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STUDIES OF CIRCADIAN CYCLES IN HUMAN SUBJECTS DURING PROLONGED ISOLATION IN A CONSTANT ENVIRONMENT USING EIGHT CHANNEL TELEMETRY SYSTEMS*

INTRODUCTION

In recent years telemetry systems have been extensively used in aerospace medicine. Cardiovascular data were monitored during F-100 flights (1), heart rate and respiration response patterns during F-105 flights (2). Simons and Prather (3) described an improved personalized radio telemetry system which took into account the demands of computer analysis.

Telemetry of physiological data has been predominantly used for intermittent monitoring and data acquisition. This was also the case in American (4) and Russian space flights (5). There is a paucity of reports on continuous telemetry of multiple physiological functions over extended periods of time, covering several weeks.

This report presents experiences obtained with the use of 8-channel telemetry systems in continuous simultaneous monitoring of six physiological functions (EEG, EKD, respiratory rate, body temperature, skin temperature, BSR) in one or two subjects during isolation experiments of two to three weeks duration. The studies were performed under NASA Contract R-24, to determine the extent of internal desynchronization in free running circadian cycles of physiological functions, under conditions of confinement in a constant environment such as those encountered in spaceflights and underwater exploration.

The enormous amount of one minute data obtained in these experiments required the development of special computer programs for the correction of artifacts in telemetered data and for the analysis of data to determine periodicities and phase shifts of circadian cycles.

METHODS

Environmental Chamber:

A climatized pressure-altitude chamber was used to provide a constant environment. Temperature was regulated by a thermistor-activated pneumatic instrument controlling a heating-cooling system to the chamber, and maintained at $27°C \pm .1°$. Barometric pressure was controlled by a pneumatically activated vent-valve. A sensitive differential pressure gauge,

referenced to a constant pressure source, provided a set-point signal
to the controlling instrument. The chamber pressure was held at 30.560
inches of mercury within a standard deviation of .004 inches. The
chamber was continuously ventilated with 100 liters/min provided by a
lubricant-free air pump. Humidity was kept at 30 per cent $\pm$ 5 per cent
by a pneumatically controlled chemical drier. Illumination was set at
30-foot candles during the subjects' day and during the night reduced
to about 3-foot candles. Communication through the chamber was by
1) one-way audio out of the chamber, 2) audio code into the chamber,
and 3) medical-lock written messages.

Physiological Data Acquisition:

The following variables were continuously monitored on each sub-
ject: 1) core temperature (rectal), 2) surface temperature (upper
arm), 3) basal skin resistance (palm), 4) EEG (occipital), 5) respi-
ration, and 6) EKG. The subjects wore an FM-FM type telemetry vest
(Biometrics). The raw data were received at a central location out-
side the chamber for preliminary reduction and recording. The core
and surface temperatures and the basal skin resistances were direct
analogue signals which passed through low pass filters before being
converted to digital form and recorded on standard IBM cards once
every minute. These low pass filters (half power frequency, $6(10)^{-3}$
cps .) were necessary to minimize "aliasing" problems during subse-
quent spectral analyses. EKG and respiratory signals were converted
to minute-rates and recorded digitally on cards once a minute, and
monitored graphically every 15 minutes for a duration of two minutes.
EEG signals were also graphically monitored every 15 minutes. More-
over, baseline crossings (indication of prominent EEG frequency) and
averaged amplitude were digitally recorded every minute. Figure 1
shows a block diagram of the total telemetry system which consisted
of two eight-channel systems (Biometrics). The sensor and transmitter
units worn by the individual subjects are displayed in Figure 2.

PROBLEMS ENCOUNTERED

Electrodes:

Electrodes are known to deteriorate very rapidly within hours.
We employed electrodes of the fluid type, which provide a low elec-
trode impedance. Such electrodes had been successfully used in the
NASA Mercury program (6). They consisted of carefully chlorided silver
discs enclosed in an inert plastic holder with a layer of modified
bentonite electrolyte between the cup and the skin of the subject.
The advantage of these electrodes were that they had special prepared
surfaces that did not tend to polarize and secondly, the electrolytic
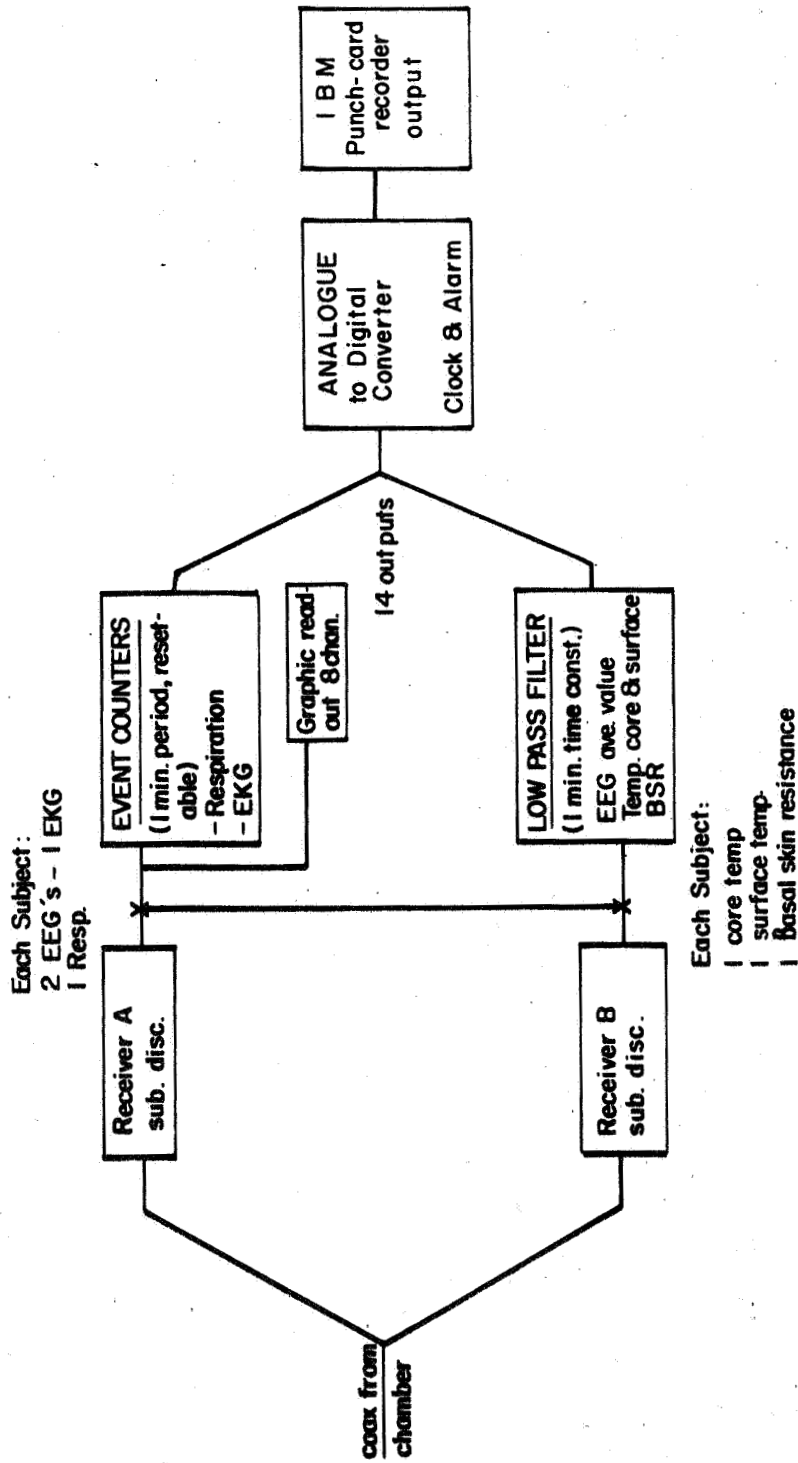
TELEMETERED DATA ACQUISITION

Each Subject:
2 EEG's – 1 EKG
1 Resp.

Receiver A
sub. disc.

EVENT COUNTERS
(1 min. period, reset-
able)
– Respiration
– EKG

Graphic read-
out 8 chan.

Receiver B
sub. disc.

LOW PASS FILTER
(1 min. time const.)
EEG ave. value
Temp. core & surface
BSR

Each Subject:
1 core temp
1 surface temp.
1 basal skin resistance

coax from
chamber

14 out puts

ANALOGUE
to Digital
Converter

Clock & Alarm

I B M
Punch-card
recorder
output

Figure 1 – Block diagram of telemetered DATA acquisition

-3-
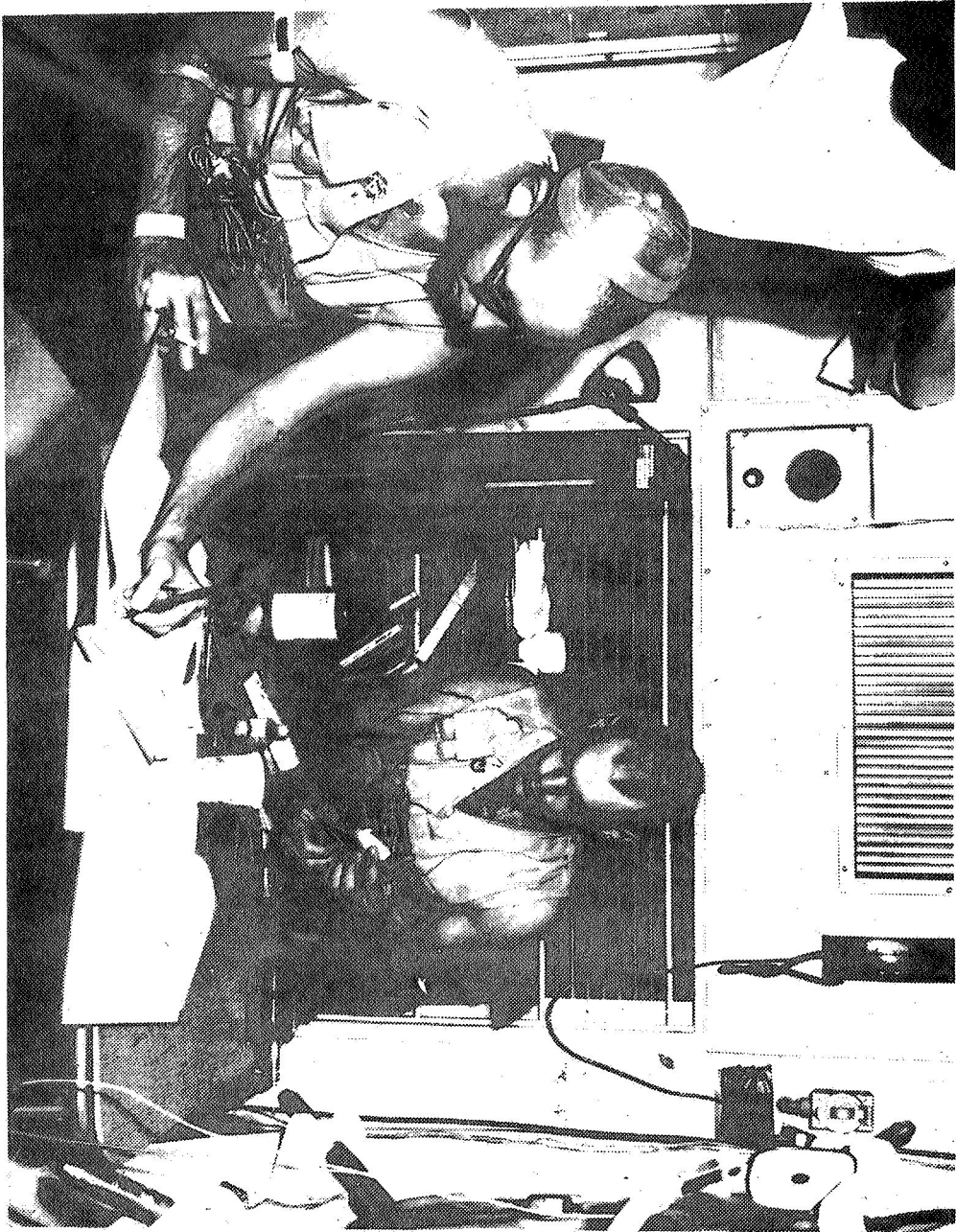
Figure 2 - Two subjects wearing eight channel telemetry packs (Biometrics): EEG (2), EKG, RESPIRATORY Rate, Body temperature, Skin temperature, BSR, Voice. The transmitters fit into the front pocket, the batteries into the breast pockets.

part used was isotonic and less prone to cause skin irritation. These electrodes lasted up to six or seven days, depending on the application. In the case of EEG electrodes, the useful time was somewhat shorter since the very low potentials were affected earlier by the slowly charging resistance of the electrodes. This deterioration prompted us to implant silver wires in subsequent experiments and we found them to last 10-12 days. The limitation of the silver or platinum wire method lies in the eventual tissue rejection.

Leads:

The second problem of the telemetry system consists of fatiguing and breaking of electrode wires, particularly of those electrodes whose connections are exposed to constant movement (EKG, BSR, palm electrodes). For this reason, we obtained special fatigue resistant wire, furnished by Cyanamid. This wire consists of 40 strands of extremely fine wire, copper wire, sufficient to make the gauge a standard 22.

Long term continuous use of telemetry equipment presents the obvious problem of obtaining routine calibrations. A decision must be made whether, at some point, it is suitable to interrupt the experiment in order to carry out recalibrations.

Signal Conditioner:

The type of data analysis determines what kinds of analog signal conditioning is to be done to the telemetry data. Rate information was desired from the EKG signals and the respiratory signals. This rate information was obtained by counting both EKG, BSR complexes and the number of inspiration signals during one minute and recording this information. It was desired to obtain an estimate of the prominent EEG frequency. The most expedient method was simply to count the number of EEG baseline crossings in one minute. The average of the EEG signal was obtained by integration of the signal for one minute. Surface temperature, core temperature and basal skin resistance were recorded essentially unmodified. The sampling theory of data analysis required that frequencies which were greater than half the sampling interval be attenuated. For this purpose, special low pass filters have been used having a time constant of three minutes. The signal conditioning equipment was developed locally and worked out very well.

Data Transmission Equipment:

The output of the signal conditioning equipment was multiplexed and converted to a digital format for punching with a standard IBM

card punch. The analog digital converter was furnished by Gulton Industries, Inc. The card punch was the weakest link in the data recording system. Reliable card punching represents a major problem for continuous long-duration experiments. In order to verify the accuracy of the card punched data, measurements were graphically recorded every fifteen minutes for a period of one minute with an Offner dynograph. Under our conditions, the use of the punch-card system was necessary because the existing computer facilities had only punch-card input. Otherwise, it would have been more feasible to use punched paper tape, or magnetic tape.

Corrections of Artifacts in Telemetered Data:

Several computer programs were developed to locate and correct many of these errors. One program corrected mechanical card-punching errors, such as false column registration, card order, etc. A second correction program detected errors in telemetry signal, e.g., loss of signals or loss of electrode contact. The data had to meet two conditions, 1) they had to be within a reasonable physiological range, and 2) the data could not display unphysiologically fast changes. Certain types of errors could be corrected by a linear approximation. The corrected data and time information were placed in standard binary-tape files.

Subjects:

Extended experiments of this type put great demands on the subjects. They must be highly motivated, intelligent and thoroughly acquainted with the experimental plan and, furthermore, must be able to make minor repairs to telemetry equipment during the experiment. Our subjects consisted of medical students who participated in the Navy's Research Clerkship Program, and research personnel.

Data Analysis for the Study of Circadian Cycles:

The finished telemetry data stored on magnetic tape was first plotted by the computer. The plots were then inspected to determine obvious artifacts in the data. Various acute-correlation analyses were performed to make estimates of the prominent low-frequencies in the data. The most successful auto-correlation analyses was based on a compromise three-day overlapping analyses. As phase information is inherently lost by this technique, a cross-correlation method was developed to determine the phase shift of the circadian periodicities. This was done by cross-correlating the data with a synthetized 24-hour periodicity of known amplitude and phase. Again, the analysed duration was three days in overlapping intervals.

RESULTS AND DISCUSSION

In the following, a few examples are given showing acquisition and analyses of telemetry data from subjects who were confined for long periods.

Figure 3 exhibits the telemetered core temperature data of two subjects. Following isolation in a constant environment, the sleep-wakefulness cycle shifts regularly about 1-2 hours per day, as indicated in the shift of the black bars denoting the sleep period. The circadian cycles of body temperature shift correspondingly. Under these conditions, in which the subjects retained their normal pattern of physical activity in isolation, all of the measured circadian cycles of physiological functions were synchronized with the sleep-wakefulness cycle.

Figure 4 exhibits the results of a three-day overlapping auto-correlation analysis of respiratory rate in a subject confined for 12 days in a constant environment. It can be seen that the 24-hour component (within the low frequency band 18-48 hours) of the spectrum analysis decreases during the first days of isolation while the 5-7 hour frequencies increase. This indicates that the stress of isolation produces a marked change in the temporal order of frequencies underlying the cycles of physiological functions.

Figure 5 gives an example of cross-correlation analysis of body temperature from one subject with a synthesized 24-hour periodicity of known amplitude and phase. The body temperature did not follow the phase shift of the sleep-wakefulness cycle indicating a desynchronization of physiological functions. These findings, which are in contrast to those shown in Figure 3, were obtained in a subject whose physical activity was greatly reduced during isolation in a constant environment. It appears that physical activity has a coordinating influence on the cycles of physiological functions.
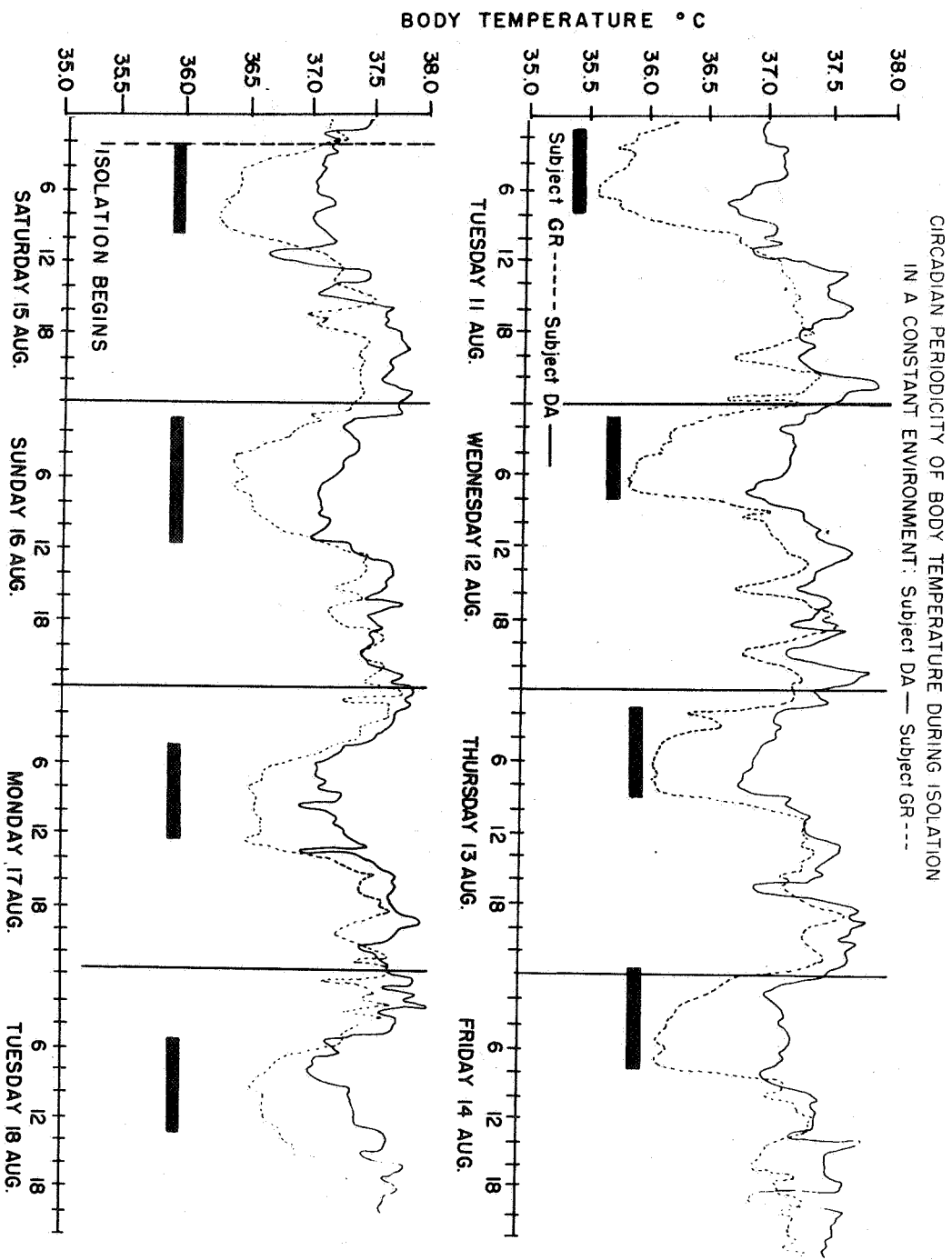
Figure 3 — Telemetered data of body temperature in two Human Subjects isolated in a constant environment for nine days, showing circadian cycles synchronized with the sleep-waking cycle. Black bars denote sleeping period, which shifts after onset of isolation.
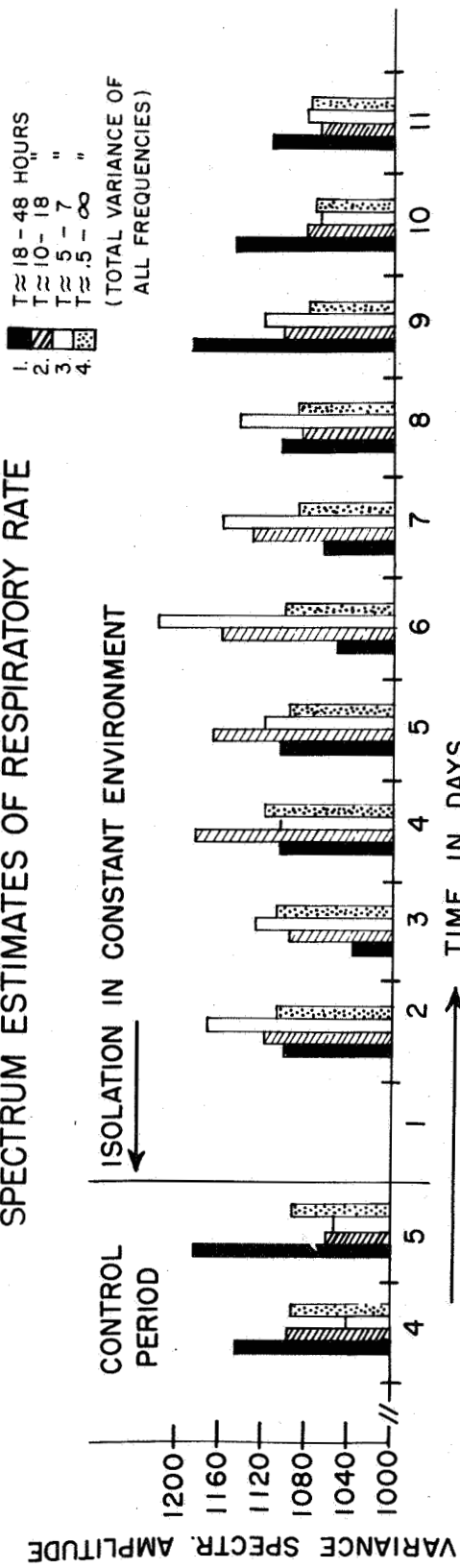
Figure 4 - Spectrum estimates of respiratory rate of a subject isolated in a constant environment. Four ranges of periodicities are shown. Following isolation, the predominances of the low frequency band 18-48 hours (black bars) containing the circadian cycles decreases while the amplitude of the higher frequencies (5-7 hours) increases. After 7 days of isolation, the distribution of periodicities returns towards normal levels.
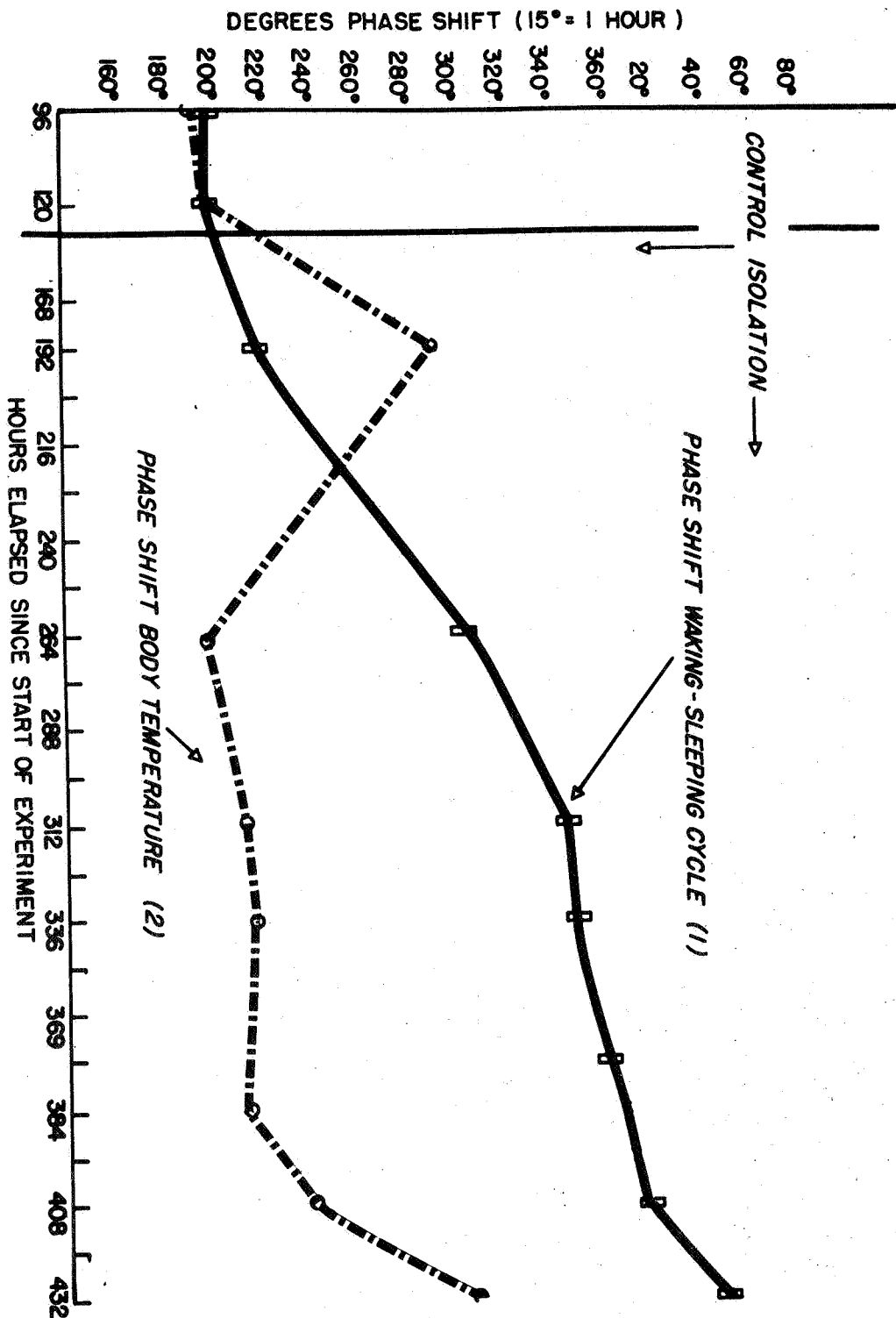
Figure 5 - Comparison of PHASE SHIFTS of WAKE-SLEEPING cycle and body
temperature cycle during isolation in a constant environment
under conditions of reduced physical activity.   (1)   Normalized
phase of wake-sleeping cycle based on the waking time of the
second day of a three-day overlapping analysis, (2) Spectrally
calculated phase relation of body temperature to a 24-hour
sinusoid.

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