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Analysing entrainment of cardiac and locomotor rhythms in humans using the surrogate data technique

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Abstract

Using the surrogate data technique we evaluated whether, during running, the synchronization between cardiac and locomotor rhythms resulted from entrainment or by chance. An electrocardiogram and an electromyogram from the right vastus lateralis muscle were monitored from ten healthy young men running at a paced rhythm of 150 steps a minute. The relationship between cardiac and locomotor rhythms was determined by examination of the occurrence of the heart beat with respect to the locomotor phase. The examination revealed that synchronization patterns were observed in all subjects. We generated surrogate data by sorting randomly the original locomotor rhythm, and no synchronization patterns were then seen. This may indicate that the synchronization between the cardiac and locomotor rhythms represented entrainment. We have provided the first evidence for the rejection of the hypothesis that when heart beat rhythm is close to the locomotor rhythm, synchronization between the two rhythms occurs by chance.

Keywords. Entrainment - Synchronization - R-R interval - Gait cycle - Running

Introduction

An oscillating function, such as heart rate, could be synchronized to an external frequency. Most biological oscillators seem to be nonlinear and in nonlinear systems, synchronization between two oscillators is often observed as an "entrainment" or as a "coupling" between two oscillators (Pavlidis 1973). However, not all synchronization phenomena represent entrainment in that synchronization between two rhythms may occur by chance when one oscillator rhythm is close to that of the other. In humans, synchronization between two rhythms such as the cardiac and locomotor rhythms (Kirby et al. 1989, Niizeki et al. 1993), the cardiac and respiratory rhythms (Palus and Hoyer 1998, Rosenblum et al. 1998, Schäfer et al. 1998, Seidel and Herzel 1998), and the respiratory and locomotor rhythms have been reported (Bechbache and Duffin 1977, Bramble and Carrier 1983, Mahler et al. 1991, Paterson et al. 1987, Raβler and Kohl 1996). Studies on the synchronization between cardiac and locomotor rhythms have included cycling, walking, and running in humans. Kirby et al. (1989) have defined entrainment as being when heart and step rates were within 1% of the closest integer ratio, while Niizeki et al. (1993) defined entrainment as being when the relative phase relationship, which is the occurrence of the heart beat with respect to the gait cycle, is fixed for more than 1 min within 10% of the phase range. These two definitions of entrainment are similar, in that both specify synchronization between two rhythms, although it is not obvious whether the synchronization represents an entrainment or if it is accidental. In the case of regular external stimuli, a phase-response curve is helpful in investigating the entrainment (Pavlidis 1973), but it is difficult to apply the phase-response curve to noisy bivariate time series as the cardiac and locomotor rhythms.

Seidel and Herzel (1998) showed that synchronization between two noisy rhythms such as the cardiac and respiratory rhythms was an entrainment phenomenon. They plotted the phase relationship between the two rhythms, and demonstrated horizontal structures. These horizontal structure indicated that when there were n heart beats in each respiratory cycle, these heart beats appear at certain n values of respiratory phases, which were constant over all cycles. They further used a surrogate data technique to estimate the probability of a horizontal structure being established by chance. The surrogate data technique is even more helpful when the system is noisy. Therefore, we have used the surrogate data technique to investigate the hypothesis that synchronization of cardio-locomotor rhythms represents an entrainment phenomenon.

Methods

Ten healthy men [mean height; 170.8 (SD 6.0) cm, mean weight; 61.4 (SD 3.5) kg, mean aged; 22.9 (SD 1.2) years] participated in the study. Each subject gave informed consent after being provided with a verbal explanation of the intent and procedures of the experiment. Three of the ten subjects were habitual smokers but abstained from smoking for at least 8 h before the experiment.

Protocols

A 5 min warm-up period was followed by at least 15 min of rest and 20 min running on a treadmill (Treadmill NT-12, Nishikawa) at a frequency of 150 steps$\cdot$min^{-1}. Electrodes for electrocardiography (ECG) and a surface electromyogram (EMG) were placed on the chest and right vastus lateralis muscles, respectively. For the first 5 min, the subjects ran at a heart rate of 120 beats$\cdot$min^{-1}. After 5–10 min, the treadmill speed was gradually raised to result in a heart rate of 150 beats$\cdot$min^{-1}, i.e., the target heart rate (THR) to be maintained for at least 5 min (Bantage XL, Canon). The treadmill speed was within the range 100–200 m$\cdot$min^{-1} while the slope was maintained at 0% when heart rate reached THR.

Data Collection

To determine the R-R interval, the ECG was recorded from the chest. The ECG signal was amplified, filtered (AB-621G, Nihonkoden) and digitized using a 1 kHz sampling by a 16-bit A-D converter (DR-Ma2, TEAC). The data were stored on an MS-DOS-formatted magnetic optical disk (MO). Detection of the R wave was carried out using a personal computer (PC9821xc13, NEC).

The EMG signals were simultaneously recorded from the right vastus lateralis muscle using bipolar surface electrodes. The inter-electrode distance was approximately 3 cm along the length of the muscle. The earth electrode was placed high on the thigh. The EMG and ECG signals were stored on the MO and processed off-line. To obtain an integrated EMG (iEMG), the signal was full-wave rectified and smoothed. The onset of muscle contraction was defined as the time when the iEMG increased above a preset trigger level.

Data Analysis

The onset of a muscle contraction was measured using a resolution of 1 ms. To analyse qualitatively the phase relationship between the cardiac and locomotor rhythms, relative phase transitions were calculated (Kenner et al. 1976, Niizeki et al. 1993). The period (t_r) at which the rth R-wave occurred in one cycle was measured from the onset of the gait cycle. We then set the period of the gait cycle as T_l. The relative phase ($\phi_{r,l}$) of the rth heart beat in one gait cycle was calculated as:

$$\phi_{r,l} = t_r/T_l,$$

where r and l are integers. To define how $\phi_{r,l}$ changed during exercise, changes in $\phi_{r,l}$ for each R-wave in the gait cycle were plotted against time. When the plot of $\phi_{r,l}$ was horizontal, it indicated phase synchronization.

To determine whether a phase synchronization was present in the transition of the $\phi_{r,l}$ obtained, the time course of a χ^2 value was evaluated (Niizeki et al. 1996). A χ^2 value using a uniformly consistent test shows a goodness of fit and uniform distribution. The larger χ^2 value of a distribution, the less uniform it is. The χ^2 value of the histogram of $\phi_{r,l}$ divided into 10 classes was calculated from 60 consecutive $\phi_{r,l}$. To obtain a time course for χ^2 value (χ^2_R), the calculation was performed every 10 points of $\phi_{r,l}$ as:

$$\chi^2_R = \frac{1}{Fe}\sum_{i=1}^{l}(Fi - Fe)^2,$$

where Fi is the frequency of each class, $Fe = 6$ because the number of sample is 60, and $l = 10$ because the number of classes is 10. The phase synchronization was defined as occurring when χ^2_R exceeded a value of corresponding to a P value less than 0.01.

To determine whether phase synchronization between cardiac and locomotor rhythms was entrained or occurred by chance, we compared the original $\phi_{r,l}$ with that developed from the surrogate data. We considered that if the $\phi_{r,l}$ trace of the surrogate data differed from the original data, the phase synchronization between cardiac and locomotor rhythms appearing in the original data did not occur by chance.

Surrogate Data

The series of gait cycles was transformed to surrogate data (Palus and Hoyer 1998). The surrogate data were generated by a random sort of the gait cycle series. To understand this process better, we consider here a simple example-two three-sample series of the R-R interval (r_1, r_2, r_3) and the gait cycle (s_1, s_2, s_3). In this study, the R-R interval series remains as (r_1, r_2, r_3), while the order of the gait cycle series is generated by a random function, (s_2, s_1, s_3).

The mean, variance, and histogram of this surrogate data should be the same as those of the original data. This approach realizes a stochastic process for mutual independence between the series of gait cycles with surrogation and the R-R interval without surrogation. Even if there is a temporal structure between bivariate time series, this randomization destroys it (Palus and Hoyer 1998).

Statistical

To determine whether the synchronization between two oscillators resulted from an entrainment, we made a histogram of all events during the experimental period divided into 10 classes. We compared the original data with the surrogate data. Significance was defined as $P < 0.05$ when we compared the χ^2 value of the histograms.

Results

The results from subject SS are shown in Fig. 1, which includes the time series of the gait cycle (A), the R-R interval (B), the traces of $\phi_{r,l}$ (C), and χ^2_R (D). The transition for the gait cycle was maintained at a steady state (Fig. 1A). The variance of the time series for the R-R interval from 11 to 13 min (Fig. 1B, a) is less than that before or thereafter.

[Insert Figure 1 here about]

Indeed, the coefficients of variance (CV) for the periods from 5 to 7 min and from 18 to 19 min were 1.24% and 1.16% respectively, while that for the period from 11 to 13 min it was 0.90%. Similarly, from 15.5 to 18 min (Fig. 1B, b) and from 18.8 to 20 min (Fig. 1B, c), CV was lower than that from 5 to 7 and from 18 to 19 min. In these periods with low CV, the $\phi_{r,l}$ trace does not show random motion but rather appears to remain at the specific phases. In other words, there are horizontal structures in the $\phi_{r,l}$ trace (Fig. 1C). Figure 1D shows the results of the trace of χ^2_R. In this study, χ^2 value of significant level was above 21.7 because 60 points and 10 classifications were used. The χ^2_R were above the significance level, from 9 to 15, 15.5 to 18, and from 18.8 to 20 min. These three periods correspond to a, b, and c in Fig. 1B.

To determine whether the phase synchronization occurred accidentally or whether it was due to entrainment of the heart beat to the locomotor rhythm during running, we analyzed the phase relationship between the cardiac and locomotor rhythms using the surrogate data technique. The results for subject SS are shown in Fig. 2 and the results of the $\phi_{r,l}$ trace of the surrogate data are shown in Fig. 2A. The horizontal structures observed before the surrogate process were destroyed, and no indication of any adherence to specific phases was observed.

[Insert Figure 2 here about]

The χ_R^2 trace with surrogate data is shown in Fig. 2B. This figure is similar to that obtained from the original data, and the periods, which are above the levels of statistically significance, are similar.

The difference between the $\phi_{r,l}$ traces of the original data and the surrogate data for the period from 9 to 15 min, corresponding to Fig. 1B, a, are shown in Fig. 3. The original data shows a tendency to be horizontal structure but it is not strict (Fig. 3A). That is the occurrence of the heart beat with respect to the locomotor phase seems to be horizontal alignment. This alignment is steady with a low variability. In contrast to the case using the original data, the surrogate data has lost its structure (Fig. 3B). This alignment is no longer steady.

[Insert Figure 3 here about]

The histograms of all events present in the original data (A) and the surrogate data (B) are shown in Fig. 4. It is shown in Fig. 4A that there were two peaks of 0.2–0.4 and 0.7–0.9 per gait cycle, which indicates the onset of a muscle contraction during the diastolic period. In that case, the χ^2 value was 812.2. However, Fig. 4B does not show a local variation, but a nearly equal distribution. In this case, the χ^2 value was 27.8.

[Insert Figure 4 here about]

The group mean and SD for the χ^2 values in a histogram for all events from the original and the surrogate data are shown in Fig. 5. The mean χ^2 values were 284 (SD 216) and 33 (SD 21) for the original and surrogate data, respectively, with the mean χ^2 value for the original data being significantly higher ($P < 0.05$). These results indicate that in the original data, $\phi_{r,l}$ was more local in the specific phases.

[Insert Figure 5 here about]

Discussion

During running, synchronization between cardiac and locomotor rhythms occurred when the cardiac rhythm was close to the locomotor rhythm paced by an acoustic signal as external input. This synchronization showed a tendency to occur at certain phases and continued the occurrence of heart beat with respect to the relative phase relationship between cardiac and locomotor rhythms. We then used the surrogate data technique to see if we could reject the hypothesis that such synchronization occurs by chance. In the surrogation results, no synchronization of the surrogate data was found. These results suggest that in the original data synchronization was likely to have been an entrainment phenomenon.

Analysis of entrainment between cardiac and locomotor rhythms

While studying the entrainment of circadian rhythm, Pavlidis (1973) found that the use of a phase-response curve was helpful. However, it is difficult to use a phase-response curve in noisy bivariate time series such as those involving cardio-locomotor rhythms. To show that synchronization between two noisy rhythms of cardiorespiratory oscillators represents entrainment, Seidel and Herzel (1998) used the surrogate data technique. They generated a random surrogate cardiac time series that fitted the autoregressive model of the original data. By so doing, they were able to determine that the two oscillators were independent because the surrogate data were adjusted to only one oscillator. The longest length of a horizontal structure in the original data was 213 beats. The probability of finding this length of synchronization in the surrogate data was about $3 \cdot 10^{-4}$. Therefore, the surrogate data technique can make obvious whether synchronization in the original data has occurred accidentally. In the present study, we applied the methods of Seidel and Herzel (1998) and Palus and Hoyer (1998) to generate surrogate data. We found three fixed horizontal structures as shown in Fig. 1C. The longest duration was 6 min. No such structure was found in the surrogate data (Fig. 2A, 3B). More specifically, our results allow us to reject the hypothesis that synchronization between cardiac and locomotor rhythms occurred by chance.

Cardiac control during entrainment of cardio-locomotor rhythms

Heart rate is modulated by respiratory movement. This is well known as respiratory sinus arrhythmia (RSA). It has been reported that subjects with no remarkable RSA have synchronization between the cardiac and respiratory rhythms, whereas subjects displaying a higher degree of RSA exhibit no distinct epochs of cardiorespiratory synchronization (Rosenblum et al. 1998, Schäfer et al. 1998). During exercise of high intensity such as the 150 beats$\cdot$min^{-1} heart rate level of our study, the heart beat included less RSA. During running in humans, synchronization between respiratory rhythm and locomotor rhythm (i.e. limbs movement) appears to be favored (Bramble and Carrier 1983, Bernasconi et al. 1995). In the present study, synchronization between the cardiac and locomotor rhythms might have been due to the synchronization between the cardiac rhythm and the respiratory rhythm that was entrained to locomotor rhythm.

The heart beat has been shown to be influenced by the timing of the muscle contraction relative to the cardiac phase (Nakamura et al. 1997, Niizeki and Miyamoto 1998, Niizeki and Miyamoto 1999), but no direct evidence for a mechanism responsible for cardio-locomotor entrainment has been claimed.

It does appear, however, that during cardio-locomotor entrainment, cardiac control is modulated by some neural circuit originating in the peripheral or central nervous system. That the cardiovascular response to exercise originates not only in the periphery, but also in the central nervous system has been proposed by Mitchell (1985, 1990). The interaction between the cardiovascular center and a locomotor rhythm generator (RG) may contribute to the entrainment of cardio-locomotor rhythms. Kawahara et al. (1993, 1994) demonstrated in paralyzed, vagotomized, and decerebrated cats that there are entrainments of cardiac, respiratory, and locomotor rhythms with respect to each other with interactions of functional hierarchical structures among three RG during fictive locomotion . However, no evidence of such an intervention has yet been found in the intact human body.

The afferent groups III and IV nerves originating from active muscle may contribute to the entrainment of cardio-locomotor rhythms. Repetitive electrical stimulation of somatic afferent nerves have been shown to entrain respiratory rhythms (Iscoe and Polosa 1976, Kawahara et al. 1988). To explain our results, during phase-dependent muscle contractions in the cardiac cycle, some afferent information from muscle through groups III and/or IV afferent nerves might have affected the cardiovascular center. Rhythmic muscle activity has been shown to causes metabolic and mechano afferent activity originating from active muscle (Kaufman et al. 1983, Mitchell 1990). In addition, there is an inhibition of the cardiac vagal component of baroreflex by groups III and IV afferent nerves (McWilliam and Yang 1991). A cardiac vagal bursting beat-by-beat (Katona et al. 1970) might be masked by that inhibition.

In conclusion, our finding provides the first evidence allowing rejection of the hypothesis that the cardio-locomotor synchronization occurs by chance when the heart beat is close to locomotor rhythm. We believe that our findings could have important implication for the understanding of the physiological mechanism(s) of heart rate stability during rhythmic exercise which is of high intensity making RSA low, and might lead to applications in the development of endurance performance.

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Legends

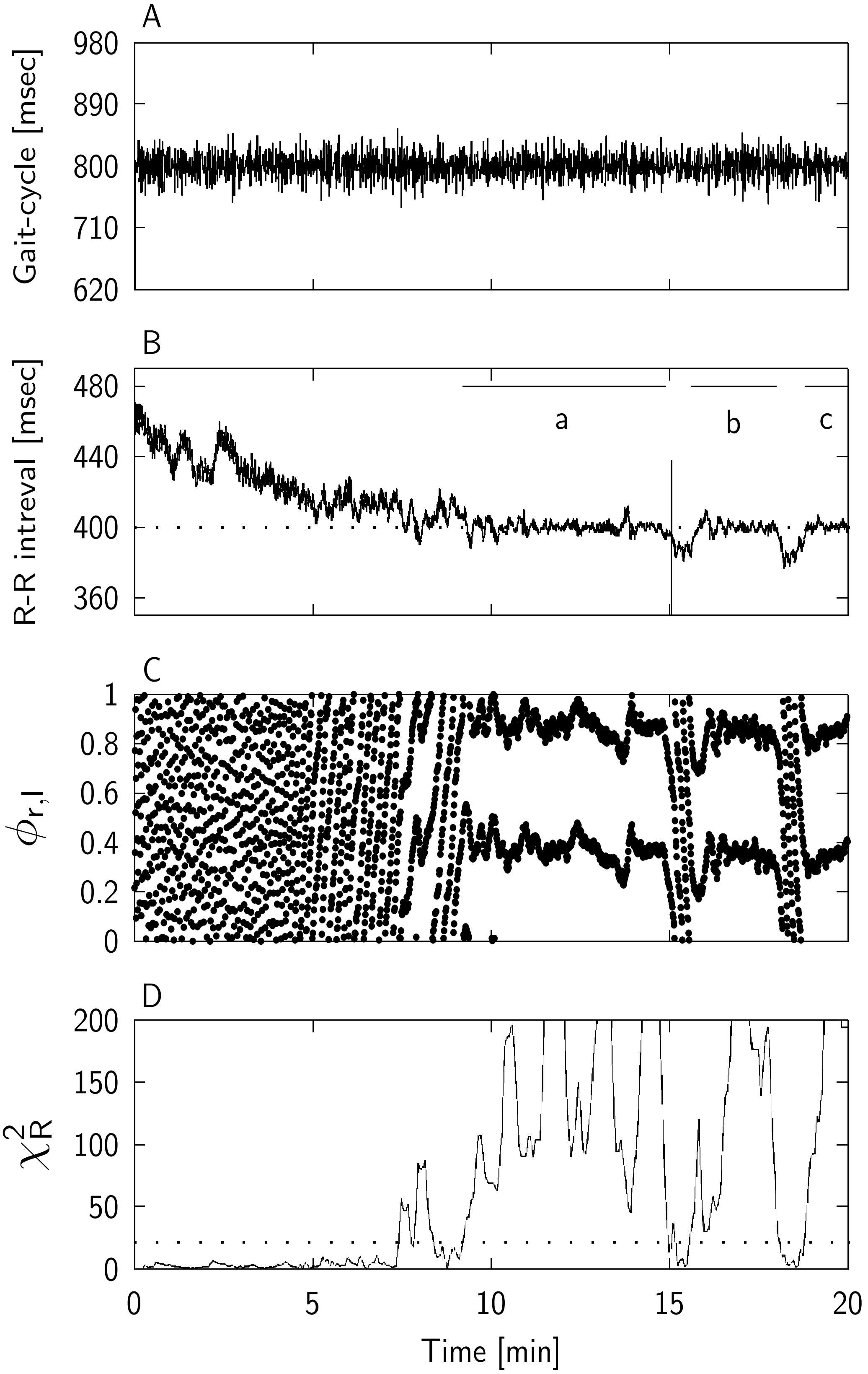
Figure 1: Time series of a gait cycle (A), R-R interval (B), and phase relationships between cardiac and locomotor rhythms [$\phi_{r,l}$, (C) and the χ^2 values of $\phi_{r,l}$, (D)] as criteria of synchronization between cardiac and locomotor rhythms in *subject* SS. A 2:1 synchronization was noted during the periods 9-15 (a), 15.5-18 (b) and 18.8-20 min (c).

Figure 2: In the surrogate data, the phase relationship between cardiac and locomotor rhythms (A) and a trace of the χ^2 values of $\phi_{r,l}$ (B) for the same *subject* as in Fig. 1. Note that the horizontal structure of the phase relationship observed in the original is destroyed by the surrogate data, but still significantly exceeds χ^2 values of $\phi_{r,l}$ as in the original data. Definition as in Fig. 1

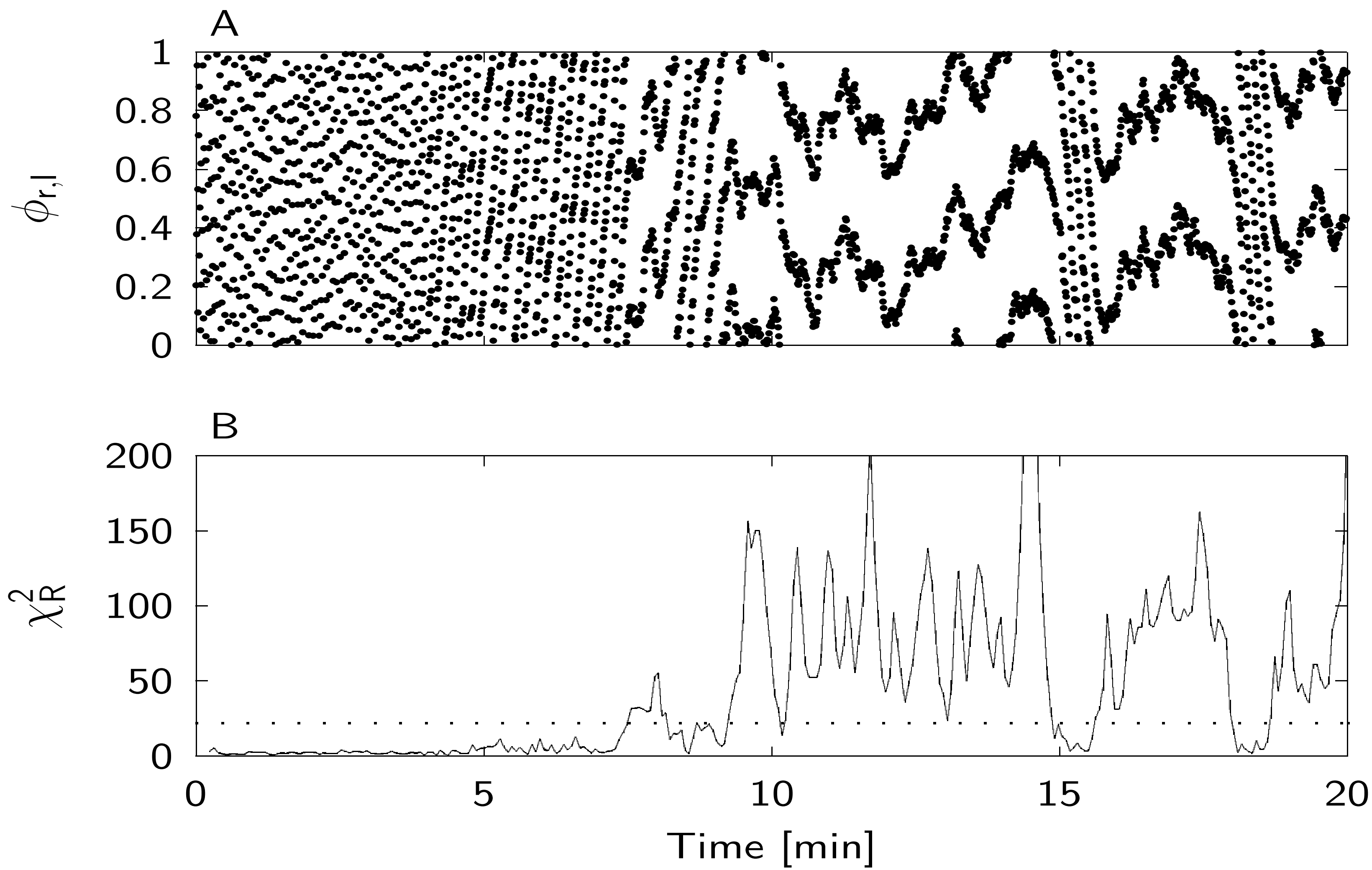
Figure 3: During the period of corresponding to Fig. 1B, a, the original data shows a typical horizontal structure (A), while the surrogate data has no such structure (B). Definition as in Fig. 1

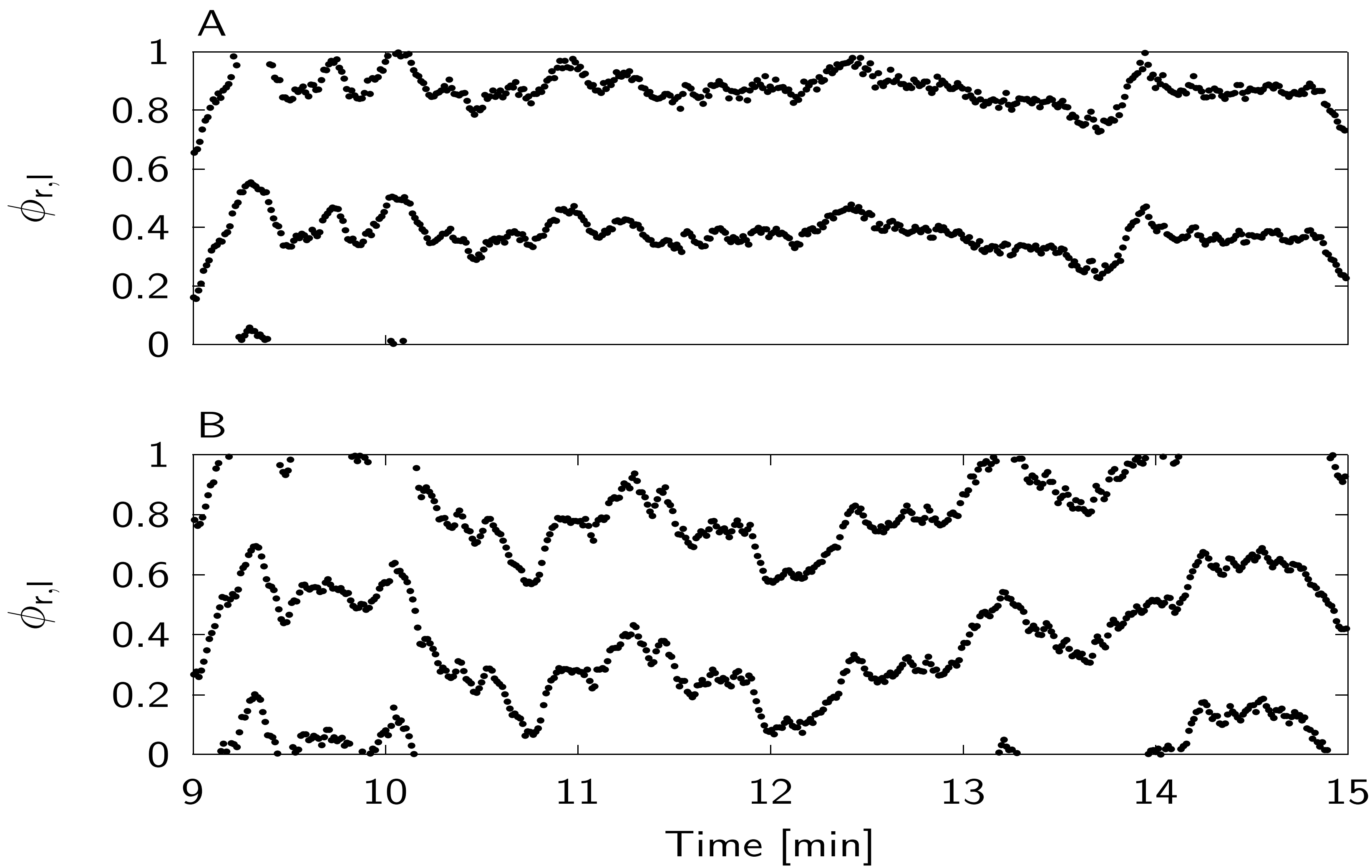
Figure 4: The distribution of all events of the phase relationship obtained during running. Original data (A), Surrogate data (B).

Figure 5: The group mean and SD of the χ^2 values of all events for all of the subjects. $*P < 0.05$.



A
980
890
800
710
620
Gait-cycle [msec]
B
480
440
400
360
R-R intreval [msec]
a
b
c
C
1
0.8
0.6
0.4
0.2
0
$\phi_{r,l}$
D
200
150
100
50
0
χ^2_R
0
5
10
15
20
Time [min]


A
B
$\phi_{r,l}$
χ^2_R
Time [min]


A
B
$\phi_{r,l}$
$\phi_{r,l}$
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0.6
0.4
0.2
0
9
10
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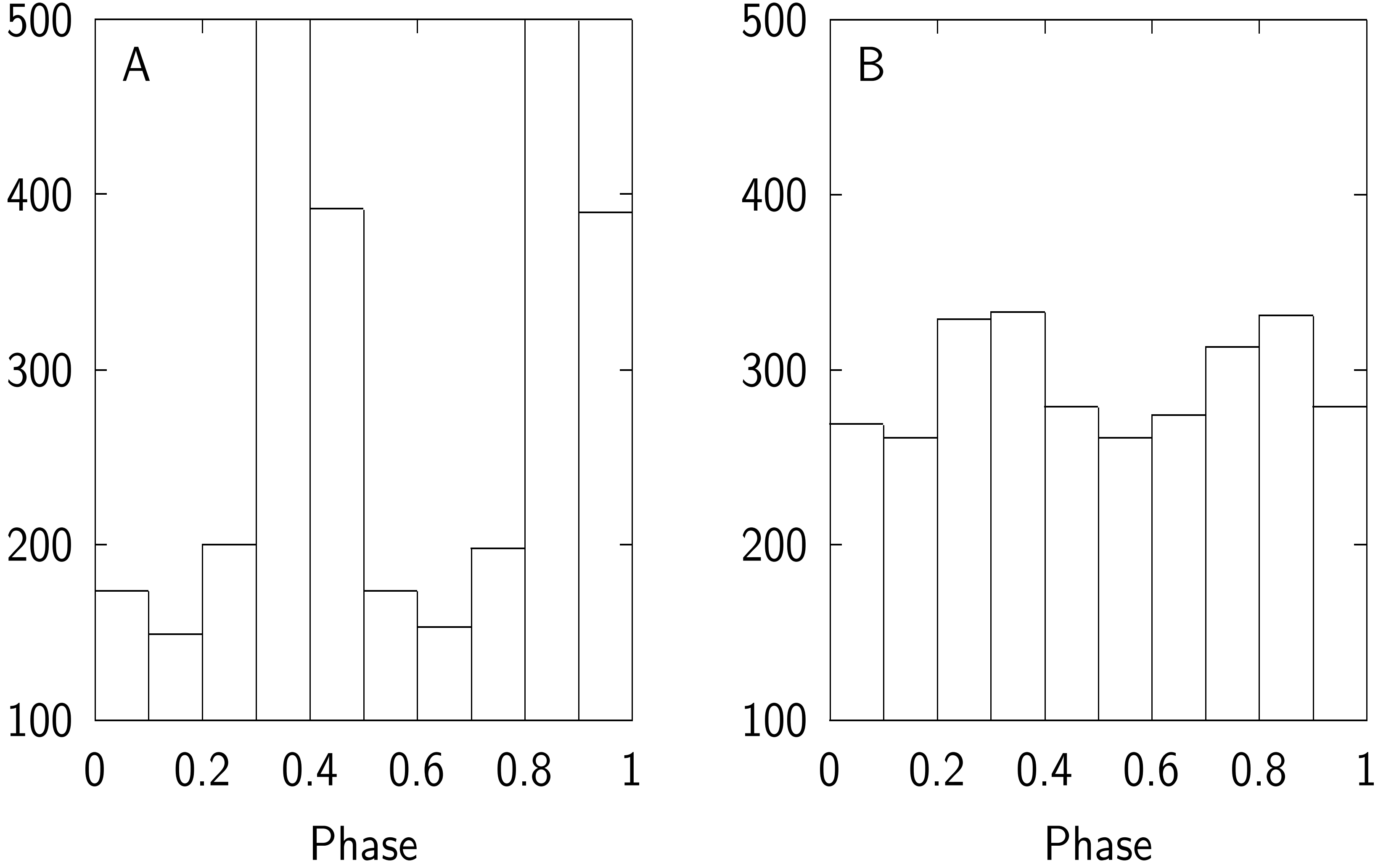
13
14
15
Time [min]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B
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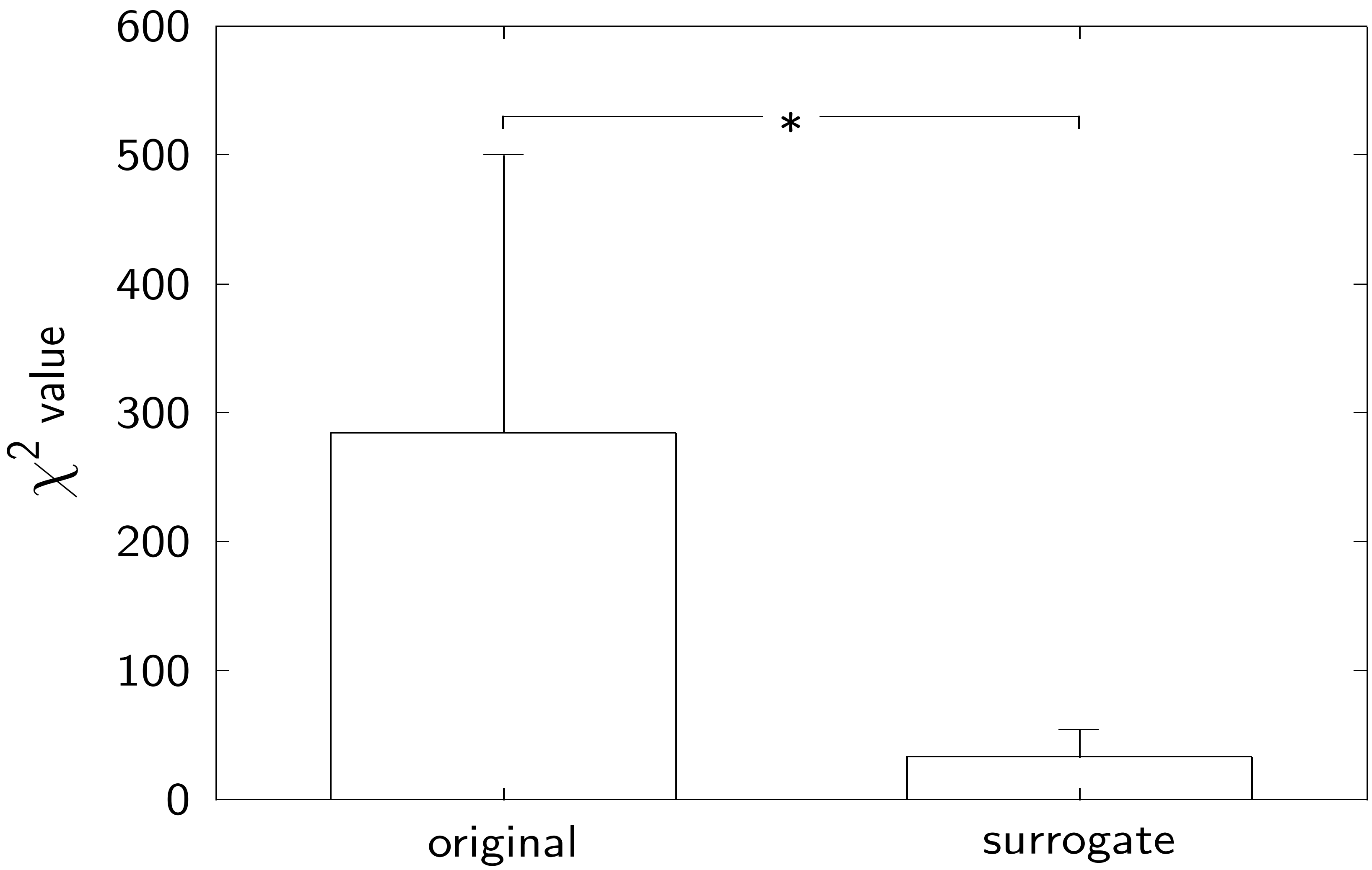
400
300
200
100
0
0.2
0.4
0.6
0.8
1
Phase



600
500
400
300
200
100
0
χ2 value
*
original
surrogate