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| journal or publication title | Tohoku psychologica folia |
| volume | 55 |
| page range | 101-106 |
| year | 1997-07-01 |
| URL | http://hdl.handle.net/10097/56194 |

Tohoku Psychologica Folia
1996, **55**, 101-106

# CHARACTERISTICS OF SPONTANEOUS ACTIVITY IN SPONTANEOUSLY HYPERTENSIVE RAT (SHR)

By

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Behavioral characteristics of spontaneously hypertensive rats (SHRs) were examined by comparing the spontaneous activity of 8 SHRs with that of 8 normotensive Wistar-Kyoto rats (WKYs) at 23-30 weeks in age in a normal homecage environment. Continuous measurement of the activity was taken over 72 hours. Analysis of the activity revealed that the circadian rhythm of the activity in SHRs was less noticeable than WKYs. This was attributed to the prominence of the ultradian variation of the activity in SHRs. This suggested the less organized circadian rhythms of sleep-wakefulness cycles in SHRs. A relationship between the cardiovascular system and the sleep-wakefulness regulation was discussed.

**Key words**: SHR, hypertension, spontaneous activity, circadian rhythm.

## Introduction

The acute raised blood pressure induces arousal in electroencephalograms of both sleeping men (Schneider-Helmert, 1983) as well as cats (Baust & Hinemann, 1967).

Recent studies reported many hypertensive persons complained of insomnia (Dimenäs, Wiklund, Dahlöf, Lindvall, Olofsson, & De faire, 1989; Müller, Montoya, Schandry, & Hartl, 1993). In addition, the hypertensives with the lowered level of blood pressure following the administration of specific antihypertensives tended not to make such a kind of complains (Rosenthal, Ben-arie, Carroll, Fiedel, Kisch, Leiba, & Traub, 1995; Werning, Thomas, & Ludwig, 1988). This suggested that the chronically raised blood pressure is involved in the sleep disorders.

According to Wagner and Storongatz (1984), however, the normotensives who believed themselves to be hypertensives show the tendency to complain the physical symptoms typically reported by hypertensives. Thus, regardless of actual blood pressure levels, the awareness of high blood pressure might cause the insomnia reported by hypertensives.

As above, mechanisms of the relationship between hypertension and sleep disorders are still unclear. In trying to investigate the mechanism, the animal studies using spontaneously hypertensive rats (SHRs), a model of human essential hypertension (Okamoto & Aoki, 1963), give a clue for elucidating blood pressure-behavior relationships in detail. The fact that SHRs characterized by chronic hypertension show higher level of the locomotor activity in an open-

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field (Sato, Shimizu, & Hatayama, 1995) suggests that a cardiovascular factor of blood pressure would affect not only physiological activity but also overt behavior. The earlier studies of day-night alternations of the spontaneous locomotor activity using nomotensive rats (Büttner & Wollnik, 1984; Honma & Hiroshige, 1978) found that they showed circadian activity rhythms. Then, supposing that cardiovascular factors are involved in insomnia reported by human hypertensives, it is inferred SHRs would be different in rest-active rhythms of the spontaneous activity from normotensive rats. In order to examine functional relationships between hypertension and the sleep-wakefulness regulation, the present study focused on delineating periodic characteristics of the spontaneous activity which SHRs showed in a homecage.

## METHOD

*Subjects*: Eight male SHRs and 8 Wistar Kyoto Rats (WKYs) as normotensive controls, amounting 16 rats in total, were used at 23-30 weeks in age. All subjects were kept in the constant darkness at the room temperature of 24 ± 2℃. Food and water were available ad libitum.

*Apparatus*: The present experiment was conducted in the sound attenuated room (SONY, STUDIO LAB) under constant darkness (DD) at the room temperature of 24 ± 2℃. Measurements of the activity were made by means of condenser-type activity monitor devices (COLUMBUS INSTRUMENTS, AUTOMEX) which made it possible to count frequency of vertical movements occurred inside a plastic homecage (17 cm × 27 cm × 14 cm).

*Procedure*: Each rat was put into the homecage. Following the habituation period of 24 hours, spontaneous activity of the rat was measured continuously throughout 72 hours. During the period of measurement, the activity was transformed to total counts per 1 minute before stored into a floppy disk in a personal computer (NEC, PC9801-UV).

*Data analysis*: The least squares spectral analysis was made to examine whether the spontaneous day-night activity would vary with circadian rhythms. To the activity data summed per 6 minutes, cosine functions were fitted within a range of periods between 1.0 - 30.0 hour in the increment 0.1-h. With these procedures, the percentage rhythm (PR) was calculated, that was the percentage of the data's variance accounted for by variations of the each fitted function. The period and the amplitude of the function with the maximum PR value were regarded as the circadian period and the circadian amplitude, respectively.

*Measurement of systolic blood pressure*: Arterial systolic blood pressure (SBP) was measured with the tail-cuff plethymography (Natsume, manometer-tachometer system KN-210) 1 week before the activity measurement.

## RESULT

*Systolic blood pressure*: The SHRs showed the mean SBP of 223.0 mmHg and their *SD* of 19.8, while the WKYs did the SBP of 130.4 mmHg and their *SD* of 4.48. One-way ANOVA revealed that the SBP in SHRs were significantly higher than in WKYs ($F(1,14)=144.9$, $p<.01$). This result confirmed that SHRs used in this study were in severe hypertension.

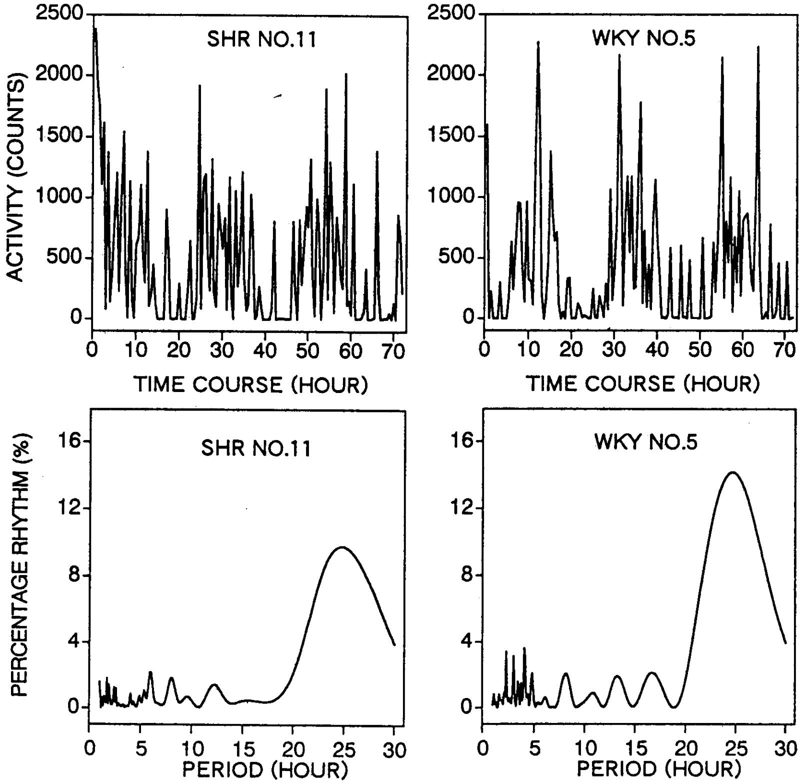


Fig. 1. Rest-active patterns of spontaneous activity (upper panels) and corresponding percentage rhythm (lower panels) of a representative individual rat of SHRs (left) and WKYs (right).

*Spontaneous activity*: Rest-active patterns of spontaneous activity and corresponding PR values for one representative animal of each strain were shown in Fig. 1. Group-averaged circadian periods were 24.2 hour in SHRs and 24.1 hour in WKYs. A one-way ANOVA revealed that there was no strain difference in the circadian period.

The PR value of the circadian variation, the circadian amplitude, and the total activity were analyzed by a one-way ANOVA, respectively. These analyses revealed that the PR value of the circadian variation in SHRs was smaller than in WKYs ($F(1,14)=22.34$, $p<.01$) (Fig. 2). The amplitude of the circadian variation in SHRs was marginally smaller than WKYs ($F(1,11)=4.03$, $p<.10$). There was no strain difference in the total activity.

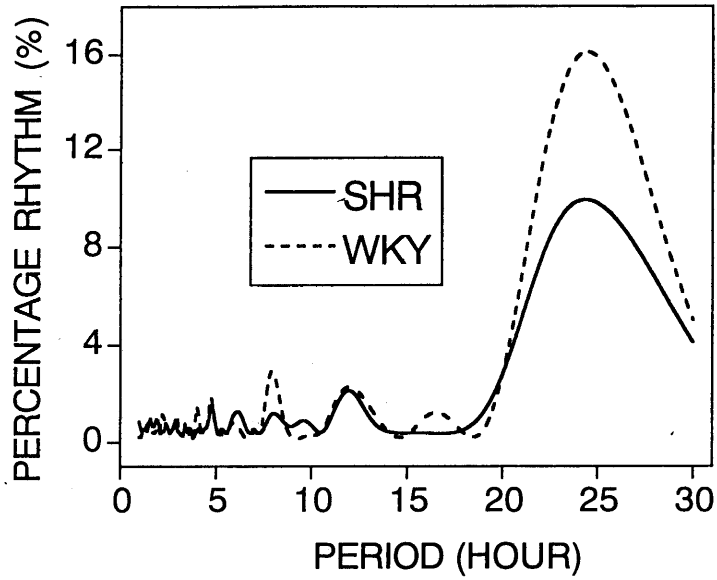


Fig. 2. Group-averaged least-squares spectra of PR values.

## Discussion

The spontaneous activity in SHRs varied with a period of about 24 hours similar to WKYs, though the circadian rhythm of the activity in SHRs was less noticeable because the amplitude and the PR value of the circadian variation in SHRs tended to be smaller than WKYs. This suggested that the differences in the activity between the subjective day and night were rather small in SHRs as well as that the fluctuation of the activity other than the circadian variation was prominent.

Borbély (1981) stated that rest-activity patterns of spontaneous activity generally corresponded to sleep-wakufulness patterns. The observed activity patterns in the present study would, if so, be accompanied by the less organized circadian sleep-wakefulness rhythms in SHRs.

The present results suggest that the cardiovascular factor of hypertension in SHRs interacts with the mechanism of the sleep-wakefulness regulation. Visual inspection of the activity patterns of SHRs in the present experiment (Fig. 1) found that the ultradian variation with a period of 1-2 hours was prominent, which make it difficult to grasp periodicity of the circadian variation. Disorganization of circadian rhythms with prominent ultradian variation, as Honma et al. (1978) suggested, may reflect the functional abnormality of the circadian clock in the central nervous system. A support of this notion is the indication (Peters, Zoller, Hennessey, Stopa, Anderson, & Alberts, 1994) that high levels of vasoactive intestinal peptide in the circadian clock (suprachiasmatic nucleus) in SHRs would lead to both the abnormal circadian rhythms and the cardiovascular activity. On the other hand, Baust et al. (1967) and Rau, Pauli, Brody, Elbert, and Birbaumer (1993) who paid attention to the feedback of peripheral blood pressure indicated that the afferent impulses from baroreceptors at the blood-vessel inner wall of arteries modulated activation level of the central nervous system both in animals and men. Additionally, Miyazaki (1995) recently found out that the salt-induced hypertensive rats also showed almost the same spontaneous activity patterns as SHRs. So, the peripheral factor of high blood pressure levels might result in the unusual activity pattern in SHRs. While a great deal is now known about the behavioral characteristics of the spontaneous activity in SHRs, much more work is needed before we will be able to elucidate how the peripheral factor interacts with the function of the central regulatory mechanisms to produce behavioral rest-active state.

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(Received December 24, 1996)
(Accepted May 7, 1997)