, and wakeup time then were scored from both the EEG and the WAM data, using the classification of awake and asleep from the discriminant analysis. The percent agreement for the number of epochs scored as awake and asleep by both sets of data then was calculated to determine the accuracy of the WAM in measuring sleep.

A second discriminant analysis was conducted in order to determine if the WAM data could be correctly classified into each of the appropriate individual stages of sleep. WAM counts were used to classify data into the categories of awake, sleep stages 1 through 4, REM sleep, and movement time as determined by the scored EEG data. Finally, correlations between EEG and WAM data for sleep onset time, wake-up time, time awake after sleep onset, and time asleep after sleep onset were calculated.

Results

Due to technical problems, the first two subjects' WAM data were lost. Therefore, only four subjects' data were analyzed. The first discriminant analysis classified the WAM data into two groups, either awake or asleep, and accuracy was determined by comparing agreement between this classification and the one based on the EEG data. The percent of correct classifications of WAM data was 61.9 percent for the awake time, and 94.1 percent for the sleep time, giving an overall correct classification of 88.8 percent. This classification function indicated that counts on the WAM from 0 to 41 were classified as asleep, and counts higher than 41 were classified as awake.

After the cutoff value of 41 for sleep was determined by the discriminant analysis, the automatic scoring program for the WAM data was used to score the data as either awake or asleep using this value. Percent agreement for each subject's data (EEG vs activity) then was computed. The highest agreement for any subject's data was 97.6 percent, with the lowest agreement being 79.9 percent. The average percent agreement for all the subjects for both days was 88.7 percent (sd=6.2).

Several comparisons of sleep time were made to determine agreement between the WAM and the EEG measures of sleep (Table 1). Sleep onset time (time from lights out to first epoch of stage 1) was calculated using both EEG and WAM. The average disagreement between these two methods was 3.1 minutes (sd=3.4), with the WAM indicating a shorter sleep onset time than the EEG. Wakeup time also was calculated using both methods. The average disagreement for this measure was 7.3 minutes (sd=10.9), with the WAM usually showing a slightly later wakeup time than the EEG. Agreement for number of minutes awake after sleep onset also was calculated.

The WAM tended to underestimate the amount of wake time after sleep onset, indicating an average of 29.4 minutes (sd=29.7) more sleep after sleep onset than was determined by the EEG. The amount of sleep calculated after sleep onset also was overestimated by the WAM, where the WAM indicated an average of 38.9 minutes (sd=32.8) more sleep than measured by the EEG.

Table 1.
Difference in sleep parameters scored by WAM and EEG.

Subject	Day	Sleep+ onset	Wakeup+	Sleep+ after sleep onset	Wake+ after sleep onset
3	1	0.5	0.0	1.5	- 4.0
3	2	0.0	1.5	13.5	-13.5
4	1	0.0	31.0	60.5	-60.5
4	2	1.0	0.5	23.5	-24.5
5	1	6.5	-1.5	-5.5	- 1.5
5	2	9.5	1.5	-88.5	93.0
6	1	-5.5	20.0	32.5	-27.0
6	2	-1.5	-2.0	-86.0	-11.5
Mean		3.6	7.3	38.9	29.4
sd		3.4	10.9	32.8	29.7

+ Difference = WAM time - EEG time; positive numbers equal a higher WAM time.

The number of awakenings of at least 1 minute duration was calculated for both the EEG and WAM. Overall, the WAM tended to overestimate the number of awakenings during the night in comparison with the EEG (Table 2). This may occur since a person may move during sleep and not awaken, but move enough to give a high number of counts on the WAM.

Table 2.
 Number of awakenings 1 minute or greater
 as scored by EEG and by WAM.

Subject	Day	WAM	EEG
3	1	5	0
3	2	1	1
4	1	7	4
4	2	1	5
5	1	4	0
5	2	9	0
6	1	7	6
6	2	6	4

A second discriminant analysis was conducted to determine the percent of correct classifications of the WAM data based on the groupings of awake, sleep stages 1 through 4, REM sleep, and movement time as indicated by the EEG data. The percent correct was 54.5 percent for the awake time, 26.8 percent for stage 1, 1.4 percent for stage 2, 74.3 percent for slow wave sleep (SWS), 5.0 percent for REM, and 46.2 percent for movement time, giving an overall correct classification of 16.4 percent.

Finally, the correlations between EEG scored sleep and WAM scored sleep were calculated. The correlations are presented in Table 3.

Table 3.
 Correlations between sleep scored by EEG and by WAM.

Parameter	r	p
Sleep onset	.31	.460
Wake-up time	.97	.001
Minutes awake after sleep onset	.85	.008
Minutes asleep after sleep onset	.81	.016

Discussion

Based on this limited comparison study, it appears that the WAM is a good instrument to use to estimate sleep time when an EEG is not possible. The percent agreement between WAM sleep time and EEG sleep time is very high, with an average of almost 89 percent. The error tended to be in the direction of overestimation of sleep time by the WAM, results supportive of those found in the comparison study by Mullaney and associates (1980).

However, despite these encouraging results, this study found that the WAM cannot be used to determine the quality of sleep. The WAM missed some awakenings for some subjects, and overestimated the number of awakenings in other subjects. These brief arousals during the night offer one measure of sleep quality, a measure which the WAM apparently is unable to reliably calculate. In addition, when sleep stages based on the EEG and the WAM were correlated, there was no evidence that the data collected from the WAM had any relationship to traditionally scored stages of sleep. The overall agreement between WAM counts and sleep stages was 16.4 percent, with the best classification being for SWS. The WAM may be able to estimate slow wave sleep better than the other stages since this stage of sleep is a quieter stage than the others, with little to no movement occurring during this period (Carskadon and Dement, 1989).

One must keep in mind that the data examined in this study were limited to the sleep period plus a 30-minute period during which the subject was awakened from sleep to perform cognitive tests. Since no EEG data were collected during the wake period, no comparisons could be made between EEG and WAM data during the wake time. Based on the experience of this Laboratory, the awake data from the WAM may be underestimated since some activity during the day (i.e., watching TV, reading, working at a desk) will give low activity counts which will be scored as sleep with an automatic sleep scoring algorithm. This is where the subjective corrections are applied in the present scoring procedure. However, unless the subject keeps a very good diary of activity, the experimenter may rescore low activity as awake, when in fact, the person took a nap during that time. However, no comparisons of this activity period were made in the present study.

In summary, it appears that the WAM is a good tool for estimating the amount of sleep a person receives in situations where an EEG recording is not possible or is too expensive and time consuming. The current method of scoring (using a set cutoff of counts) is a suitable method. However, an overestimation of sleep most likely will occur when this method is used. Therefore whenever actigraphs are used, a conservative interpretation of the data is to discuss "rest time" instead of "sleep time." In

addition, the quality of sleep as determined by normal EEG sleep staging cannot be assessed by the WAM.

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Appendix A.

Volunteer consent forms.

VOLUNTEER REGISTRY DATA SHEET

THIS FORM IS AFFECTED BY THE PRIVACY ACT OF 1974

1. AUTHORITY: 5 USC 301; 10 USC 1071-1090; 44 USC 3101; EO 9397
2. Principal and Routine Purposes: To document participation in research conducted or sponsored by the U.S. Army Medical Research and Development Command. Personal information will be used for identification and location of participants.
3. Mandatory or Voluntary Disclosure: The furnishing of the SSN is mandatory and necessary to provide identification and to contact you if future information indicates that your health may be adversely affected. Failure to provide the information may preclude your participation in the research study.

PART A-INVESTIGATOR INFORMATION (To Be Completed By Investigator)

PLEASE PRINT, USING INK OR BALLPOINT PEN

1. Study NR: _____ 2. Protocol Title: Ability to return to sleep upon midsleep awakening using triazolam and temazepam
3. Contractor (Laboratory/Institute Conducting Study): USAARL
4. Study Period: From: 01/___/___ To: 15/___/___
(DAIMOYR) (DAIMOYR)

5. Principal/Other Investigator(s) Names(s)

6. Location/Laboratory

- (1) Caldwell J. Lynn Fort Rucker/ USAARL
(Last) (First) (MI)
- (2) Comperatore Carlos Fort Rucker/ USAARL
- (3) _____ / _____

PART B-VOLUNTEER INFORMATION (To Be Completed By Volunteer)

PLEASE PRINT, USING INK OR BALLPOINT PEN

7. SSN: ___/___/___
8. Name: _____
(Last) (First) (MI)
9. Sex: M ___ F ___
10. Date of Birth: ___/___/___
11. *MOS/Job Series: ___
12. *Rank/Grade: ___
13. Permanent Home Address (Home of Record) or Study Location Address:

(Street) (P.O. Box/Apartment No.)

(City) (Country) (State) (Zip Code)
()

(Perm Home Phone No)

14. *Local Address (If Different From Permanent Address):

(Street) (P.O. Box/Apartment No.)

(City) (Country) (State) (Zip Code)
()

(Local Phone No)

15. *Military Unit: _____ Zip Code: _____
Organization: _____ Post: _____ Duty Phone No. () _____

PART C-ADDITIONAL INFORMATION
(To Be Completed By Investigator)

PLEASE PRINT, USING INK OR BALLPOINT PEN

16. Location of Study: _____

17. Is Study Completed: Y__ N__

Did volunteer finish participation: Y__ N__ If YES, Date finished: / /
(DAJMOIYR)

If NO, Date withdrawn: / / Reason withdrawn: _____
(DAJMOIYR)

18. Did Any Serious or Unexpected Adverse Incident or Reaction Occur: Y__N__ If YES, Explain: _____

19.*Volunteer Followup: _____

Purpose: _____

Date: / / Was contact made: Y__N__ If No action taken, explain:
(DAJMOIYR)

20.*Hard Copy Records Retired: Place: _____ File NR: _____

21.*Product Information:

Product: _____

Manufacturer: _____

Lot NR: _____ Expiration Date: _____

NDA NR: _____ IND/IDE NR: _____

*Indicates that item may be left blank if information is unavailable or does not apply.
Entries must be made for all other items.

VOLUNTEER AGREEMENT AFFIDAVIT

For use of this form, see AR 70-25 or AR 40-38; the proponent agency is OTSG

PRIVACY ACT OF 1974

Authority: 10 USC 3013, 44 USC 3101, and 10 USC 1071-1087

Principle Purpose: To document voluntary participation in the Clinical Investigation and Research Program. SSN and home address will be used for identification and locating purposes.

Routine Uses: The SSN and home address will be used for identification and locating purposes. Information derived from the study will be used to document the study; implementation of medical programs; adjudication of claims; and for the mandatory reporting of medical conditions as required by law. Information may be furnished to Federal, State and local agencies.

Disclosure: The furnishing of your SSN and home address is mandatory and necessary to provide identification and to contact you if future information indicates that your health may be adversely affected. Failure to provide the information may preclude your voluntary participation in this investigational study.

PART A(1) - VOLUNTEER AFFIDAVIT

Volunteer Subjects in Approved Department of the Army Research Studies

Volunteers under the provisions of AR 40-38 and AR 70-25 are authorized all necessary medical care for injury or disease which is the proximate result of their participation in such studies.

I, _____, SSN _____

having full capacity to consent and having attained my _____ birthday, do hereby volunteer/give consent as legal representative for _____ to participate in _____

the study entitle "Ability to return to sleep upon midsleep
awakening using triazolam and temazepam"
(Research study)

under the direction of Dr. J. Lynn Caldwell

conducted at USAARL/ Fort Rucker, AL
(Name of Institution)

The implications of my voluntary participation/consent as legal representative; duration and purpose of the research study; the methods and means by which it is to be conducted; and the inconveniences and hazards that may reasonably be expected have been explained to me by

Dr. Caldwell

I have been given an opportunity to ask questions concerning this investigational study. Any such questions were answered to my full and complete satisfaction. Should any further questions arise concerning my rights/the rights of the person I represent on study-related injury, I may contact

LTC George Sisson, Command Judge Advocate General

at HQ USAMRDC, Ft Detrick, Frederick, MD AV 343-2065 Com 301-663-2065
(Name, Address and Phone Number of Hospital (Include Area Code))

I understand that I may at any time during the course of this study revoke my consent and withdraw/have the person I represent withdrawn from the study without further penalty or loss of benefits; however, I/the person I represent may be required (military volunteer) or requested (civilian volunteer) to undergo certain examination if, in the opinion of the attending physician, such examinations are necessary for my/the person I represent's health and well-being. My/the person I represent's refusal to participate will involve no penalty or loss of benefits to which I am/the person I represent is otherwise entitled.

PART A (2) - ASSENT VOLUNTEER AFFIDAVIT (MINOR CHILD)

I, _____, SSN _____ having full

capacity to assent and having attained my _____ birthday, do hereby volunteer for _____
_____ to participate in _____

(Research Study)

under the direction of _____

conducted at _____
(Name of Institution)

(Continue on Reverse)

PART A(2) - ASSENT VOLUNTEER AFFIDAVIT (MINOR CHILD) (Cont'd.)

The implications of my voluntary participation; the nature, duration and purpose of the research study; the methods and means by which it is to be conducted; and the inconveniences and hazards that may reasonably be expected have been explained to me by

I have been given an opportunity to ask questions concerning this investigational study. Any such questions were answered to my full and complete satisfaction. Should any further questions arise concerning my rights I may contact

at _____
(Name, Address, and Phone Number of Hospital (Include Area Code))

I understand that I may at any time during the course of this study revoke my assent and withdraw from the study without further penalty or loss of benefits; however, I may be requested to undergo certain examination if, in the opinion of the attending physician, such examinations are necessary for my health and well-being. My refusal to participate will involve no penalty or loss of benefits to which I am otherwise entitled.

PART B - TO BE COMPLETED BY INVESTIGATOR

INSTRUCTIONS FOR ELEMENTS OF INFORMED CONSENT: *(Provide a detailed explanation in accordance with Appendix C, AR 40-38 or AR 70-25.)*

See Attached Sheets.

I do do not *(check one & initial)* consent to the inclusion of this form in my outpatient medical treatment record.

SIGNATURE OF VOLUNTEER	DATE	SIGNATURE OF LEGAL GUARDIAN <i>(If volunteer is a minor)</i>	
PERMANENT ADDRESS OF VOLUNTEER	TYPED NAME OF WITNESS		
	SIGNATURE OF WITNESS		DATE

REVERSE OF DA FORM 5303-R, MAY 89 .

You are being asked to participate in a study which will determine the ability of a person to return to daytime sleep after being awakened during the sleep period. You will take either Halcion (triazolam) or Restoril (temazepam) to help induce sleep. Additionally, you will be required to remain awake each night before your test days and to sleep in the laboratory during the day.

You are to come to the laboratory in advance of your test days in order to undergo a medical screen for possible sensitivities to benzodiazepines and any other medical situation which may be complicated by use of a benzodiazepine. After the medical monitor has approved your participation in the study, you will be scheduled for two days of participation. During that time, you will stay awake during the night and sleep during the day with the help of a benzodiazepine. On your scheduled visits, you are to come to the laboratory at 0700, sleep during the day, and you will be released at approximately 1700. You should return to the laboratory at 0700 the next day for the same procedure.

In order to monitor your activity throughout the study period, you will be asked to wear a small activity monitor on your wrist. This monitor records wrist movements which are an indication of your general level of activity. This will aid us in assessing how well you are able to stay awake at night and sleep during the day. Whenever you take a shower or participate in heavy physical activity (weight lifting, basketball, etc.), remove the monitor, and then replace it whenever you have finished the activity, recording the time you removed it and the time you replaced it. The monitor is very sensitive to water and to bumps.

In order to monitor your daytime sleep, we will connect small sensors to your scalp which will permit us to monitor the electrical activity from your brain. Before the sensors are applied, your scalp will be cleaned with acetone to ensure good sensor placement. The sensors will be attached with collodion and filled with electrode gel to aid in recording of your brain waves. You may feel a slight discomfort when your scalp is cleaned, however, this will be very mild and will dissipate rapidly. If you feel any irritation once the sensors are removed, an emollient with an antibiotic will be applied to the affected area(s). Once the sensors are attached, you will be administered the sleeping aid assigned to you and then taken to a private bedroom. You will sleep until awakened, after which you will be required to take some computerized tests. These tests will last approximately 30 minutes, after which you will be allowed to return to bed and sleep for the remainder of the sleep period. At the end of the

Participant's Initials _____

Witness's Initials _____

sleep period, you will be awakened, the sensors will be removed, and you will be questioned by the medical monitor for any possible side effects from the medication. After release by the medical monitor, you are free to return to your home. You should have someone come to take you home or we will provide you a driver to take you home. You should not operate any equipment such as automobiles, lawn mowers, heavy equipment, etc. Additionally, you must not consume any alcoholic beverages during the night. At 0700 you will return to the laboratory for the second day of tests. Again, someone should drive you to the laboratory or we will provide a driver for you. This day will be exactly like the first day. After awakening at the end of the sleep period, you will once again be checked by the medical monitor for any side effects from the medication. Upon release by the medical monitor, we will provide you with a driver to take you to your home. Again, you should not operate any automobiles, lawn mowers, heavy equipment, etc., or consume alcoholic beverages for at least 10 hours after leaving the laboratory. If you feel any discomfort upon returning home and for 2 days after your final visit to the laboratory, call one of the numbers provided to you.

The medications which you will receive are standard sleep medications prescribed for people who have problems sleeping. As with any medication, there is the slight possibility of side effects. Please note the possible adverse effects of each of the medications listed below.

Halcion: When taken without going to sleep, the known central nervous system (CNS) effects of triazolam are drowsiness, headache, dizziness, nervousness, lightheadedness, and coordination disorder. Nausea and vomiting have also been known to occur in less than 5% of the patients reporting symptoms. In less than 1% of patients, euphoria, tachycardia, tiredness, confusional states/memory impairment, cramps/pain, depression, and visual disturbances have been reported. In less than 0.5% of patients, constipation, taste alterations, diarrhea, dry mouth, dermatitis/allergy, dreaming/nightmares, insomnia, paresthesia, tinnitus, dysesthesia, weakness, congestion, death from hepatic failure have been reported. Additionally, the following symptoms have been reported at least once during the use of triazolam: anterograde amnesia with appropriate or inappropriate behavior, disorientation, derealization, depersonalization, clouding of consciousness, dystonia, anorexia, fatigue, sedation, slurred speech, jaundice, pruritus, dysarthria, changes in libido, menstrual irregularities, incontinence, and urinary retention. Factors which may contribute to some of these reactions include concomitant intake of alcohol or other drugs, sleep deprivation,

Participant's Initials _____

Witness's Initials _____

or an abnormal premorbid state. Other events reported include restlessness, irritability, excitation, increased muscle spasticity, sleep disturbances, hallucinations, aggressiveness, falling, somnambulism, inappropriate behavior and other adverse behavioral effects.

Restoril: The most common adverse reactions reported after consuming temazepam and not sleeping were drowsiness, dizziness, and lethargy. Other effects which have been reported include confusion, euphoria and relaxed feeling. Less commonly reported were weakness, anorexia and diarrhea, with tremor, ataxia, lack of concentration, loss of equilibrium, falling, and palpitations being rarely reported. Hallucinations, horizontal nystagmus and paradoxical reactions (excitement, stimulation and hyperactivity) were reported in less than 0.5% of the cases. If temazepam is combined with other drugs having known hypnotic properties or CNS-depressant effects, additive effects are a potential result.

Please note the following requirements for your safety:

1. Do not consume any alcoholic beverages at least 24 hours before your scheduled appointments and at least 10 hours after your final release from the laboratory.
2. Do not take any medications at least 24 hours before your scheduled appointments and at least 24 hours after your final release from the laboratory.
3. Do not operate any automobiles, heavy equipment, lawn mowers, etc., at least 10 hours after your final release from the laboratory.
4. Do not participate in any activities which may require sound judgement or important decisions at least 10 hours after your final release from the laboratory.

The risks associated with this protocol are listed in the contraindications of each of the medications you may take. There are no risks associated with wearing the wrist monitor. The risk associated with EEG recordings is a possibility of slight skin irritation from wearing the sensors on your scalp. This irritation will be treated with standard skin lotion.

Participant's Initials _____

Witness's Initials _____

You may withdraw from the study at any time without prejudice. If you choose to complete the study, the benefits to you include an assessment of your sleep quality after taking a sleep medication, as well as a contribution to the design of future sleep studies. None of the information obtained from this study which identifies you in any way will be released without your express consent. All names and other identifying information will be removed from all records and replaced with a subject number for future identification.

Should any question/problems occur during the period of the study, you may reach Dr. Lynn Caldwell at 255-6857 between 0700 and 1630, and at 1-735-3344 at other hours.

I have received a copy of this consent form.

Participant's Initials _____

Witness's Initials _____

Appendix B

Manufacturers' list.

Precision Control Design, Inc.
646A Anchors St.
Fort Walton Beach, FL 32548

Grass Instrument Company
101 Old Colony Avenue
P.O. Box 514
Quincy, MA 02169

Nihon Kodan (American), Inc.
17112 Armstrong Avenue
Irvine, CA 92714