

AD-A283 180



NTATION PAGE

RT DATE

3. REPORT TYPE (AND DATE COVERED)  
ANNUAL 01 Sep 92 TO 31 Aug 93

4. TITLE AND SUBTITLE

(FY91 AASERT), BASIC MECHANISMS AND IMPLICATIONS OF NON-PHOTIC ENTRAINMENT OF CIRCADIAN RHYTHMICITY

F49620-92-J-0347

61103D

3484/S4

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8. PERFORMING ORGANIZATION REPORT NUMBER

AEOSR-TR- 94 0451

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)

AFOSR/NL  
110 DUNCAN AVE SUITE B115  
BOLLING AFB DC 20332-0001

10. SPONSORING/MONITORING AGENCY REPORT NUMBER

Dr Haddad

DTIC  
ELECTE  
AUG 12 1994  
S G D

11. SUPPLEMENTARY NOTES

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13. ABSTRACT (Maximum 200 words)

The studies showed that afternoon exposure to exercise increases TSH levels and tends to delay the onset of nocturnal TSH secretion on the following night. Analysis of the melatonin levels is under progress. Mr Trabb learned to recruit, screen and supervise research volunteers, to record EEG activity, and all the basic skills of clinical research. He also participated in studies examining the effects of carbohydrate intake on vigilance and performance. Mr Salchli was responsible for incorporating the new computerized data collection and analysis system into the laboratory. His computer skills were vital in allowing the laboratory to begin using this new system. He used this system to determine the phase shifting effects of light pulses of varying intensity on the free-running circadian rhythm of locomotor activity in both young and old hamsters. He was able to demonstrate that old hamsters are about 20 times less sensitive to the effects of light on the circadian clock, despite there being little if any effect of age on the amount of light being transmitted through the eyes. These results raise the possibility that age-related changes in the circadian organization in animals, including humans, could be due to a decreased sensitivity to the entraining agents in the environment. Thus, a countermeasure that could be used to reverse the effects of aging on the circadian clock would be to

14. SUBJECT TERMS increase the strength of the entraining agents.

15. NUMBER OF PAGES

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT

(U)

18. SECURITY CLASSIFICATION OF THIS PAGE

(U)

19. SECURITY CLASSIFICATION OF ABSTRACT

(U)

20. LIMITATION OF ABSTRACT

(U)

NSN 7540-01-280-5500

DTIC QUALITY INSPECTED 1

94-25320



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FY91 - AASERT F49620-92-J-0347  
**Basic Mechanisms and Implications of Non-Photic Entrainment of  
 Circadian Rhythmicity**

YEAR 1 - TECHNICAL REPORT  
 Sept 1, 1992 - Aug 30, 1993

Principal Investigator: Eve Van Cauter  
 Dept of Medicine  
 University of Chicago

Students supported

Jeffrey Trabb- SS#212-04-5135 - On grant from 9/1/92-8/31/93

Frederick J. Salchli-SS#111-40-5100- On grant from 9/1/92-12/31/92

There were only funds to cover one student for one year and a second student for only 4 months.

Jeffrey Trabb:

Grades: 5As, 4Bs and 1C

Mr. Trabb did both animal research and human research on the basic mechanisms of non-photic entrainment of circadian rhythmicity

## ANIMAL RESEARCH

Project title: Phase-shifting effects of triazolam on the biological clock of the Tau mutant hamster.

**Background:** The first single gene mutation that is associated with a major change in the mammalian circadian clock was found in the golden hamster. This mutation in the heterozygous state results in a shortening of the circadian period of the activity rhythm from 24 to 22 hrs, while in the homozygous state the period of the activity rhythm is 20 hrs. Very little is known about how this mutation affects other circadian properties. Previous studies had demonstrated that the Phase Response Curve (PRC) to light pulses may be different between tau mutant and wild-type animals. In view of the recent demonstration that induced-changes in the activity-rest cycle of the hamster can induce phase shifts in the circadian clock regulating the activity rhythm of hamsters, Mr. Trabb sought to determine

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if the phase shifting effects of an activity-inducing stimulus on the clock differed between tau mutant and wild-type hamsters.

**Experiments and Conclusions:** Tau mutant animals for studies at Northwestern University were obtained from Dr. Michael Menaker at the University of Virginia. Tau mutant and wild-type hamsters were housed in cages with a running wheel, and movement of the wheel was recorded on-line by a recently developed computerized system. Mr. Trabb learned how to use this system, as well as the sophisticated software used in data analysis. Animals were allowed to free-run under conditions of constant light, before receiving a single injection of triazolam at different circadian times. Previous studies had shown that treatment with triazolam induces an acute increase in locomotor activity which in turn is responsible for inducing phase shifts in the free-running rhythm of activity. The PRCs generated in mutant and wild-type animals were similar, indicating that this mutation does not alter the feedback effects of activity on the circadian clock.

#### HUMAN RESEARCH

**Project title:** direct and phase-shifting effects of exercise on circadian profiles of TSH and melatonin

**Background:** in a previous series of studies designed to examine the phase-shifting effects of nighttime exposure to a 3-hour period of exercise, we demonstrated that delay shifts of the profiles of TSH and melatonin occurred one day after exposure. We also unexpectedly observed direct stimulatory effects of exercise on TSH secretion. The next series of experiments were designed to examine whether daytime exercise exposure had similar effects

**Experiments and conclusions:** the studies showed that afternoon exposure to exercise increases TSH levels and tends to delay the onset of nocturnal TSH secretion on the following night. Analysis of the melatonin levels is under progress. Mr. Trabb learned to recruit, screen and supervise research volunteers, to record EEG activity, and all the basic skills of clinical research. He also participated in studies examining the effects of carbohydrate intake on vigilance and performance.

**Frederick Salchli**

**Grades: 8 As, 4 Bs and 1 C.**

**Project Title: Effects of age on the response of the clock to the phase-shifting effects of light.**

**Background:** In both rodents and humans, advanced age is associated with a number of different alterations in the expression of behavioral, endocrine and physiological rhythms. For example, in old animals entrained to a light-dark cycle there is much more variability from day-to-day in the onset of activity, and the activity pattern itself becomes highly fragmented. It is not clear if this breakdown in the normally coherent activity/rest cycle is due to alterations in the circadian clock itself or in the entrainment pathways. As a first step to address this question, Mr. Salchli participated in studies to determine if there is any change in sensitivity to the effects of light on the circadian clock with advanced age in hamsters.

**Experiments and Conclusions:** Mr. Salchli was responsible for incorporating the new computerized data collection and analysis system into the laboratory. His computer skills were vital in allowing the laboratory to begin using this new system. He used this system to determine the phase shifting effects of light pulses of varying intensity on the free-running circadian rhythm of locomotor activity in both young and old hamsters. He was able to demonstrate that old hamsters are about 20 times less sensitive to the effects of light on the circadian clock, despite there being little if any effect of age on the amount of light being transmitted through the eyes. These results raise the possibility that age-related changes in the circadian organization in animals, including humans, could be due to a decreased sensitivity to the entraining agents in the environment. Thus, a countermeasure that could be used to reverse the effects of aging on the circadian clock would be to increase the strength of the entraining agents.