33rd Annual International Conference of the IEEE EMBS
Boston, Massachusetts USA, August 30 - September 3, 2011

HRV Response of Vegetative State Patient with Music Therapy

Yaw-Chern Lee[1], Chun-Yang Lei[1], Yi-Sen Shih[1], Wen-Chih Zhang[1], Hui-Min Wang[1], Cheng-Lung Tseng[1], Mark C. Hou[1,2], [3]Hui-Ya Chiang, and Sheng-Chieh Huang[1]
[1]sense/tcm SOC Lab., Department of Electrical Engineering, National Chiao Tung University, Hsinchu, Taiwan
[2]Department of Chinese Medicine, Changhua Christian Hospital, Changhua, Taiwan
[3]Department of Humanities and Social Sciences, National Chiao Tung University, Hsinchu, Taiwan
e-mail: microsoft.com.tw@gmail.com

Abstract—This case study centered on the effects of Music Therapy (MT) on vegetative state (VS) patients for a continuous 41-day experiment with electrocardiogram (ECG) recorded. Mahler's Second Symphony was used for this MT. There are various elements in Mahler's second symphony, with string, wind, drum, and even voice; providing the subject a strong and dynamic stimulation. There are some significant changes after 14-day stimulation: both standard deviation of all normal RR intervals (SDNN) and root mean square successive differences (RMSSD) in heart rate variability of the subject increased, indicating the activity of the cardiovascular system was enhanced. Although there's only one subject in this experiment, the results are still encouraging.

I. INTRODUCTION

Studies showed that mood and cognitive function of stroke patients improved significantly after a long-term period of music therapy (MT) [1]. For patients in vegetative state (VS), their emotional response to music is still similar to that of the general population in some examples [2] and few cases have significant changes of cardiovascular response [3]. In fact, the quantitative physiological measurements such as electroencephalogram (EEG), electrocardiogram (ECG) and blood pressure have been used to assess the level of consciousness of patients in VS [4]. Some phenomena of MT were observed in our previous publication, including decreased heart rates and increased heart rate variability (HRV) in one VS patient [5]. Although there are few examples, other researchers have confirmed this result [3]. This article elaborates the relevance of music and cardiovascular signals in the VS patient.

Car accidents and/or hypoxia (e.g., stroke) are two major reasons of brain injury and usually cause patients to be in a coma. Some of them recover quickly, while the others are in VS, Locked-In Syndrome (LIS) or brain death (BD) [6]. Some obvious features on the coma are no significant sleep/wake cycle, no response to verbal stimulation, no spontaneous eye opening, and no purposeful movement [7].

Since 1995, BD is defined as follows. Began as a coma with absence of confounding factors, including hypothermia, drugs, electrolyte, and endocrine disturbances. The main observations include absence of brainstem reflexes, absent motor responses and apnea. The repeated assessments are advised more than six hours [8]. Computed tomographic angiography (CTA) is an easy-implemented method to determine BD in recent years. If blood flow is not observed in acute arterial phase of the CTA, BD can be determined and no other testing is necessary [9].

Patients of LIS typically are fully conscious, but completely unable to move by themselves. The syndrome is usually due to brainstem lesions. By EEG, LIS patients have abnormal cortical sources of resting state eyes-closed alpha and delta rhythms [10]. For example, a patient suffered a rare stroke to the brainstem; only his left eye and brain escaped damage. He refused to give up his life and wrote a memoir through the blink of an eye [11].

VS [12] can be divided into persistent vegetative state (PVS) [13, 14] and minimally conscious state (MCS) [15-17]. Compared with coma patients, the most distinctive characteristics are that PVS patients have spontaneous arousal and sleep/wake cycles [13]. Studies have shown that despite the lack of evidence can be directly observed, some patients in VS are still conscious [14]. Different measurements of the level of consciousness in VS have still been explored [14]. There is a small group of patients whose status is between coma and PVS. Named as MCS, the patients still have some signs of consciousness [15]. Diffusion tensor imaging (DTI) is a modified magnetic resonance imaging (MRI) technique. The latest DTI study showed that the MCS and PVS patients differed significantly in subcortical white matter and thalamic regions [17]. Despite significant working experience, MCS and PVS are both poorly defined by most neuropsychologists and speech and language therapists [16].

The other sections of this paper are organized as follows. In section II, the works about MT, heart rate variability, and the relations with VS will be reviewed. In section III, we describe subjects, music for stimulus, the reason of music selection and the experiment procedure. In section IV and V, the results are presented and discussed. Finally, in section VI, we summarize this work.

II. PRELIMINARY

Of healthy control subjects and patients in VS, almost all linear parameters of HRV were similar in some experiments [22].

A. Music Therapy and Vegetative State

Although there is no comprehensive rehabilitation, MT has also been used in VS patients [36-39]. Traditionally, the

selection of music was based upon the tempo of the patient's breathing or pulse pattern [36]. Sometimes vertical motions on a trampoline synchronized with live music were included to regain awareness through activation of brain function. The developed method was named as musicokinetic therapy (MKT) [39]. Auditory stimulation with emotional significance was preferred to reveal residual functioning and elicit optimal behaviors. However, therapists should be careful against misinterpreting limbic responses of selected music [38].

B. Heart Rate Variability

Emotion affects ANS [43], and music is a common stimulus to trigger emotional reactions [44]. Among various physiological measurements, HRV is a simple and non-invasive way to assess cardiac autonomic control. Since the milestone paper proposed [40], HRV has become a widely used tool in many research fields [41].

A standard routine of electrocardiogram (ECG) signal processing includes a few stages. The detection of heartbeats (QRS complexes) is the first step. R-wave is the peak of the complex. SDNN is the standard deviation of time sequence (normal-to-normal RR-intervals). Through the Fast Fourier Transform (FFT), the low frequency (LF) and high frequency (HF) power could be obtained. LF/HF ratio is viewed as an index of sympatho-vagal balance of autonomic nervous system. To further understand these steps, the associated algorithms are listed in [42].

III. Method

A. Music Used for the Investigation

People in VS still have auditory responses of varying degrees [18-21]. To select the stimulus, music is better than speech in middle cerebral artery stroke patients [1]. Hence for the rehabilitation of brain, music is an ideal stimulus for patients in VS.

Emotion and consciousness share most of the same structures in the brain [26]. In most people's brain circuits, music can affect the limbic system and insula (both areas dealing the emotional responses) through the primary auditory cortex [27]. Emotional reactions of normal people in the limbic system [28] and some VS patients [29] are similar. The consistency of emotional reaction between normal subjects and patients in VS is confirmed through HRV measurements [2, 23-25]. The effectiveness would decrease if the same piece of music was repeated listening [30]. To select the proper music stimulus for the rehabilitation of VS patients, the musical emotion should be strong, but must avoid remaining in the same style.

The emotional expressions were omnipresent in the musical pieces of Tchaikovsky and Rachmaninov [31]. However, to satisfy the needs of high contrast [30], the masterpieces of Mahler are the more appropriate candidates. Gustav Mahler (1860–1911) was a late-Romantic composer [32,33]. His main works include nine symphonies [34] and a number of songs. Symphony No. 2 in C minor "Resurrection" [35] was chosen as the main stimulus. The version we chose was a two-CD box set (Orchestra: London Symphony Orchestra, Conductor: Gilbert Kaplan, Audio CD: September 14, 1998, Label: RCA, ASIN: B00000F1BI). Thirty minutes of silence were added as baseline before the audio tracks. More detailed information is shown in Table I.

B. Subjects

The subject participating in this study lived with his wife in Changhua County, Taiwan. Mr. S was in his middle 40s when this experiment was conducted from March to May in 2009. He had suffered from left intracerebral hemorrhage due to arterio-venous-malformation twice, which occurred on Nov. 2000 and May 2008, respectively. He recovered from the first stoke well, while the latter one further resulted in VS, diagnosed by doctors in Changhua Christian Hospital. He had been unconscious and bed-ridden for almost three years. His coma scale was E1M2Vt when the study was carried out.

C. Experimental Apparatus

The ECG signal was captured by a 3-channel portable device (MSI E3-80, FDA 510(k) K071085) at 500Hz sampling rate from the chest surface of body. Only the channel 1 (Lead 1) data was analyzed.

D. Procedures

Each data collection sessions lasted about 210 minutes and was separated from day to day, continuing for almost 6 weeks (from March 26, 2009 to May 5, 2009). As a reference line, no music was played in the first week (six days: from March 26 to March 31) and each session was 180 minutes. From the second week, the time session was changed to 210 minutes. On the first day, no music was played. From the second day to the seventh day of the following weeks, the audio program (Table I) was conducted with a headphone on the patient's head to an MP3 player. Every session was handled by his wife under a circumstance with no noisy interruptions in the bedroom of Mr. S, with a portable ECG data recording device installed on Mr. S.

E. Data Analysis and Statistics

Qualitative and quantitative data analysis was performed and used three software packages: C programming language, MATLAB and Microsoft Excel. At first, each 210-min session, on the basis of convenience, was divided into forty-two 5-min epochs with C programming language. Each epoch was then imported into MATLAB. Pattern analysis was then used by Excel.

The ECG data were not available in three days (April 20, May 4 and 5). The first 5-min and last 5-min epochs of all days was omitted to avoid inappropriate data from the movements and the instrument operation. Hence there were a total of 1484 (34*6+40*32) epochs. There were 3 records (0.2%) of SDNN data and 9 records (0.6%) of RMSSD data

due to signal error. The values were replaced by mean of their two neighboring data.

The experiment days were separated into two groups: the rest days and music days. The rest days included first week (6 days) and first days of the other weeks.

On music days, the complete audio session was performed. Each session was separated into two parts: non-symphony (NS) session and symphony (S) session. NS session was the first 75 minutes of the complete session. S session was the remaining 135 minutes. S and NS sessions are considered for the comparison of "Music Effect."

IV. Results

Two important time-domain parameters: SDNN and RMSSD were derived from the R-R interval measured from the subject. There are two parts: Day Effect, the different from the first day to the last (Fig. 1 and Fig. 2); and Music Effect, comparing from non-symphony session to symphony session (Fig. 3 and Fig. 4).

V. Discussion

- Day Effect: By the continuous music stimulation, SDNN and RMSSD (Fig. 1, Fig. 2) increased obviously especially after the critical turning point 04/17. And the R-squared of SDNN is high, 0.50.
- Music Effect: By observation, most SDNN and RMSSD on Symphony Sessions are higher than those on non-Symphony Sessions (Fig. 3, Fig. 4).
- From Fig. 1, Fig. 2, Fig.3 and Fig. 4, SDNN and RMSSD both are increasing obviously; especially the rising rate of SDNN is linear. In addition, Fig. 3 and Fig. 4 show that SDNN raises more than RMSSD does.

VI. Conclusions

SDNN and RMSSD significantly increased after 14 days continuous MT, showing that the condition of the subject's circulatory system is enhanced. This article introduced a music therapy process used in vegetative state (VS). Even though there's only one subject, the results are encouraging.

SDNN increased significantly about 100% in music days compared with that in rest days. Meanwhile, RMSSD also increased slightly. And the longer SDNN indicates the improvement of body circulation.

Acknowledgment

The authors want to thank the patient and family whose case vignette has been included in this paper.

References

[1] T. Särkämö , *et al.*, "Music listening enhances cognitive recovery and mood after middle cerebral artery stroke," *Brain,* vol. 131, pp. 866-876, Mar 2008.

[2] F. Riganello, *et al.*, "Heart rate variability: An index of brain processing in vegetative state? An artificial intelligence, data mining study," *Clinical Neurophysiology,* vol. 121, pp. 2024-2034, Dec 2010.

[3] J. Gutierrez, *et al.*, "Heart rate variability changes induced by auditory stimulation in persistent vegetative state," *International Journal on Disability and Human Development,* vol. 9, pp. 357-362, 2010.

[4] M. Wieser, *et al.*, "Quantitative description of the state of awareness of patients in vegetative and minimally conscious state," in *Engineering in Medicine and Biology Society (EMBC), 2010 Annual International Conference of the IEEE*, 2010, pp. 5533-5536.

[5] B. S. Yen, *et al.*, "The relationship between music processing and electrocardiogram (ECG) in vegetative state (VS)," in *Circuits and Systems (ISCAS), Proceedings of 2010 IEEE International Symposium on*, 2010, pp. 2239-2242.

[6] S. Laureys, "Eyes open, brain shut," *Scientific American,* vol. 296, pp. 84-89, May 2007.

[7] G. Teasdale and B. Jennett, "Assessment of coma and impaired consciousness: A practical scale," *The Lancet,* vol. 304, pp. 81-84, 1974.

[8] S. Laureys and J. J. Fins, "Are we equal in death? Avoiding diagnostic error in brain death," *Neurology,* vol. 70, pp. E14-E15, Jan 2008.

[9] C. M. Berenguer, *et al.*, "Brain death confirmation: Comparison of computed tomographic angiography with nuclear medicine perfusion scan," *Journal of Trauma-Injury Infection and Critical Care,* vol. 68, pp. 553-558, Mar 2010.

[10] C. Babiloni, *et al.*, "Resting state eyes-closed cortical rhythms in patients with locked-in-syndrome: An EEG study," *Clinical Neurophysiology,* vol. 121, pp. 1816-1824, Nov 2010.

[11] J. Bauby, *The diving bell and the butterfly*: Knopf Group E-Books, 2008.

[12] N. Shea and T. Bayne, "The vegetative state and the science of consciousness," *British Journal for the Philosophy of Science,* vol. 61, pp. 459-484, Sep. 2010.

[13] B. Jennett and F. Plum, "Persistent vegetative state after brain damage: A syndrome in search of a name," *The Lancet,* vol. 299, pp. 734-737, 1972.

[14] P. Nachev and P. M. S. Hacker, "Covert cognition in the persistent vegetative state," *Progress in Neurobiology,* vol. 91, pp. 68-76, May 2010.

[15] J. Giacino, *et al.*, "The minimally conscious state: definition and diagnostic criteria," *Neurology,* vol. 58, p. 349, 2002.

[16] F. C. Wilson, *et al.*, "Vegetative and minimally conscious state(s) survey: Attitudes of clinical neuropsychologists and speech and language therapists," *Disability and Rehabilitation,* vol. 29, pp. 1751-1756, 2007.

[17] D. Fernández-Espejo , *et al.*, "Diffusion weighted imaging distinguishes the vegetative state from the minimally conscious state," *Neuroimage,* vol. 54, pp. 103-112, Jan 2011.

[18] S. Laureys, *et al.*, "Auditory processing in the vegetative state," *Brain,* vol. 123, pp. 1589-1601, Aug 2000.

[19] M. Boly, *et al.*, "Auditory processing in severely brain injured patients: Differences between the minimally conscious state and the persistent vegetative state," *Archives of Neurology,* vol. 61, pp. 233-238, Feb 2004.

[20] M. Boly, *et al.*, "Cerebral processing of auditory and noxious stimuli in severely brain injured patients: Differences between VS and MCS," *Neuropsychological Rehabilitation,* vol. 15, pp. 283-289, Jul-Sep 2005.

[21] A. M. Owen, *et al.*, "Residual auditory function in persistent vegetative state: A combined PET and fMRI study," *Neuropsychological Rehabilitation,* vol. 15, pp. 290-306, Jul-Sep 2005.

[22] M. Sara, *et al.*, "Heart rate non linear dynamics in patients with persistent vegetative state: A preliminary report," *Brain Injury,* vol. 22, pp. 33-37, 2008.

[23] F. Riganello, *et al.*, "Heart rate response to music: An artificial intelligence study on healthy and traumatic brain-injured subjects," *Journal of Psychophysiology,* vol. 22, pp. 166-174, 2008.

[24] G. Dolce, *et al.*, "Personal interaction in the vegetative state: A data-mining study," *Journal of Psychophysiology,* vol. 22, pp. 150-156, 2008.

[25] F. Riganello, *et al.*, "Heart rate variability, emotions, and music," *Journal of Psychophysiology,* vol. 24, pp. 112-119, 2010.
[26] N. Tsuchiya and R. Adolphs, "Emotion and consciousness," *Trends in Cognitive Sciences,* vol. 11, pp. 158-167, Apr 2007.
[27] J. Warren, "How does the brain process music?," *Clinical Medicine,* vol. 8, pp. 32-36, Feb 2008.
[28] S. Brown, *et al.*, "Passive music listening spontaneously engages limbic and paralimbic systems," *Neuroreport,* vol. 15, pp. 2033-2037, Sep 2004.
[29] N. D. Schiff, *et al.*, "Residual cerebral activity and behavioural fragments can remain in the persistently vegetative brain," *Brain,* vol. 125, pp. 1210-1234, Jun 2002.
[30] M. Iwanaga, *et al.*, "Heart rate variability with repetitive exposure to music," *Biological Psychology,* vol. 70, pp. 61-66, Sep 2005.
[31] J. Sloboda, "Music structure and emotional response: Some empirical findings," *Psychology of Music,* vol. 19, p. 110, 1991.
[32] T. Adorno and E. Jephcott, *Mahler: A musical physiognomy*: University of Chicago Press, 1996.
[33] P. Franklin, *The life of Mahler*: Cambridge Univ Pr, 1997.
[34] D. Hurwitz, *The Mahler symphonies: An owner's manual*: Amadeus Pr, 2004.
[35] G. Kaplan, "How Mahler performed his second symphony," *The Musical Times,* vol. 127, pp. 266-271, 1986.
[36] D. Aldridge, et al., "Where am I? Music therapy applied to coma patients," Journal of the Royal Society of Medicine, vol. 83, p. 345, 1990.
[37] W. L. Magee, "Music therapy with patients in low awareness states: Approaches to assessment and treatment in multidisciplinary care," Neuropsychological Rehabilitation, vol. 15, pp. 522-536, Jul-Sep 2005.
[38] W. L. Magee, "Music as a diagnostic tool in low awareness states: Considering limbic responses," Brain Injury, vol. 21, pp. 593-599, 2007.
[39] R. Noda, et al., "Therapeutic time window for musicokinetic therapy in a persistent vegetative state after severe brain damage," Brain Injury, vol. 18, pp. 509-515, May 2004.
[40] A. J. Camm, et al., "Heart rate variability - Standards of measurement, physiological interpretation, and clinical use," Circulation, vol. 93, pp. 1043-1065, Mar 1996.
[41] U. Rajendra Acharya, et al., "Heart rate variability: A review," Medical and Biological Engineering and Computing, vol. 44, pp. 1031-1051, 2006.
[42] H. M. Wang, et al., "A ±6ms-accuracy, 0.68mm2 and 2.21μW QRS detection ASIC," in Circuits and Systems (ISCAS), Proceedings of 2010 IEEE International Symposium on, 2010, pp. 1372-1375.
[43] S. D. Kreibig, "Autonomic nervous system activity in emotion: A review," *Biological Psychology,* vol. 84, pp. 394-421, Jul 2010.
[44] R. Ellis and J. Thayer, "Music and autonomic nervous system (dys) function," *Music Perception,* vol. 27, pp. 317-326, 2010.

Audio Program		
Start Time	Length	Remark
0:00	30:00	Silence
30:00	7:57	String
37:57	26:10	Piano
54:07	21:53	Talk
76:00	22:22	1st Movement
98:22	5:00	Silence
103:22	10:15	2nd Movement
113:37	10:40	3rd Movement
124:17	5:34	4th Movement
129:51	34:26	5th Movement
164:17	30:00	Silence
194:17	30:00	Silence
224:17	/	End

Table I. The Audio Program for the VS patient

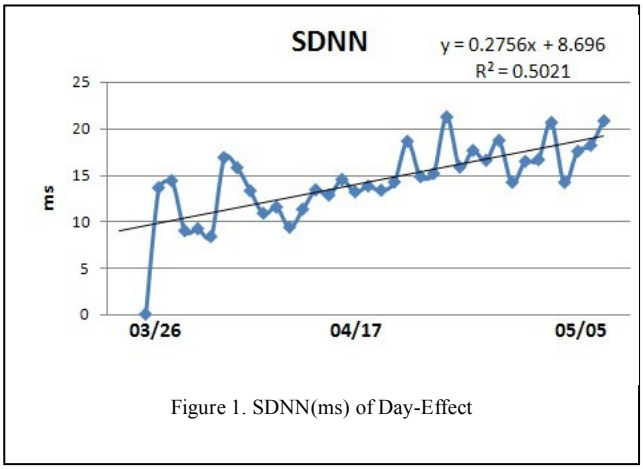

Figure 1. SDNN(ms) of Day-Effect

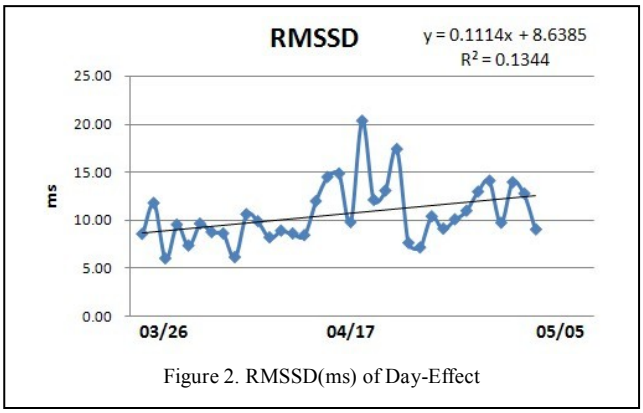

Figure 2. RMSSD(ms) of Day-Effect

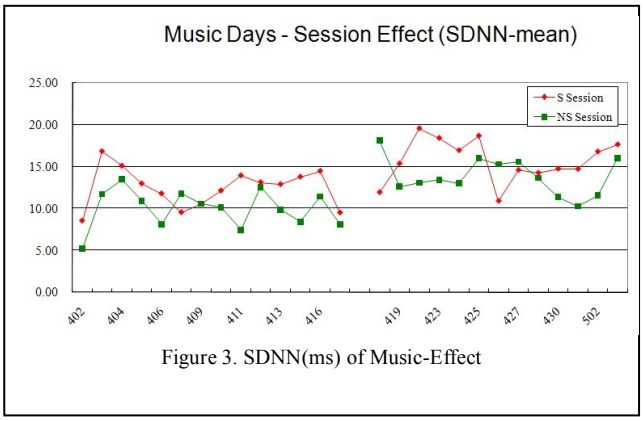

Figure 3. SDNN(ms) of Music-Effect

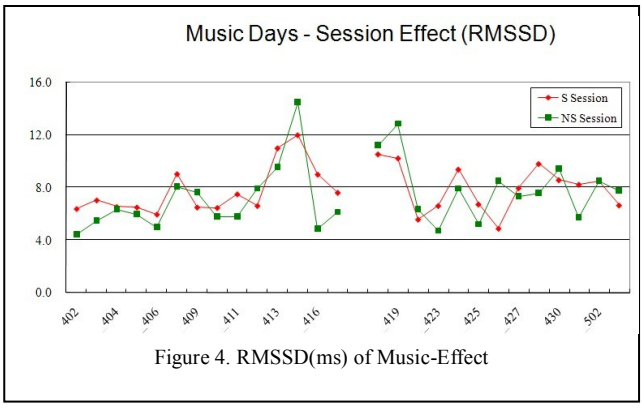

Figure 4. RMSSD(ms) of Music-Effect