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A simple method for recording and analysing circadian rhythms in man

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We describe a method for recording human rest–activity and body temperature. A small automatic cordless electronic device has been developed in order to record circadian rhythmicity of rest–activity for a period of one week. A comparable device connected to a small temperature transducer by means of a flexible probe was designed to register body temperature. These devices can register human circadian rhythms without interfering with their normal daily activity.

Introduction

Circadian rhythms are a fundamental feature of all living systems. Different biological phenomena such as rest–activity, sleep–wakefulness, body temperature and cognitive performance, all exhibit a profound ‘circadian’ rhythmicity, i.e. they reveal a free-running period of about 24 h.

Most human sleep–wake studies have been carried out for relatively short periods of time. Continuous recording over several days, which is generally required in studies on circadian rhythms (Pittendrigh and Daan, 1976), is currently performed by multiple electrode attachments and a heavy ambulatory recorder which interferes considerably with the activity of the subjects. In the present communication, we describe methods for long-term continuous recording and subsequent analysis of the human rest–activity cycles (which

is comparable to the sleep–wake cycle) and of body-temperature rhythms. Since we are interested in effects of aging and of Alzheimer’s disease on human circadian rhythms, examples of such recordings are also presented to show the practicality of these methods in practice.

Materials and Methods

The devices consist of an automatic cordless electronic unit for recording rest–activity (called ‘RA-24’) and a similar unit with a temperature transducer (called ‘BT-24’) attached to a flexible wire for registering body temperature. The RA-24 consists of a box measuring $9 \times 4 \times 2$ cm, and weighs 140 g. This box can be worn on the arm or leg. The used acceleration detector (Entran, Type EGB-125;50) has an acceleration response range between -50 and $+50$ g. A crystal clock determines the time. Any motor activity that induces acceleration is detected by the acceleration detector, amplified and passed through a level detector. When the preset level is exceeded, a binary counter is incremented and the input to the counter is

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blocked for 16 s. Every hour the number of counts is stored in an EEPROM (electrical erasable read only memory; model X2804 with 512 addresses) after which the counter is reset. Since 225 is the (dividable) number of data that can be recorded into each address of the EEPROM, the minimum interval for each hour registration, dividing 3600 s (1 h) by 225, is 16 s. However, if necessary the accelerations can be recorded per second and stored into EEPROM every 225 s. Nevertheless, in the latter case an EEPROM with a larger memory (2048 addresses; model X2816) should be used if the registrations are going to be continued for many days. Two small, long-life lithium batteries (1/2AA 3.5 V) are used as power supply. Fig. 1 shows the detailed circuit diagram of RA-24.

We have developed a similar device called 'BT-24' for recording body-temperature rhythm using a small temperature transducer (type AD590) in place of the acceleration detector. This device records body-temperature changes between 30 and 40 °C in steps of 0.1 °C. The BT-24 can be carried in one's pocket; its transducer (AD590) is attached to the skin in the subaxillary area using adhesive tapes. A flexible wire carries the signal to the BT-24 (12 × 4 × 2 cm; 160 g) where, after A-D conversion, the output of the transducer is written into an EEPROM (X2804) once every hour. If necessary, the output can be stored with minimum intervals of 15 min. Fig. 2 shows the detailed circuit diagram of BT-24.

A FORTRAN program has been developed to read the rest-activity or temperature data stored in the EEPROM. This program runs on a VAX 11/780 (Digital) computer. The data are read by means of an 'AVAL PKW1000' EEPROM programmer, which is connected to a terminal port on the VAX by means of RS232 communication lines. The rest-activity or temperature data are read by a FORTRAN program and stored in a data file on the VAX computer, together with some administrative data such as the recording date, the start time of the acquisition and a test identification code. The program also has options to make simple histograms of the test data (both on screen and on hard copy). Nevertheless, no specific interface or computer programs are required, and, in fact, the data could be handled by any microcomputer.

Results

For analysing the circadian rhythmicity of the rest-activity data, the 'Chi-square' periodogram was used. This test determines whether the rest-activity signal is significantly different from a random signal (and the extent of the deviation) as well as the period of the rhythm (Sokolov and Bushell, 1978). Displays of rest-activity and results of the analysis of circadian rhythms of one young and one old healthy subject, as well as an Alzheimer patient recorded with 'RA-24', are illustrated in Fig. 3. Pilot studies have shown that the subject's profession and amount or type of daily activity do not substantially influence the circadian rhythmicity of the data. In 11 healthy subjects of both sexes ranging in age from 28 to 78 years, we could observe a clear circadian rhythm of the rest-activity cycle. Fig. 4 demonstrates diurnal rhythmicity of rest-activity and body temperature in a 37-year-old male volunteer wearing both RA-24 and BT-24.

Devices for a similar purpose, but essentially different in configuration from our RA-24 have previously been developed. Borbely et al. (1981, 1983) built a 'solid-state motor activity monitor' and applied it in various pharmacological studies in humans. Their device uses a piezoelectric transducer as movement detector. When a voltage induced by a movement exceeds a preset threshold, a pulse is generated. The pulses are counted during a preset time interval. Data are stored as an 8-bit word in a programmed 1024-word memory. Recently, another system using a similar principle became commercially available by AMI, New York (see Redmond and Hegge, 1985). However, both systems store data on 'RAM' (random access memory, as used in most computers) and need a specific interface unit for data recovery. Our system differs from these two in several aspects:

(1) Using a similar principle, we are able to record body temperature as well.

(2) For recording motor activity we use an acceleration detector which is based on a strain gauge and is connected as a half wheatstone bridge. This unit is made as a complete device by Entran, thus self-construction is not required as is the case with piezoelectric transducers.

Fig. 3. Left panel: raw data of subjects' rest-activity recorded over several days are double-plotted. Right panel: the Chi-square periodogram statistical analysis of the data are presented; the straight line indicates the level of statistical significance below which a signal is considered to be random (Sokolov and Bushell, 1978). Top and middle data are from a 41-year-old (D.F.S.) and a 78-year-old (L.I.S.) healthy control; data from an Alzheimer patient (aged 79) are illustrated in the 2 bottom panels. Note the peak of rest-activity rhythm at 24 h for control subjects, deviating significantly from the straight line; a much smaller peak not significant from a random signal was found in the Alzheimer patient.

Fig. 4. Data simultaneously recorded continuously with both the RA-24 and the BT-24 from a 37-year-old (M.M.) healthy subject over a period of 3 successive days. Bars indicate amount of activity (A); solid thick line shows body temperature (T).

(3) No specific interface is required for data recovery (as is required for previous devices), except for an EEPROM reader which is used for many purposes in most laboratories having computer facilities.

(4) All data are lost in the two models cited above whenever there is a power supply failure, whereas all data collected up to the moment of failure are preserved in our device. This is of practical importance in long-term studies.

(5) The system described in the present paper can be made in any laboratory having even limited electronic facilities; this, in turn, creates significant savings compared with the other two models.

Discussion

The present paper describes a simple way of recording and analysing circadian rhythmicity of the human rest-activity cycle. Furthermore, for the first time, a fully automatic method for continuous long-term recording of body temperature in humans has been described. The time bin for registration used in the present study was every 1 h, because our interest centres on circadian rhythms. However, for those interested in using this system to examine the number and periodicity of movements as well as ultradian changes of body temperature, the time can easily be reduced to as short as 225 s for rest-activity registrations and to 15 min for body-temperature recordings. This method might be of potential value in research programs concerned with a variety of biological rhythms.

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Addendum

The FORTRAN program can be obtained from the authors by supplying a 1600 BPI tape. EEPROMs can be obtained from Xicor, CA, U.S.A., and accelerators from Entran, NJ, U.S.A.

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