Effects of Heart Rate Variability Biofeedback Therapy on Patients with Poststroke Depression: A Case Study

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INTRODUCTION

Poststroke depression (PSD) is one of the common complications of cerebrovascular diseases. Drug therapy and cognitive behavioral therapy are two commonly used methods in current clinical treatments of PSD. However, either method has its own drawbacks: The former has problems such as the slow onset of action and various side effects, and patients often have a poor response to the latter.[1] Recently, scientists have started using the heart rate variability (HRV) biofeedback approach to treating patients with depression and found significant clinical efficacy. HRV biofeedback requires patients to synchronize heart rate (HR) oscillations, and breathe by slow abdominal breathing (about 6 times/min; i.e., at the resonance frequency of 0.1 Hz), and thus maximizes HRV.[2] The objective of this study is to examine the impacts of HRV biofeedback on patients’ emotional improvement and to explore the potential of this approach as an effective, side-effect-free supplement for comprehensive recovery.

METHODS

Patient selection

Subjects of the study were recruited among the rehabilitation inpatients in Beijing Bo Ai Hospital from February 2013 to May 2014. Eligible subjects were selected according to the inclusion criteria and exclusion criteria as shown in Table 1. The study protocol was approved by the Ethics Committee of Beijing Bo Ai Hospital and Written informed consent was obtained from all participants.

Procedure and randomization

Patients enrolled in the experiment were divided into feedback and control groups according to the randomized controlled trials table. All the subjects received regular rehabilitation treatments, including physical therapy, psychotherapy, and medication (fluoxetine 20 mg daily). The patients in the feedback group were given additional HRV biofeedback treatments (30 min each time, 3 times/week for 4–6 weeks, and 10 times as a course), following the protocol of study of Lehrer et al. in 2003.[3] The patients in the control group received the relaxation therapy without a feedback signal to guide them breathe quietly and stay awake. The clinical outcome was evaluated using the Hamilton Depression Scale (HAMD), Pittsburgh Sleep Quality Index (PSQI), simplified Fugl-Meyer Motor Assessment (FMA), National Institutes of Health Stroke Scale (NIHSS), modified Barthel index (MBI), and the monitoring of indices of HRV included standard deviation of normal RR intervals (SDNN), HR, low frequency (LF), high frequency (HF), LF/HF ratio, etc., before and after the treatments, respectively.

Statistics analysis

We evaluated the differences between the two groups. Paired samples t-test on data before and after the experiment and one-way analysis of variance (ANOVA) on data of the

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two groups were calculated using IBM SPSS Statistics for Windows, version 19.0 (IBM Corp., Armonk, NY, USA). When the data were not normally distributed, the Wilcoxon rank-sum nonparametric tests were used to compare the data before and after the experiment and between groups. A P < 0.05 was considered as statistically significant.

## Results

### Patient characteristics

A total of 24 patients meeting all the requirements were recruited and enrolled in the experiment. They were randomly assigned to the feedback group (n = 13) and the control group (n = 11), respectively. The general demographic data of these patients are listed in Table 2. No significant differences were found between the two groups in terms of any demographic [Table 2] or baseline variables [Table 3].

### Impacts on depression

We found statistically significant drops in scores of the following factors which measure levels of depression: Anxiety/somatization (P = 0.00), cognitive impairment (P = 0.00), total score of HAMD (P = 0.00), weight (P = 0.02), block (P = 0.01), and desperation (P = 0.02) in HAMD scale. In contrast, for patients in the control group, only the anxiety/somatization factor score decreased significantly between before and after treatment (P = 0.05). The posttreatment scores of feedback group for sleep disturbance (P = 0.01) and block (P = 0.04) were statistically lower than those of the control group, indicating that the clinical symptoms of depression were improved significantly through HRV biofeedback.

### Impacts on sleep

We found statistically significant drops in scores of the following factors: Sleep disturbance component score (P = 0.03), global PSQI score (P = 0.02), Subjective sleep quality component score (P = 0.03), sleep duration component score (P = 0.03), and daytime dysfunction component score (P = 0.05) in PSQI scale. In contrast, the difference between before and after treatment was not found in the control group. There were significant differences after the treatments between the feedback and control groups for the factor scores for global PSQI score (P = 0.01), Subjective

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### Table 1: Inclusion criteria and exclusion criteria of patients

| Patient inclusion criteria                                                                 | Feedback group (n = 13) | Control group (n = 11) |
|-------------------------------------------------------------------------------------------|-------------------------|------------------------|
| Aged between 18 and 75 years, regardless of gender                                         |                         |                        |
| Meeting the diagnostic criteria for stroke confirmed by head CT or MRI and in the first stage of stroke |                         |                        |
| Having stable vital signs verified by the test taken in 2–6 months after the stroke onset |                         |                        |
| Being conscious, of complete orientation, and having a total score greater than 27 in the MMSE |                         |                        |
| The education level being elementary or above                                              |                         |                        |
| Being able to cope with the tests and treatments, and having signed the form of informed consent |                         |                        |

### Table 2: Basic characteristics of control and feedback groups

| Characteristics                        | Feedback group (n = 13) | Control group (n = 11) |
|----------------------------------------|-------------------------|------------------------|
| Age (years), mean±SD                   | 54.38 ± 13.33           | 59.64 ± 12.44          |
| Gender, n                              |                         |                        |
| Female                                 | 8                       | 3                      |
| Male                                   | 5                       | 8                      |
| Education, n                           |                         |                        |
| Elementary                             | 2                       | 1                      |
| High school                            | 4                       | 7                      |
| Graduate                               | 7                       | 3                      |
| Married, n                             | 13                      | 11                     |
| Diagnosis, n                           |                         |                        |
| Infarction                             | 8                       | 6                      |
| Hemorrhage                             | 5                       | 5                      |
| Effect side, n                         | Left                    | 10                     | 6                  |
|                                       | Right                   | 3                      | 5                  |
| Course of disease (months), mean ± SD   | 3.62 ± 2.18             | 3.36 ± 1.43            |
| Involved part, n                       |                          |                        |
| Parietal                               | 1                       | 2                      |
| Temporal                               | 4                       | 5                      |
| Prefrontal                             | 5                       | 1                      |
| Basal                                  | 12                      | 10                     |
| Single lesion, n                       | 6                       | 7                      |
| Medical history, n                     |                          |                        |
| Hypertension                           | 10                      | 11                     |
| Diabetes                               | 3                       | 2                      |
| Heart disease                          | 3                       | 0                      |
| Hyperlipidemia                         | 4                       | 8                      |
| Mood, n                                | Depression              | 3                      | 4                  |
|                                        | Anxiety                 | 10                     | 7                  |

SD: Standard deviation.

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Table 3: Comparisons of impacts on depression, sleep, functional disorder, and HRV indices between control and feedback groups (mean ± SD)

| Items                        | Control group (n = 11) | Feedback group (n = 13) | F or Z | P     | Control group (n = 11) | Feedback group (n = 13) | F or Z | P     |
|------------------------------|------------------------|-------------------------|--------|-------|------------------------|-------------------------|--------|-------|
| HAMD                         |                        |                         |        |       |                        |                         |        |       |
| Anxiety/somatization         | 5.13 ± 1.81            | 6.18 ± 2.40             | 1.09   | 0.31  | 3.13 ± 2.03†           | 2.55 ± 1.70*            | 0.46   | 0.51  |
| Cognition impairment         | 3.38 ± 2.33            | 3.27 ± 1.95             | 0.01   | 0.92  | 1.38 ± 0.92            | 0.82 ± 1.25*            | 1.14   | 0.30  |
| Sleep disturbance            | 4.88 ± 1.89            | 3.55 ± 2.42             | 1.67   | 0.21  | 4.38 ± 1.60            | 1.91 ± 2.07             | 7.88   | 0.01  |
| Total scores                 | 23.63 ± 8.28           | 25.73 ± 5.36            | 0.45   | 0.51  | 16.88 ± 5.84           | 11.45 ± 5.56*           | 4.23   | 0.06  |
| Weight                       | 0.88 ± 0.84            | 0.91 ± 0.70             | −0.13† | 0.89  | 0.50 ± 0.76            | 0.18 ± 0.41†            | −1.02† | 0.31  |
| Diurnal variation            | 0.13 ± 0.35            | 0.27 ± 0.91             | −0.16† | 0.88  | 0.00 ± 0.00            | 0.27 ± 0.65             | −1.24† | 0.22  |
| Block                        | 5.50 ± 2.73            | 6.27 ± 1.49             | −0.42† | 0.68  | 4.25 ± 1.58            | 2.55 ± 1.81*            | −2.10† | 0.04  |
| Desperation                  | 4.00 ± 2.93            | 4.64 ± 1.69             | −0.38† | 0.71  | 3.25 ± 2.19            | 2.64 ± 1.03*            | −0.68† | 0.50  |
| PSQI                         |                        |                         |        |       |                        |                         |        |       |
| Sleep duration               | 2.38 ± 0.92            | 1.82 ± 1.25             | 1.15   | 0.30  | 2.13 ± 1.36            | 1.09 ± 0.94             | 3.87   | 0.07  |
| Sleep efficiency             | 1.38 ± 1.30            | 1.55 ± 1.29             | 0.08   | 0.78  | 1.00 ± 1.07            | 0.55 ± 0.82‡             | 1.11   | 0.31  |
| Global PSQI score            | 13.38 ± 5.01           | 12.00 ± 6.66            | 0.24   | 0.63  | 12.13 ± 3.40           | 7.18 ± 3.82‡             | 8.49   | 0.01  |
| Subjective sleep quality     | 2.38 ± 0.74            | 1.73 ± 1.01             | −1.43† | 0.15  | 1.88 ± 0.84            | 1.00 ± 0.63‡             | −2.47† | 0.01  |
| Sleep duration               | 1.63 ± 1.30            | 1.64 ± 1.36             | −0.04† | 0.97  | 1.38 ± 1.41            | 0.45 ± 0.93‡             | −1.63† | 0.1   |
| Sleep disturbance            | 1.00 ± 0.00            | 1.18 ± 0.60             | −0.93† | 0.35  | 1.13 ± 0.35            | 1.00 ± 0.45             | −0.65† | 0.52  |
| Daytime dysfunction          | 2.38 ± 0.92            | 2.45 ± 0.69             | 0.00†  | 1.00  | 2.63 ± 0.74            | 1.64 ± 0.81†             | −2.35† | 0.02  |
| Assessment for functional disorder |                  |                         |        |       |                        |                         |        |       |
| FMA                          | 24.75 ± 10.57          | 48.64 ± 30.36           | −1.82† | 0.07  | 32.38 ± 11.35*         | 53.64 ± 30.22†           | −1.49† | 0.14  |
| NIHSS                        | 10.25 ± 1.67           | 6.82 ± 5.08             | −1.08† | 0.28  | 8.00 ± 1.93*           | 4.91 ± 4.11*             | −1.37† | 0.17  |
| MBI                          | 36.25 ± 12.17          | 55.91 ± 23.86           | −1.78† | 0.08  | 51.25 ± 15.30*         | 67.27 ± 19.67*           | −1.62† | 0.11  |
| HRV indices                  |                        |                         |        |       |                        |                         |        |       |
| HR (beats/min)               | 78.87 ± 12.60          | 80.20 ± 9.46            | 0.07   | 0.80  | 74.65 ± 15.30          | 79.97 ± 14.28            | 0.61   | 0.45  |
| SDNN (ms)                    | 35.15 ± 35.50          | 36.19 ± 24.15           | −0.50  | 0.62  | 18.22 ± 11.27          | 44.62 ± 32.23            | −2.23  | 0.03* |
| LF (ms)                      | 77.69 ± 147.72         | 62.18 ± 114.91          | −0.50† | 0.62  | 16.36 ± 25.63          | 273.93 ± 462.78†         | −2.97† | 0.00  |
| HF (ms)                      | 190.56 ± 405.96        | 71.31 ± 84.77           | −0.58† | 0.56  | 23.95 ± 39.93          | 98.80 ± 218.17           | −1.32† | 0.19  |
| LF/HF                        | 0.82 ± 0.62            | 0.97 ± 0.70             | −0.79† | 0.43  | 2.01 ± 2.19            | 8.52 ± 16.66†            | −1.32† | 0.19  |

*P<0.01, comparison of the feedback group before and after treatment; †P<0.05, comparison of the feedback group before and after treatment; ‡Z values. SDNN: Standard deviation of normal RR intervals; SD: Standard deviation; HRV: Heart rate variability; HAMD: Hamilton Depression Scale; PSQI: Pittsburgh Sleep Quality Index; FMA: Fugl‑Meyer Motor Assessment; NIHSS: National Institutes of Health Stroke Scale; MBI: Modified Barthel Index; LF: Low frequency; HF: High frequency; HR: Heart rate.

sleep quality component score (P = 0.01), and daytime dysfunction component score (P = 0.02), which implied that the symptoms of sleep disorder were improved significantly through HRV biofeedback.

**Impacts on motor function, damage levels, and activities of daily living**

We found statistically significant increases in the total scores of FMA scale (P = 0.01) and NIHSS scale (P = 0.00), and significant decrease in the score of MBI scale (P = 0.00) in the feedback group after the treatment. Meanwhile, the increases in the total scores of FMA scale (P = 0.00) and NIHSS scale (P = 0.00) and the decrease in the score of MBI scale (P = 0.00) are also significant in the control group after treatment. There was no significant difference between the two groups in FMA, NIHSS, and MBI scales. That is, the functional disorder had no change through HRV biofeedback.

**Impacts on heart rate variability indices**

We found significant increases in the scores of LF (P = 0.05) and LF/HF (P = 0.03) in the feedback group after the treatment. In contrast, the rank and test of the control group had no differences. The posttreatment scores of SDNN (P = 0.03) and LF (P = 0.00) of the feedback group were significantly higher than those of the control group, indicating that the autonomic nervous system function was improved significantly through HRV biofeedback.

**Discussion**

This study has shown that the 10 times as a course of HRV biofeedback treatments can be an effective treatment for PSD patients with no side-effects caused by the intervention of antidepressant drugs. In HRV indices, the scores of LF of the feedback group after treatment was significantly higher than that of the control group (P = 0.00), indicating that the autonomic nervous system function was improved significantly through HRV biofeedback. As the most important index of HRV biofeedback, the more significantly LF increases, the stronger patients’ feedback awareness and...
ability as well as their regulation on autonomic function level. This finding is consistent with those of most experiments, that is, LF increases significantly in the feedback process. Obviously, HRV biofeedback strengthens sinus arrhythmia and enhances its volatility and variability, and under certain conditions, there is a synchronous effect between such fluctuations and baroreflex. Using this type of behavioral therapy, patients can learn to self-regulate autonomic nervous functions, which indicate the improvement of functional activity of vagus nerve.\(^3,4\)

On the other hand, we have found in our experiments that although the depressive symptoms of feedback group were obviously enhanced, unlike the study of Karavidas et al.\(^5\) which resulted in significant improvement, the depression levels of subjects in our feedback group still did not reach the clinical cure levels after a course of 10 treatments. A possible reason is that patients with PSD are not as sensitive to HRV biofeedback as patients with only strokes or depression. The specificity of PSD disease may account for the outcome. The pathogenesis of PSD is complex, and most scholars believed that the parts of the brain damaged, and neurotransmitters are important factors in determining whether stroke patients suffer from depression. Previous studies have shown that PSD patients had a greater impact on HRV than mere strokes or depression, and its damage on the autonomic nerve is more serious. We thus conjecture that the specific characteristics of the pathogenesis of PSD, as well as its special occurrence and development processes, have caused the effectiveness of HRV biofeedback on PSD to be different from the results of prior studies treating other types of depressions. In our experiments, patients receiving a course of 10 times biofeedback treatments were still in the recovery process and not completely cured. Future studies may increase the frequency and intensity of training to investigate the long-term effects of this type of treatment on PSD patients.

The experiment also found that HRV biofeedback can significantly improve sleep disorder of PSD patients, which is a bright spot of our results. HRV biofeedback promote a conversion of autonomic nervous activity to be conducive to sleep and also a decline in awakened level, which will then induce sleep, increase depth of sleep, improve sleep quality, and shorten sleep latency. Our experiment has found that patients felt significant improvements of their daytime function. This may be due to shorter sleep time and an overall improvement of sleep quality, so that patients get adequate rest and can energetically engage in various rehabilitation activities in the daytime, which is of great clinical value in the improvement of neurological deficit and activities of daily living for stroke patients.

Our findings suggested that our HRV biofeedback treatment was an effective adjuvant treatment for PSD patients, especially on the improvement of depression levels and sleep disorder. In the future, we will increase subjects and extend the long-term follow-up time.

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**Conflicts of interest**

There are no conflicts of interest.

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