A Method for Monitoring Autonomic Nervous Activity by Pupillary Flash Response

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SUMMARY

This paper proposes a noninvasive method for estimating autonomic nervous activity from changes in dynamic parameters of a pupillary flash response. Our method is derived based on an analysis that clarifies the relationship between the autonomic nervous activity and the dynamic parameters using the human pupillary muscle plant model developed in our previous study. Moreover, we show that pupillary responses to an identical flash vary depending on the initial pupil diameter when evaluating autonomic nervous activity by means of changes in the dynamic parameters. The efficacy of this method is demonstrated by applying it to a subject whose autonomic nervous activity is modified by drugs affecting the autonomic nervous system. © 2000 Scripta Technica, Syst Comp Jpn, 31(4): 22–31, 2000

Key words: Pupil; iris sphincter; iris dilator; autonomic nervous system; biomechanical model; range nonlinearity.

1. Introduction

The pupillary control system, which regulates the light intensity on the retina and spatial frequency characteristics, focal depth, and lens aberration of the optical system, is considered as a suitable system for the study of biological feedback control systems [1]. Moreover, the pupil has also attracted attention by means of noninvasive monitoring of autonomic nervous activity because it is innervated by both the sympathetic and parasympathetic nervous systems. Observation of autonomic nervous activity, which performs an essential role in regulating homeostasis, has been desired from medical, psychological, and ergonomic points of view. In space medicine, it is important to examine the effects of a long-term stay in a microgravity environment on the homeostatic regulation of astronauts. Currently, a monitoring method utilizing the heart rate variability has been widely used. This method evaluates the low-frequency (LF) and high-frequency (HF) components of the heart rate power spectrum. It is understood that the LF component, originating from blood pressure rhythm (Mayer wave), reflects sympathetic and parasympathetic
nervous activity. The HF component, originating from respiratory rhythm (respiratory sinus arrhythmia), reflects parasympathetic nervous activity only [2]. However, the frequency bands of LF and HF components have not been determined clearly [3, 4], and the components cannot always be separated in the spectrum [5, 8]. Consequently, this method is not appropriate for independent evaluation of sympathetic and parasympathetic nervous activity. In contrast, since the pupil is controlled by two kinds of muscles whose dynamics and innervation are different (iris sphincter innervated by parasympathetic nervous system and iris dilator innervated by sympathetic nervous system), it has a potential to allow independent evaluation of both types of nervous activity.

Several methods utilizing the pupil have been proposed. It is known that the pupillary fluctuation under steady light intensity (pupil noise) synchronizes with respiratory rhythm [6, 7]. The pupil noise method [9] evaluates parasympathetic nervous activity from this respiratory component in the same manner as the heart rate method. However, sympathetic nervous evaluation is not considered in this method. Therefore, it can be said that this method does not sufficiently use given characteristics of the pupil, that is, the possibility of both types of nervous evaluation. Another method mathematically estimates the autonomic nervous input to the pupil using the inverse model of the pupillary muscle plant model [10–12]. This method has an advantage of being able to quantitatively estimate pure nervous activity because the inverse dynamic model eliminates the nonlinear properties of the muscle plant. However, the disadvantage of this method is that the solution of the inverse model can only be derived under the condition that the balance of reciprocal innervation of both types of nervous activity remains unchanged. This condition is not satisfied in most situations in which autonomic nervous activity should be evaluated, and this method is thus not practical for many pertinent studies.

In the field of neuro-ophthalmology, a method using the dynamic parameters (e.g., maximum constriction amount, maximum constriction velocity) of a flash response has been proposed (hereafter referred to as the conventional method) [13–15]. Since nonlinear characteristics inherent in the pupillary muscle plant are reflected in the change of dynamic parameters, it is difficult to quantitatively estimate the pure nervous activity as in the inverse model method. The conventional method, however, is practical because it enables evaluation of both types of nervous activity by simple differential processing. The main drawback of the conventional method is that it can evaluate only four autonomic nervous states: increase or inhibition of sympathetic nervous activity or increase or inhibition of parasympathetic nervous activity. It does not evaluate the case in which both types of nervous activity change simultaneously. Acute idiopathic pandysautonomia and Parkinson’s disease, which can be diagnosed from pupil behavior, are known to occur due to neurological impairments of both types of nervous systems [16, 17]. Additionally, situations in which both types of nervous activity change are common. Astronauts’ autonomic nervous activity in microgravity environments may involve changes in both types of activity. Therefore, a method which enables independent evaluation of both types of nervous activity is strongly desired.

In this paper, a new method for monitoring both types of nervous activity independently and simultaneously is proposed. This method is a major modification of the conventional method. First, in the following section, the problems of the conventional method associated with the separate evaluation of both types of nervous activity are explained in detail. Also, the results of computer simulation and experiment for resolving the problems are shown. In Section 3, a new method developed based on these results is introduced. Finally, in Section 4, the efficiency of the method is confirmed by applying it to a drug experiment.

2. Problem of Conventional Method and Its Improvement

2.1. Problem of conventional method

In order to evaluate autonomic nervous activity, the conventional method refers to changes in dynamic parameters (see Fig. 2) such as initial pupil diameter or area ($D_{\text{init}}$), latency ($\tau$), maximum constriction amount ($\Delta D$), maximum constriction velocity ($V_{cmax}$), maximum dilation velocity ($V_{dmax}$), and maximum constriction acceleration ($A_{cmax}$) of a flash response [13–15]. $A_{cmax}$ is not used in some cases [14] because changes in $A_{cmax}$ and $V_{cmax}$ have a high correlation [13]. The methodology of the conventional method is explained below in detail.

First, drugs for activating or inhibiting the sympathetic or the parasympathetic nervous activity are instilled into normal subjects. Next, the averaged patterns of change in each dynamic parameter before and after drug administration are obtained (see four patterns of Table 1). In addition, the measured normal values of each dynamic parameter are averaged and categorized by age and sex. After these preparations, dynamic parameters of the patient are recorded and the difference in the dynamic parameters between the patient and the normal subject is calculated (patient’s pattern). Diagnosis is made by comparing patient’s pattern with the four kinds of pattern of Table 1 [14]. If the patient’s pattern does not coincide with any of those in Table 1, the most similar pattern is chosen as a patient’s symptom. This method is currently being applied clinically.
However, there are two problems with the sympathetic and parasympathetic evaluations.

The first problem is that only the four kinds of autonomic nervous activity shown in Table 1 can be monitored with this method. That is, the conventional method can be applied in the case in which only the sympathetic or only the parasympathetic nervous activity is changed. Expanding Table 1 by adopting mixed drugs is one solution to this problem. However, before using a mixed drug method, the dangers associated with additive action and side effects of the chemical changes of the ingredients must be sufficiently studied. This difficulty means that expansion of Table 1 is unreasonable. Another way to clarify the problem is to find parameters which have sensitivity to either the sympathetic or the parasympathetic nervous activity alone. Such parameters would allow independent evaluation of both types of nervous activity even when both change simultaneously.

The second problem with the conventional method is that the patterns of parasympathetic activation and sympathetic inhibition, and the pattern of parasympathetic inhibition and sympathetic activation in Table 1 are very similar. As mentioned previously, the patient’s pattern and the patterns of Table 1 do not always coincide. Sometimes it is difficult to select the most similar pattern from Table 1 [14]. There are at least two possible reasons for the similarities of patterns of two autonomic nervous states. One is that the conventional method only refers to dynamic parameters which show similar changes in parasympathetic activation (inhibition) and sympathetic inhibition (activation). This complication can be resolved if dynamic parameters that independently reflect sympathetic and parasympathetic nervous activity are obtained as the solution of the first problem. The second reason regards the characteristic termed the range nonlinearity (RNL) [18]. It is known that the dynamic parameters change depending on $D_{init}$ even if the nervous activity is normal [19]. The conventional method does not consider this RNL effect. Table 1 shows that when $D_{init}$ changes in a particular direction, the remaining dynamic parameters also change in a particular direction. There is a high possibility that such similarity in pattern occurs because of RNL.

The first problem is discussed in Section 2.2 and the effects of RNL are discussed in Section 2.3.

### 2.2. Determination of dynamic parameters for independent evaluation

In order to determine the dynamic parameters which can evaluate sympathetic and parasympathetic nervous activity independently, it is necessary to know clearly how each type of nervous activity is reflected in the dynamic parameters through the internal mechanisms of the pupillary muscle plant. To date, the relationships between the two have not been clarified in detail. A major reason for this failure is that the inverse problem of the pupillary muscle plant is an ill-posed problem [10]. It is possible to estimate the difference of the tension between the sphincter and dilator muscles. It is not possible, however, to know the tension of each muscle from observation of the pupillary response only. Thus, using this formulation, contribution of each type of nervous activity to pupillary response is also unknown. Still, if the autonomic nervous input to the pupillary muscle plant can vary freely, such interaction can be determined. For example, if the parasympathetic nervous input can be eliminated, the flash response generates only sympathetic nervous activity and vice versa. These data provide useful information about the relationship between each type of autonomic nervous activity and dynamic parameter. However, if one type of nervous activity is blocked or enhanced by drugs, the recorded pupillary response reflects not only the nervous state modified by the drugs but also the effect of RNL (explained in detail in Section 2.3) due to the change in $D_{init}$. Therefore, it is difficult to investigate the exact relationship between autonomic nervous activity and dynamic parameters experimentally. The pupillary muscle plant model [11, 12], however, can realize the above experiment by a simple computational simulation.

#### 2.2.1. Pupillary muscle plant model

The pupillary muscle plant model (Fig. 1) [11, 12] has a structure reflecting physiological and anatomical evidence. Since each parameter of this model is determined by fitting model output to flash response experimental data, unique characteristics dependent on the subjects or experimental conditions are reflected in the model. An example of such fitting is shown in Fig. 2. The experimental data in Fig. 2 are measured by a helmet-type infrared TV pupillometer [20]. The model parameters are estimated by BFGS

<table>
<thead>
<tr>
<th>Drug effect</th>
<th>$D_{init}$</th>
<th>$L$</th>
<th>$\Delta D$</th>
<th>$V_{max}$</th>
<th>$V_{min}$</th>
</tr>
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<tbody>
<tr>
<td>Parasympathetic activation</td>
<td>$\downarrow$</td>
<td>$\rightarrow$</td>
<td>$\downarrow$</td>
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<tr>
<td>Parasympathetic inhibition</td>
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<td>Sympathetic activation</td>
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<td>Sympathetic inhibition</td>
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$db$ : $20\log\left(\frac{R_{post}}{R_{pre}}\right)$, where $R_{pre/post}$:
- pre/post-drug value of right eye, $L_{pre/post}$:
- pre/post-drug value of left eye. The drugs were instilled to right eye.
a nonlinear optimization method. All parameters are estimated within the range of physiological and physical requirements determined by previous studies. This model has been confirmed by comparing model behavior with experimental evidence reflecting both basic and compound properties of the pupillary muscle plant. The model can reproduce or predict (1) pupil diameter at death, (2) movable range of the pupil, (3) effect of drugs on the pupil size, (4) difference in velocities of change in the sphincter and dilator tension, (5) differences between flash responses of the normal and sympathectomized pupil, and (6) pupillary responses to steps in sympathetic and parasympathetic nervous stimulus. Among those, (4), (5), and (6) are related to the interactions and dynamic properties of the sphincter and dilator as they receive sympathetic and parasympathetic nervous inputs. Thus, this model is a reliable analysis tool.

2.2.2. Relationship between autonomic nervous activity and dynamic parameter

Because the model explicitly describes characteristics of each muscle and each nervous input, it is possible to selectively simulate either the sympathetic or parasympathetic response by eliminating one of the nervous inputs to the model. Normal, sympathetic, and parasympathetic flash response components are shown at the top of Fig. 2. The latency of each component is different. The parasympathetic component shows a transient response, while the sympathetic component shows a sustained response. Because of these differences in dynamics, a single flash response can be divided into three distinct periods which reflect different nervous activity.

**Period I** reflects only parasympathetic nervous activity.
From the parasympathetic component action (beginning of the pupillary constriction) to the sympathetic component action.

**Period II** reflects both types of nervous activity.
From the sympathetic component action to the end of the parasympathetic component response.

**Period III** reflects only sympathetic nervous activity.
From the end of the parasympathetic component response to the end of the sympathetic component response.

These periods mean that it is not necessary to refer to several dynamic parameters at the same time, as in the conventional method. The sympathetic nervous activity can be assessed by referring to only one parameter of Period III and parasympathetic nervous function can be evaluated solely by one parameter of Period I. In addition to this, a parameter that is highly sensitive to changes in a single type of nervous activity is desired. Also, ease of calculation is important for practical use. Since response, velocity, and acceleration curves can be simply calculated by differentiation, the dynamic parameter should be selected from these three kinds of waveforms. Figure 3 shows cases in which these waveforms vary with sympathetic and parasympa-
thetic inputs to the model. From this figure, the dynamic parameters having the desired properties can be determined.

First, the dynamic parameter that is the index of the parasympathetic nervous activity is determined. Figure 3(a) shows the effect of varied parasympathetic inputs to the model. The gray area at the bottom of the figure denotes differences of the curve. This figure indicates that $V_{cmax}$ and $A_{cmax}$ reflect the parasympathetic nervous activity with high sensitivity in Period I. Thus, the parasympathetic nervous activity can be assessed by referring to either $V_{cmax}$ or $A_{cmax}$. The high correlation between $V_{cmax}$ and $A_{cmax}$ pointed out in previous studies (mentioned in Section 2.1) [13] can be explained from these results. However, $A_{cmax}$ is extracted from the second-derivative curve of the flash response and is therefore more easily influenced by the experimental noise than $V_{cmax}$. Thus, $V_{cmax}$ is suitable for parasympathetic evaluation.

Second, the dynamic parameter that is the index of the sympathetic nervous activity is determined. As can be seen in Fig. 2, no dynamic parameter referred to in the conventional method appears in Period III. Thus, a new dynamic parameter belonging to Period III must be defined for sympathetic evaluation. Figure 3(b) shows the results of the sympathetic input change to the model. It is seen that the beginning of Period III of the response curve is the most sensitive. Based on this, a new dynamic parameter, $RA$ (Recovery Amount), is defined as the difference of $D_{ini}$ and the pupil diameter in the beginning of Period III. Extracted time of $RA$ must be determined after obtaining Fig. 2 because the starting time of Period III differs depending on the stimulus intensity or the subject.

As can be seen in Fig. 3, $V_{cmax}$ and $RA$ change in magnitude which correspond to changes in the magnitude of the sympathetic and parasympathetic nervous activity. The behavior of each dynamic parameter with respect to each nervous change is shown in Table 2, which reveals that increase (decrease) of $V_{cmax}$ and $RA$ indicate parasympathetic activation (inhibition) and sympathetic inhibition (activation), respectively.

2.3. Range nonlinearity

RNL is the factor of the second problem of the conventional method. It is a nonlinear gain characteristic dependent on the sphincter and dilator muscle length [18,
If \( D_{init} \) changes due to the background light intensity, the dynamic parameter of the response to identical flash stimuli changes even under normal autonomic nervous conditions. In Table 1, \( D_{init} \) changes significantly in any state of autonomic nervous activity. The effect of RNL, however, is not considered in this table.

According to the simulation results shown in Fig. 3 and Table 2, \( V_{cmax} \) is not changed by sympathetic input changes. \( V_{cmax} \) is increased by parasympathetic activation. \( V_{dmax} \) which reflects both types of nervous activity should increase (decrease) by the parasympathetic activation (inhibition). These model predictions are inconsistent with Table 1. Moreover, in Table 1, two kinds of autonomic nervous states cause \( D_{init} \) changes in the same direction with similar patterns. Presumably these occur due to the effect of RNL. Therefore, when the autonomic nervous activity is evaluated by \( V_{cmax} \) and \( RA \), the effect of RNL can be eliminated from changes in parameters. To accomplish this, it is important to know how \( V_{cmax} \) and \( RA \) change depending on \( D_{init} \).

### 2.3.1. Range nonlinearity experiment

The flash interval was set to 10 seconds. This allows the pupil diameter to recover to steady state (corresponding to the initial pupil diameter). \( D_{init} \) was controlled by adjusting the background light intensity. The background light was exposed in the eye not subjected to flash stimulation while avoiding a high gain condition. Thus, the flash-stimulated eye maintains its dark adaptation state. The flash stimulation method was not the Maxwellian View and the system remained in closed-loop condition. In these conditions, the flash intensity reaching the retina changes depending on \( D_{init} \). Therefore, not only RNL but also the differences of flash intensity dependent on \( D_{init} \) affect the changes in dynamic parameters. However, if the same stimulating method is used for control measurement (corresponds to this experiment) and is used in the experiment for autonomic nervous evaluation, these experimental conditions do not affect the final evaluation. In the experiment, after dark adaptation of more than 20 minutes, the background light was exposed step by step. The flash response was measured after sufficient adaptation at each background intensity level. The subjects were five healthy males in their early 20s.

### 2.3.2. Relationship between range nonlinearity and dynamic parameter

Examples of experimental results are shown in Fig. 4. Each response is the average of 10 flash responses of which \( D_{init} \) were within \( \pm 0.2 \) mm of the mean value. This figure indicates that, depending on \( D_{init} \), dynamic property of responses and velocity curves are clearly different. In order to visualize the effect of RNL on each parameter, Fig. 5 (hereafter referred to as the RNL map) plots \( D_{init} \) as the abscissa and \( V_{cmax} \) and \( RA \) as the ordinate. The shape of the RNL map of each dynamic parameter is different. Moreover, the shape of the RNL map differs by subject even for the same parameter. Similar tendencies are confirmed in

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Fig. 4. Examples of flash response (upper) and velocity curves (lower) with various initial pupil diameters. Each curve is the average of 10 flash responses whose initial pupil diameters range within the mean \( \pm 0.2 \) mm.
three other subjects. Therefore, to evaluate autonomic nervous activity, the RNL map of the normal condition should be obtained as control data for each subject. The dynamic parameters measured in experimental conditions should be compared with control data in the same range to eliminate the effect of RNL.

3. Proposed Method

Based on the results in Sections 2.1 and 2.3, a new method for monitoring the autonomic nervous activity utilizing the pupillary flash response is proposed. The methodology is summarized as follows:

(1) Measure flash response at different initial pupil diameters. Extract $D_{init}$, $V_{cmax}$, and $RA$, and build RNL maps of control data for each subject.

(2) Measure flash response to the identical light stimulus under various experimental conditions and extract $D_{init}$, $V_{cmax}$, and $RA$.

(3) Compare $V_{cmax}$ and $RA$ of (2) with those of control measurements taken in (1) in the same $D_{init}$ range, correcting for RNL. Sympathetic evaluation by $V_{cmax}$ and parasympathetic evaluation by $RA$ are made by referring to Table 2. Changes in the magnitude of the sympathetic and parasympathetic nervous activity correspond to changes in the magnitude of $V_{cmax}$ and $RA$.

4. Accuracy of the Method

In this section, the proposed method of autonomic nervous monitoring is applied to a subject whose autonomic nervous activity has been modified by drugs in order to confirm whether the method can accurately predict the effect of drugs.

4.1. Drug experiment

The experiment employed two kinds of drugs, tropicamide 0.01% and dipivaryl epinephrine (DPE) 0.1%. Tropicamide inhibits parasympathetic nervous activity and DPE activates the sympathetic nervous activity. These drugs were also used to obtain Table 1 in the conventional method [14]. Here the concentration is diluted to half for safety. After applying the drug of sympathetic activation or parasympathetic inhibition, the maximum pupil diameter under dark adaptation becomes larger than the normal condition. $V_{cmax}$ and $RA$ of the drug-induced states cannot be compared with $V_{cmax}$ and $RA$ of normal states in the same $D_{init}$ range. To counteract, the pupil diameter was set to about 6 mm before instilling drugs by adjusting the background intensity. The method for measuring the flash response and exposing the background light were the same as in Section 2.3.1. The subject was the same person used in Fig. 4. After dark adaptation of more than 20 minutes, the drug was instilled into the right eye two times in 5-minute intervals. The flash response was recorded 5 minutes after instillation, and again every 15 minutes for 120 minutes. In each session, about 10 responses were recorded.

4.2. Evaluation

The experimental results were evaluated according to the steps in Section 3. The RNL map of step (1) was measured in advance under the normal conditions (corresponding to subject M.I.’s RNL map in Fig. 5). The experimental results of Section 4.1 correspond to step (2). In step (3), the comparison of dynamic parameters of the drug-induced condition and the normal condition in the same $D_{init}$ range was done as follows. As shown in Fig. 6, data recorded during the drug experiment are superimposed onto the RNL maps of $V_{cmax}$ and $RA$. Next, drug data are compared with the RNL map of which $D_{init}$ is within its range. An asterisk denotes that the difference between values is significant ($P < 0.01\%$).

Figure 6(a) shows the time course of each dynamic parameter after instilling tropicamide. The results reveal that at 45 and 60 minutes after drug instillation, $V_{cmax}$ significantly decreases. According to Table 2, this result indicates that parasympathetic nervous activity was inhibited at that time. After this, $V_{cmax}$ gradually returned to the normal value, although there were some variations. These results agree with clinical findings [23, 24] that the maximum effect of tropicamide is manifested between 30 and 60 minutes after instilling the drug. $RA$ during this time overlaps the normal data, accurately showing that tropi-
camide does not affect sympathetic nervous activity. These results demonstrate that parasympathetic nervous activity can be assessed by the proposed method.

$D_{init}$ was determined by the tension balance of the sphincter (parasympathetic nervous input) and the dilator (sympathetic nervous input). Changes in this balance reflect changes in sympathetic and parasympathetic nervous activity. Since the sympathetic nervous activity is unchanged in the experiment of Fig. 6(a), the change of $D_{init}$ (dilation) reflects the effect of parasympathetic inhibition caused by tropicamide. Even 120 minutes after instillation, when $V_{cmax}$ is almost back to its normal value, $D_{init}$ is still large compared to the $D_{init}$ value 5 minutes after instillation. This inconsistency is due to the difference in the sensitivities of $V_{cmax}$ and $D_{init}$ to parasympathetic nervous change. $D_{init}$ has a higher sensitivity to parasympathetic change than $V_{cmax}$ in the pupil diameter range between 6 and 9 mm [25]. But since $D_{init}$ reflects both types of nervous activity, $V_{cmax}$ must be used for parasympathetic evaluation.

The results of the DPE experiment were similarly evaluated. As shown in Fig. 6(b), RA significantly decreases after 60 minutes. The maximum decrease is detected 105 minutes after instillation. According to Table 2, this means that the sympathetic nervous activity is activated during that time. The maximum effect of DPE is known to occur between 60 and 180 minutes after instillation [26, 27]. Since significant change in $V_{cmax}$ is not observed, this indicates there is no change in parasympathetic nervous activity. These results correspond to the evidence known from the effects of DPE. Thus, sympathetic nervous activity can be accurately assessed by this method.

Section 2.1 detailed the two major problems of the conventional method. The first problem is that sympathetic and parasympathetic nervous activity cannot be evaluated independently. The method proposed here can be used to evaluate each type of nervous activity from the changes in $V_{cmax}$ and RA. The second problem is due to the similar patterns in Table 1. In Table 1, the patterns of the effects of tropicamide and DPE are similar; therefore, there is a possibility that each symptom cannot be easily judged by the conventional method. However, the method proposed here accurately evaluated the changes in both types of nervous activity without any confusion. These results show that the proposed method overcomes the problems of the conventional method. In the future, further investigation of this method will be made with drugs which affect parasympathetic activation and sympathetic inhibition.
5. Conclusions

In this study, a new method for monitoring the sympathetic and parasympathetic nervous activity from the pupillary flash response is proposed and verified. The monitoring method proposed in this paper is expected to be applicable to various research areas. However, since the RNL map as normal condition data of a patient cannot be obtained in clinical applications, a substitute RNL map, such as an averaged RNL map of a normal person, must be used. In this case, the autonomic nervous activity is evaluated more accurately if the $D_{\text{aut}}$ range, which shows minimal variations among individuals, is determined in advance and the flash response of a patient is measured at that $D_{\text{aut}}$ range. On the other hand, the proposed method is useful in situations in which the autonomic nervous evaluation of the normal subject is conducted under special experimental conditions.

The authors are in the process of evaluating human nervous activity under a microgravity environment. We believe that application of our method will provide new insights to space medicine.

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REFERENCES


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