Time and Frequency Domain Measures of Heart Rate Variability in Schizophrenia

Saime A. Akar, Sadık Kara,
Institute of Biomedical Engineering,
Fatih University,
İstanbul, Turkey
e-mail: {saimeakar, skara}@fatih.edu.tr

Fatma Latifoğlu
Biomedical Engineering Department,
Erciyes University,
Kayseri, Turkey
flatifoglu@erciyes.edu.tr

Vedat Bilgiç
Bakırköy Mental and Nervous Diseases Training and Research Hospital,
İstanbul, Turkey
e-mail: vbilgic@gmail.com

Abstract — It has been reported that schizophrenia patients have altered cardiac autonomic regulation and changed heart rate variability. The goal of this study was to analyze whether schizophrenia patients may exhibit distinctive Heart rate variability time and frequency domain parameters for control subjects compared both at rest and during auditory stimulation periods. Photoplethysmographic signals of thirteen schizophrenic patients and thirteen healthy subjects were used in the analysis of heart rate variability. Results show that heart rate in patients was higher than that of control subjects indicating autonomic dysfunction throughout the entire experiment. In comparison with control subjects, patients with schizophrenia exhibited lower high frequency power and a greater low-frequency to high-frequency ratio. Moreover, while alerting stimulus decreased parasympathetic activity in healthy subjects, no significant changes in heart rate and frequency-domain HRV parameters were observed between the auditory stimulation and rest periods in schizophrenia patients.

Keywords*-schizophrenia; heart rate variability; photoplethysmography; time and frequency domain measures.*

I. Introduction

Schizophrenia is a mental disorder characterized by some positive symptoms such as hallucinations, delusions and negative symptoms such as loss of motivation, lack of interest, disturbances in cognitions and emotions [1, 2]. According to the theories about symptom development in schizophrenia, it is claimed that indication of psychosis is related to autonomic dysfunction [3]. Therefore, there have been numerous studies that analyze disturbances of autonomic activity in schizophrenia patients [4-6].

Heart rate variability (HRV), which describes the variation in heartbeat intervals, is an important measure for investigation of the autonomic nervous system (ANS) activity. HRV analysis has been widely used to assess ANS activity in myocardial infarction, diabetic neuropathy, cardiac transplantation, myocardial dysfunction, tetraplegia [7], diabetes mellitus and renal failure [8]. Moreover, HRV analysis has been widely used in schizophrenia patients due to the relationship between symptoms of the disorder and cardiac autonomic irregularities [3, 9-12]. Results for altered cardiac autonomic regulation and changed HRV in schizophrenia patients are reported. It has been found that they have higher rates of cardiac disease and morbidity due to the dysregulation of ANS activity.

Most of these studies in schizophrenia patients are restricted to electrocardiogram (ECG) based HRV signal analysis. However, there are some of the problems of this technique such as drift, electromagnetic and biologic interference, the number of wires, and the complex morphology of the ECG [13]. On the other hand, photoplethysmogaphy (PPG) is reported as a simpler and easier process than analyzing HRV parameters from ECG data according to the results of a previous study [14]. In previous studies, HRV signal is usually analyzed in the time and frequency domain. While time domain measures of HRV have been used to evaluate the interbeat interval (IBI) variability, spectral analysis of sequences of IBIs can be used to assess the distribution of power across different frequency bands and reflects the sympathovagal balance between the sympathetic and parasympathetic activity.

The aim of the present study is to identify the differences in PPG based HRV measures during alertive acoustic white noise (WN), sedative Classical Turkish Music (CTM), and restive (no stimulation) periods for schizophrenia patients and healthy control subjects. While Section II is related to data acquisition and analysis techniques, Section III, IV and V are about results, discussion and conclusion of the study, respectively.

II. Methods

A. Subjects

Thirteen schizophrenia patients diagnosed by the DSM-IV (Diagnostic and Statistical Manual, Fourth Edition) [15] and thirteen healthy subjects, approximately matched in age and gender, participated in the study. Table I lists the demographic and clinical data of the participants. None of the subjects had history of diabetes mellitus, hypertension, respiratory diseases, cardiovascular diseases, hearing difficulties and co-morbidity in terms of psychiatric problems. Both the university and hospital ethics committee approved the protocol, and a written informed consent was obtained from all participants before the study was conducted.

 ISBN: 978-1-61208-243-1

TABLE I. DEMOGRAPHIC AND CLINICAL DATA OF THE PARTICIPANTS

	Participants	
	Controls	*Patients*
Number	13	13
Male/Female	8/5	7/6
Age (years ± std. deviation)	33.95 ± 8.33	33.39 ± 6.86
Age of onset in male/female	-	20.82 ± 5.21 / 20.08 ± 6.37
Medication status (drug-naïve/drug-free)	-	13/0

B. Data Acquisition

The study was carried out whilst participants seated in a quiet, temperature controlled and illuminated room without moving in Bakırköy Mental and Nervous Diseases Training and Research Hospital. The PPG data were recorded using Biopac MP150WSW data acquisition unit, PPG100C amplifier, TSD200 transducer and associated Acknowledge Software, which is an interactive program that measure, analyze and transform data.

The transducer was strapped on to the middle finger of the non-dominant hand of the participant and connected to the amplifier. A baseline data recording was obtained prior to the experiment. Data were recorded for 2 min. resting state (resting 1, R1) before auditory stimuli exposure, then following 2 min. period of WN exposure, following 2 min. period of music exposure and a 2 min. post-exposure resting (resting 2, R2) period and were digitized at a sampling rate of 250 Hz. The subjects listened to stimuli binaurally through headphones with the intensity of 75 dB.

WN is a kind of sound of rain on a river and was selected because of its uncomfortable, annoying evaluation from previous studies [16, 17]. On the other hand, CTM was selected as a sedative music period [18]. According to the Turkish philosopher Farabi, the effect of this kind of music induces serenity and ease [19].

C. Heart Rate Variability Analysis

Matlab 7.6® software package was used for data analysis. The PPG data were first low-pass filtered using a Butterworth filter (8^{th} order, cut-off 8 Hz). A detection algorithm, which finds min and max points of waveform, was implemented to detect peaks of the PPG signal and tachograms were plotted. Then, an interpolation with a sampling rate of 4 Hz was applied and data were detrended using a least-squares polynomial fitting detrending technique, which is explained in our previous study [18, 20].

In the time domain analysis of HRV, the mean length of all PP intervals (PPint) and the heart rate (HR) in each measurement period (2 min.) were computed. In the frequency domain analysis, spectral analysis was performed using the Welch's algorithm, which is an averaging modified periodogram to estimate the power spectrum [21]. The power spectrum of the HRV signal was divided into three bands: very low frequency-VLF (0-0.04 Hz), low frequency-LF (0.04-0.15 Hz) and high frequency-HF (0.15-0.5 Hz). The power spectral density of the LF and the HF band were computed by integration of the power spectrum over the related frequency range (square milliseconds-ms2) in each period. While the LF band reflects sympathetic activity, the HF band is related to parasympathetic activity. The ratio of LF to HF power (LF/HF) was calculated to assess the sympathovagal balance for indicating the function of the ANS activity.

D. Statistical Analysis

All statistical analyses were performed using the SPSS (version 20.0) statistical software package. Comparisons of HRV features between the patients and controls in each period were executed using an independent sample Student's t-test. Under the null hypothesis, defined as "no difference in the HRV features of patients and controls", the data follows a normal distribution. To compare the differences in HRV between sequential periods, paired sample Student's t-tests were performed on both groups, separately. The student's t-test was chosen based on a finding from Levene's test. Due to confidence level of 95 %, results were considered as significant at the level of $p<0.05$.

III. RESULTS

In this study, PPG signals were recorded during varying measurement periods, in which time and frequency domain measures of HRV were computed for the PPint of healthy control subjects and schizophrenia patients. In Table II, the differences in HRV measures observed between schizophrenia patients and control subjects are summarized.

A. Comparisons of HRV measures between groups

Time domain measures of HRV for patients and control subjects during measurement periods are shown in Fig. 1.

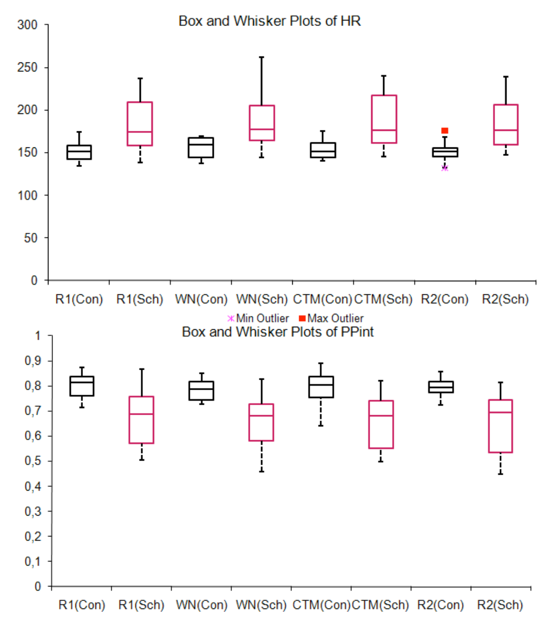

Figure 1. Box and Whisker plot comparison of HR and PPint between schizophrenia and control groups during different experimental periods.

TABLE II. TIME AND FREQUENCY DOMAIN HEART RATE VARIABILITY MEASURES.

	Controls				***Patients***			
	R1	***WN***	***CTM***	***R2***	***R1***	***WN***	***CTM***	***R2***
Mean HR	151.6 (11.7)	156.5 (10.8)	153.3 (10.3)	151.3 (10.1)	181.8 (34.0)	187.7 (36.7)	185.7 (32.6)	183.2 (30.7)
Mean PP interval	0.7978 (0.053)	0.7860 (0.044)	0.7879 (0.074)	0.7944 (0.036)	0.6799 (0.123)	0.6602 (0.117)	0.6636 (0.112)	0.6586 (0.134)
LF pow. (ms2)	41.6 (3.13)	50.9 (2.68)	47.6 (3.62)	43.1 (3.73)	42.7 (3.81)	49.4 (3.11)	47.1 (3.54)	45.4 (3.77)
HF pow. (ms2)	33.3 (3.36)	29.8 (2.34)	32.8 (2.79)	33.2 (2.61)	27.2 (3.32)	24.7 (2.12)	25.2 (3.25)	26.5 (3.27)
LF/HF	1.26±0.14	1.72±0.15	1.46±0.18	1.31±0.14	1.58±0.16	2.01±0.23	1.90±0.31	1.74±0.27

The schizophrenia patients showed a significantly higher HR than control subjects during all periods of the procedure ($p<0.05$). However, healthy subjects exhibited a high degree of HRV, which is described by the variation in mean PPint ($p<0.05$).

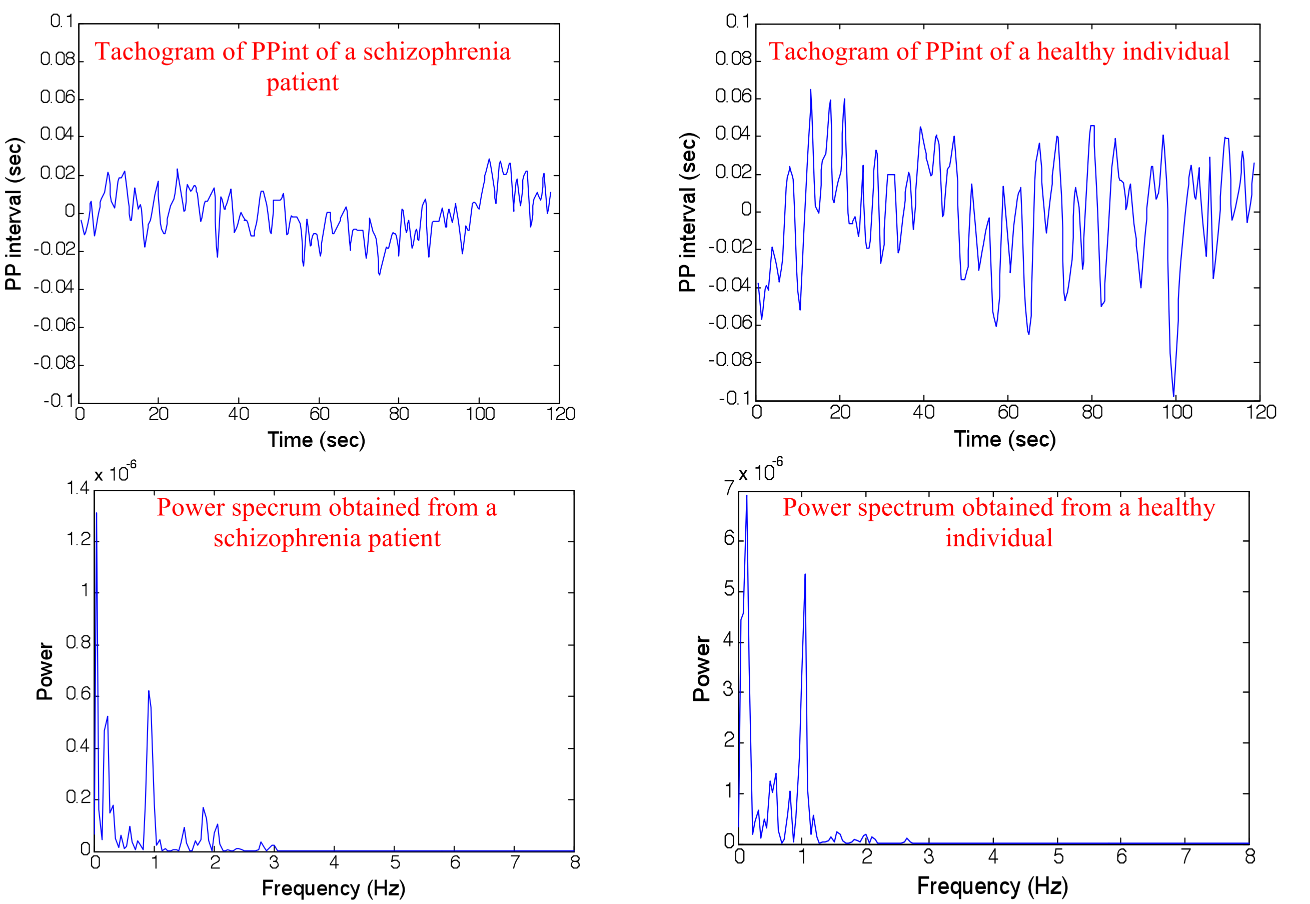

Figure 2. Spectral analysis of HRV in restive condition in a healthy subject and schizophrenia patient. Top: Interbeat interval tachogram of a schizophrenia patient (left) and a healthy individual (right). Bottom: Corresponding power spectrum obtained from the patient (left) and control subject (right)

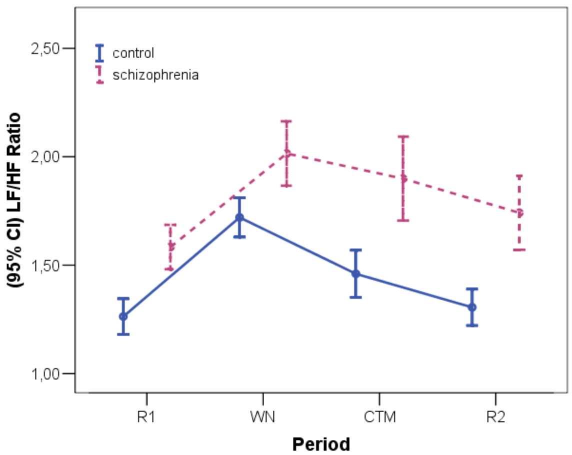

Figure 3. Comparison of the changes in the LF/HF of HRV between patients with schizophrenia and healthy subjects

The baseline tachograms (top panels) and their corresponding power spectra (bottom panels) of a patient in the schizophrenia group (left) and an individual in the control group (right) are shown in Fig. 2. From here, it may be seen that, the individual with schizophrenia exhibited a higher HR, shorter PPint, and decreased HRV during the restive baseline period as compared to the healthy subject. The PPint feature of the schizophrenia patients during the whole procedure was significantly lower than that of the control subjects ($p<0.05$). While the LF power in schizophrenia patients was not different from that in control subjects, the HF power was significantly reduced in the patients ($p<0.05$) during all periods of the procedure. Moreover, schizophrenia patients showed increased LF/HF ratio as compared to control subjects during both stimulation and restive periods (Fig. 3).

B. Comparisons of HRV measures within groups

Auditory stimulation caused an increase in HR in both groups as compared to that during restive periods. While the control group showed the greatest HR during the WN exposure, no significant HR change was reported during the WN period and CTM period in schizophrenia patients. Although HR decreased during CTM as compared to the WN period, this difference did not reach significant levels in either the control ($p=0.1$) subjects or schizophrenic patients ($p=0.18$). The decrease in HR continued in the R2 period for both the control subject and patient groups. However, for both groups, no significant change was reported over the CTM and R2 periods. The results indicate that there was an insignificant decrease in PPint between restive periods (R1 and R2) and stimulation periods (WN and CTM) in both groups.

Auditory stimulation evoked an increase of LF power and LF/HF ratio from the baseline and a decrease of HF power in the HRV in both groups ($p<0.05$). While the LF power increased more during WN than during CTM, the WN evoked a more deceleration of HF power from the baseline as compared to CTM in the control group. The LF/HF ratio of healthy subjects was higher during WN than during CTM. In contrast, there were no significant differences in terms of LF, HF, and LF/HF ratio when the different auditory stimuli were heard by the group of schizophrenia patients. The restive period (R2) after stimulation periods caused a significant decrease in LF power in healthy individuals, whereas LF power did not change significantly during the R2 period in the schizophrenia group.

IV. DISCUSSION

It has been reported that altered autonomic function is associated with higher rates of cardiac disease and morbidity in schizophrenia patients [22]. Therefore, HRV analysis has become a powerful and useful tool in clinical research to assess ANS activities in schizophrenia patients. By combining the knowledge about impairment in auditory stimuli discrimination with altered autonomic regulation of schizophrenia patients, we aimed to investigate the PPG based HRV parameters during different types of auditory stimuli in patients. It was found that schizophrenia patients had higher HR and shorter PPint than control subjects during all periods of the procedure. This may be observed as a result of disorder-related autonomic nervous system changes [3]. Schizophrenia group also exhibited a similar LF power, a significant decrease in HF power and an increase in the LF/HF ratio as compared to healthy subjects during all the periods of the procedure.

Although HR increased during auditory stimulation periods in both groups, changes between the two stimulus periods were not significant for schizophrenia patients. The LF power and the LF/HF ratio increased during stimulation periods as compared to restive periods in both schizophrenia and control groups. However, the LF power was higher during WN exposure than during sedative CTM exposure in the control group. On the other hand, HF power was higher during CTM than WN, but remained the same in both restive and CTM periods. Namely, while alerting stimulus increased sympathetic activity more, it caused a reduction in parasympathetic activity in healthy subjects. Therefore, the LF/HF ratio was highest during WN in the control group. This confirms the result of a past study that states the HF power, which is decreased by uncomfortable stimuli, may be sensitive to stress reduction in resting state [23]. In contrast, there were no significant differences in terms of LF, HF, and LF/HF ratio in schizophrenia patients during these two different auditory stimuli periods. This may be related to impairments of schizophrenia patients in auditory discrimination [24] or related to cardiac autonomic dysfunction in schizophrenia patients.

A post hoc power analysis revealed that on the basis of the mean a limited statistical power because of the modest sample size. Therefore, it is suggested to increase the number of participants in each group for future studies.

V. CONCLUSION

In conclusion, the results obtained for HRV measures support that the variations in cardiac autonomic activity during the restive baseline and other stimulation periods are different between schizophrenia patients and healthy individuals. The reduced parasympathetic activity in schizophrenic patients can be considered as strongly relating the risk factor of cardiac morbidity.

ACKNOWLEDGMENT

This work is supported by the Scientific Research Fund of Fatih University under the project number P50060901.

REFERENCES

[1] K. T. Mueser and S. R. McGurk "Schizophrenia" Lancet, vol. 363 (9426), pp. 2063-72, 2004.

[2] R. Tandon, H. A. Nasrallah, Keshavan M. S., "Schizophrenia, "just the facts" 4. Clinical features and conceptualization" Schizophr Res, vol. 110 (1-3), pp. 1-23, 2009.

[3] K. J. Bar, A. Letzsch, Jochum T., Wagner G., Greiner W., Sauer H. "Loss of efferent vagal activity in acute schizophrenia" J Psychiatr Res, vol. 39 (5), pp. 519-527, 2005.

[4] E. Kraepelin Psychiatry: A Textbook for Students and Physicians. Canton: Watson Publishing International; pp. 110–111; 2002.

[5] L. H. Lindstrom, "Clinical and biological markers for outcome in schizophrenia: a review of a longitudinal follow-up study in Uppsala schizophrenia research project" Neuropsychopharmacology, vol. 14, pp. 23–26, 1996.

[6] S. Grossberg, "The imbalanced brain: from normal behavior to schizophrenia" Biol Psychiatry, vol. 48, pp. 81–98, 2000.

[7] Anonymous, "Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology" Eur Heart J, vol. 17 (3), pp. 354-381, 1996.

[8] F. Javed, P. M. Middleton, P. Malouf, G. S. Chan, A. V. Savkin, N. H. Lovell, E. Steel, J. Mackie, "Frequency spectrum analysis of finger photoplethysmographic waveform variability during haemodialysis" Physiol Meas, vol. 31 (9), pp. 1203-1216, 2010.

[9] J. S. Chang, C. S. Yoo, S. H. Yi, K. H. Hong, H. S. Oh, J. Y. Hwang, S. G. Kim, Y. M. Ahn, Y. S. Kim, "Differential pattern of heart rate variability in patients with schizophrenia" Prog Neuropsychopharmacol Biol Psychiatry, vol. 33 (6), pp. 991-995, 2009.

[10] J. S. Chang, C. S. Yoo, S. H. Yi, K. H. Hong, Y. S. Lee, H. S. Oh, D. C. Jung, Y. S. Kim, Y. M. Ahn, "Changes in heart rate dynamics of patients with schizophrenia treated with risperidone" Prog Neuropsychopharmacol Biol Psychiatry, vol. 34 (6), pp. 924-929, 2010.

[11] B. L. Henry, A. Minassian, M. P. Paulus, M. A. Geyer, W. Perry, "Heart rate variability in bipolar mania and schizophrenia" J Psychiatr Res, vol. 44 (3), pp. 168-176, 2009.

[12] M. N. Castro, D. E. Vigo, E. M. Chu, R. D. Fahrer, D. deAchaval, E. Y. Costanzo, R. C. Leiguarda, M. Nogues, D. P. Cardinali, S. M. Guinjoan, "Heart rate variability response to mental arithmetic stress in patients with schizophrenia: autonomic response to stress in schizophrenia" Schizophr Res, vol. 99 (1-3), pp. 294-303, 2008.

[13] M. Bolanos, H. Nazeran, E. Haltiwanger, "Comparison of heart rate variability signal features derived from electrocardiography and photoplethysmography in healthy individuals" Conf Proc IEEE Eng Med Biol Soc, 2006, pp. 4289-4294.

[14] N. Selvaraj, A. Jaryal, J. Santhosh, K. K. Deepak, S. Anand, "Assessment of heart rate variability derived from finger-tip photoplethysmography as compared to electrocardiography" J Med Eng Technol, vol. 32 (6), pp. 479-484, 2008.

[15] E. Falkum, G. Pedersen, S. Karterud "Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, paranoid personality disorder diagnosis: a unitary or a two-dimensional construct?" Compr Psychiatry, vol. 50 (6), pp. 533-541, 2009.

[16] J. H. Sohn, E. Sokhadze, S. Choi, and K. H. Lee, "Autonomic, respiratory and subjective effects of long-term exposure to aversive loud noise," Korean Journal of Science of Emotion and Sensibility, vol. 3, pp. 37–42, 2000.

[17] E. Sokhadze, K. H. Lee, Y. K. Kim, M. K. Park, J. H. Sohn, "Effects of long-term exposure to loud noise on tonic autonomic responses," Proceedings of the 5th International Congress on Physiological Anthropology, Korea, 2000.

[18] S. A. Akar, S. Kara, and V. Bilgiç, "Respiratory variability during different auditory stimulation periods in schizophrenia patients" Methods of Information in Medicine, pp. 29-38, doi: 10.3414/ME10-01-0087.

[19] R. Kalender, "Türk Musikisinde Kullanılan Makamların Tesirleri" Ankara Üniversitesi Dergisi, vol. 29, pp. 361-375.Turkish, 1987.

[20] S. A. Akar, S. Kara, F. Latifoğlu, and V. Bilgiç, "Spectral Analysis of Photoplethysmographic Signals: The Importance of Preprocessing" Biomedical Signal Processing and Control, doi:10.1016/j.bspc.2012.04.002, in press.

[21] P. D. Welch, "The use of fast fourier transform for the estimation of power spectra: A method based on time averaging over short, modified periodograms" IEEE Transactions on Audio and Electroacoustics, vol. 15 (2), pp. 70-73, 1967.

[22] C. H. Hennekens, A. R. Hennekens, D. Hollar, D. E. Casey, "Schizophrenia and increased risks of cardiovascular disease" Am Heart J, vol. 150 (6), pp. 1115-1121, 2005.

[23] M. Iwanaga, A. Kobayashi, C. Kawasaki, "Heart rate variability with repetitive exposure to music" Biol Psychol, vol. 70 (1), pp. 61-66, 2005.

[24] C. S. Li, M. C. Chen, Y. Y. Yang, M. C. Chen, P. K. Tsay, "Altered performance of schizophrenia patients in an auditory detection and discrimination task: exploring the 'self-monitoring' model of hallucination" Schizophr Res, vol. 55 (1-2), pp. 115-128, 2002.