Assessment of Autonomic Function in Children with Autism and Normal Children Using Spectral Analysis and Posture Entrainment: A Pilot Study

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Abstract

Objective: The dysfunction of the autonomic nervous system investigated in Children with Autism compared with healthy one. Cardiovascular autonomic disturbances are possibly associated with the pathogenesis of Autism in children. The purpose of this study is to use the spectral and coherence analysis of heart rate variability signal (HRV), respiration signal and peripheral blood flow signal (PBF) to assess the autonomic activity of normal children and children with Autism for the clinical usefulness of the applied methods of signal processing and time-frequency analysis for screening and treatment of Autism in children.

Methods: Twenty four children who had Autism and who were not taking any medications and Twenty three age and sex matched controls (Children) were participated in this study at Department of Neurology at Johns Hopkins Hospital, Baltimore, MD, USA and Regional Medical Center, Cookeville, TN, USA. PBF and respiration signals as well as HRV signal derived from Electrocardiogram (ECG) were measured during supine and standing positions. Autopower, cross power and coherence spectra were produced to investigate the sympathetic and parasympathetic activity in both groups.

Results: The results clearly indicate that in children with Autism, the coherence values are less than in control group in both low frequency (LF) and high frequency (HF) bands at coherence spectra between HRV and PBF as well as HRV and respiration in both supine and standing position. Also, the ratio of amplitude at nearly frequency of 0.1 Hz in auto power spectra and coherence spectra is less in Autism group than in matched control ($p<0.001$).

Conclusion: Autopower and coherence spectra analysis for Children with Autism compared to normal Children seems useful in the assessment of autonomic function for Autism patients. The decreased of autonomic function specially parasympathetic activity in patients with Autism revealed by auto power and coherence spectra analysis is significant and may be related to the effective of treatment of Autism children in this disorder compared to controls. Further studies is needed using other tests and methods of signal analysis to introduce clinical indices for early detection of autonomic function in patients with Autism.

Keywords: Autonomic system; Heart rate variability analysis; Power spectral analysis; Coherence spectra

Introduction

The short term power spectral analysis of HRV signal (heart rate variability) has been used to assess autonomic control of heart rate [1,2]. Impaired autonomic function has been associated with an increased risk of mortality in autonomic dysfunction in randomly selected general populations. Autonomic dysfunction involving both sympathetic and parasympathetic systems has also been demonstrated in different diseases using cardiovascular reflex tests based on heart rate to various stimuli [1-6]. However, the clinical significance and pathophysiology of these findings in many diseases associated with autonomic malfunction are poorly understood. Conventional time and frequency domain analysis techniques based on the linear fluctuation of heart rate insufficient in outline the changes in heart rate dynamics [7,8], therefore, new methods based on system dynamics have been introduced. The combined application of power spectral analysis of heart rate variability (HRV), Peripheral Blood Flow (PBF) and their coherence to assess the autonomic function to patients using standing specially in short term, is used in this study. HRV and PBF signals in healthy subjects manifested a balance between sympathetic and parasympathetic systems [9-12]. A high variability in heart rate and PBF signal means adaptability implying a healthy individual with well-functioning autonomic control mechanisms [9-12]. Conversely, lower variability is often an indicator of less adaptability of the autonomic nervous system. Reduced heart rate variability has emerged as a strong indicator of risk related to adverse events in patients with range of diseases [5-8,13-17]. In fact, HRV analysis is a practical reproducible and considered noninvasive method to detect early autonomic dysfunction and also permitting better quantitative and qualitative evaluation of sympathovagal modulation of cardiovascular function [18]. Studies of autonomic control of autonomic function in Autism specially in children patients are few and their study population were not homogenous [19].

The aim of this study to assess the autonomic function of a series of randomly selected Autism children and were not taking any medication related to Autism using stimulus standing position by evaluating the power spectra and coherence of several signals including HRV, PBF and respiration signals compared with healthy children.

Methods and Patients

The study was performed at Johns Hopkins university hospital, Baltimore, Maryland, USA, over more than one year period. The study group of patients was composed of 24 children newly diagnosed Autism (10 ± 2.43) years and were not taking medication. For each patient, one healthy age and sex matched control children on no medication was selected. In all cases routine physical examination, a 12 lead surface electrocardiographs, routine biochemistry tests (liver and renal function tests), serum electrolytes, basic hematological parameters were obtained and none of the cases had any evidence of cardiovascular or non-cardiovascular disease. None of patients had clinical signs of autonomic dysfunction, history of myocardial infraction, arterial

hypertension, diabetes or pulmonary disease. The subjects and the control groups during the study used no drugs that could affect the HRV parameters. Therefore, the final group consisted of 24 male patients with Autism (mean 10 ± 2.43 years) and 23 healthy age and sex matched controls (mean 10 ± 1.57 years). All guardians of children agreed to participate in the research prior to their inclusion in the study and the consent of ethical committee was obtained and approved the study protocol. With each subject lying supine on a bed and physiological measuring devices are connected. The breathing signal measured using a thermistor placed on the nose. The ECG is taken from wrists and the ankle (lead II). An infrared plethysmograph placed on finger indicates PBF signal simultaneously for the duration of experiments. All measurements are interfaced to laptop PC and stored in CD. The second phase of experiments entail that all subjects asked to standup and all the signal measured in this position. The duration of measurements in supine and standing position is 10 min.

Generation of HRV signal and estimation of coherence function

Figure 1 illustrates the derivation of HRV signals from ECG. The technique used in this study to produce HRV signals is based on the hardware circuits described by Ahmed et al. [12] to detect R-R interval and produce HRV signals. The HRV signals were then passed through two 12 bit A/D converters at 10 Hz sampling rate and then interfaced to Laptop PC. A/D converters were designed so that the first conversion would occur when the first R wave of ECG was detected. The stored HRV signals of 24 Autism patients and 23 control subjects were then transferred to spectral package prepared by the author at Tennessee Tech University based on Fast Fourier Transform (FFT) or autoregressive method. The package was stored on PC to produce auto-power spectrum, cross power spectrum and coherence spectrum between different signals including HRV, respiration signal and PBF in supine and standing positions. A rank sum test, a nonparametric analog of independent–samples, t-test, was applied to the data of both groups and results indicate patients with Autism are significantly different from control at 0.001 ($p > 0.001$). The estimation of
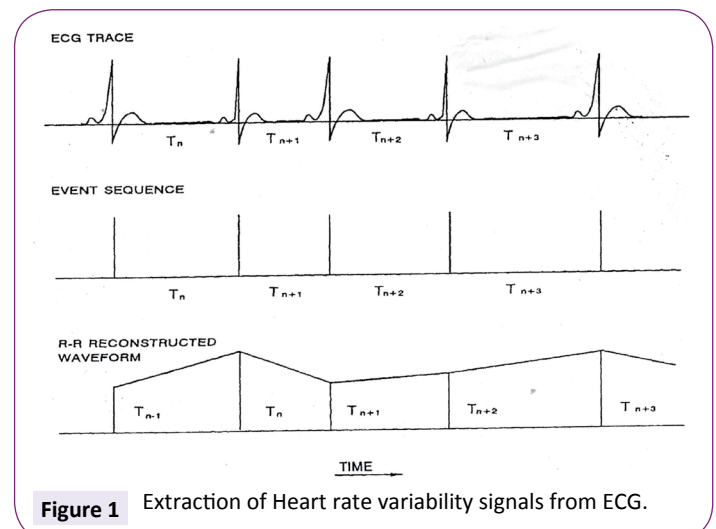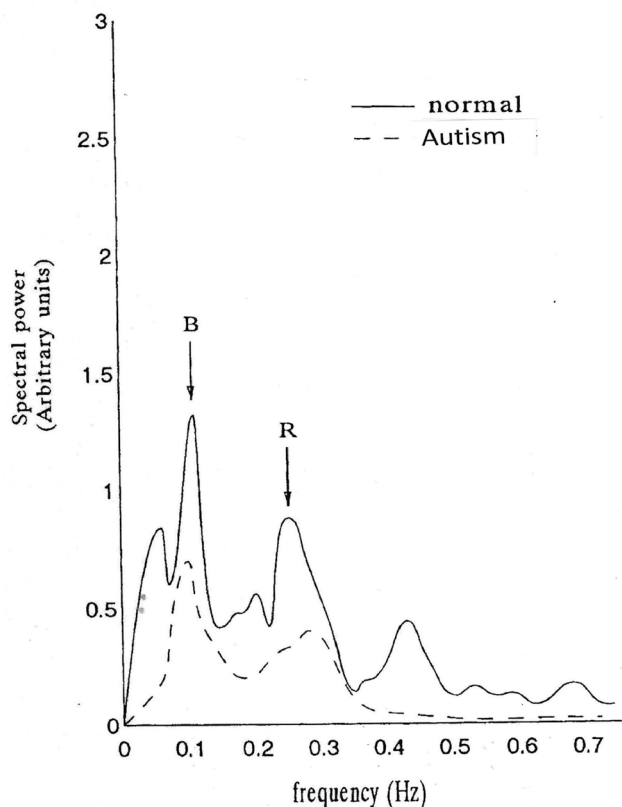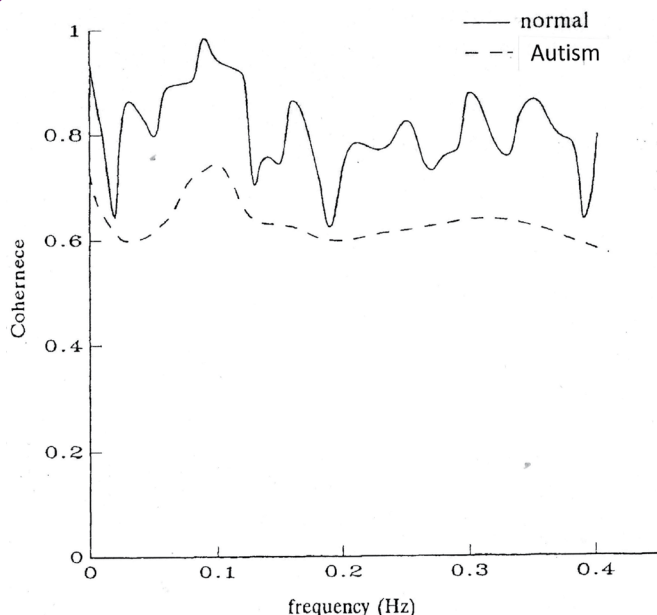

Figure 1   Extraction of Heart rate variability signals from ECG.

Figure 2 Typical power spectra upon standing for Autistic child and Normal child.

Figure 3 Typical Coherence spectra between Respiration and HRV signal for Autistic child and normal child upon standing.

coherence function is explained in Appendix.

Results

Table 1 Illustrates the number of subjects (control and Autism

patients) exhibiting amplitude entrainment after standing position at Traube–Herring Mayer component (THM) i.e. at frequency at 0.1 Hz expressed in ratio of amplitude at 0.1 Hz at standing to the same frequency (0.1Hz) at Supine position.

Figure 2 represents the typical HRV spectrum for control subject and Autistic patient in standing positions respectively. Similar Figures are obtained for PBF. B Peak represents peak oscillation at 0.1 Hz and R Peak represents Peak oscillation of respiration.

Figure 3 represents the typical coherence spectra between breathing and HRV signals for Autism patient and control subject at standing stimulus.

Discussion

Until now, only some researchers have assessed autonomic function in children with Autism by means of a neurophysiological methods [6,11]. However, this study is directed to use the power spectra and coherence spectra of heart rate variability signals(extracted from Cardiovascular signal ECG) and Peripheral Blood flow signal (PBF) to assess the function of autonomic system in Autism children patients compared with normal subjects. **Figure 2** shows the change in blood pressure frequency which oscillates at 0.1 Hz and shown in power spectrum of heart rate variability signals in **Figure 2** in the standing position for both Autism patients and normal control subjects. The ratio of amplitude of component of blood pressure at 0.1 Hz between standing and supine positions for control subjects and Autism patients extracted from the autopower spectrum of HRV signal is shown in **Figure 2** and demonstrated in **Table 1**.

Referring to **Table 1**, it appears for control healthy subjects 15 out of 23 (65%) that have ratios in the range of 1.4-1.59. However, for Autism patients 14 out of 24 (60%) have lower ratios in the range of 1-1.19. This is clear indication of the effect of standing as natural stimulus to autonomic system to mediate the stimulus signal via baroreceptor to the heart [17-19]. Using coherence spectra between HRV and breathing signals are demonstrated in **Figure 3**. **Figure 3** illustrates the low coherence values of HRV for autism patients with respect to control healthy subjects. Once again, this may indicate that autonomic system (both sympathetic and parasympathetic) cannot convey the control oscillations (thermoregulatory oscillation at 0.03 Hz, blood pressure oscillation at 0.1 Hz and respiration oscillation at nearly 0.25Hz) as manifested in coherence spectrum.

Table 1 Number of Subjects (Control and Autism patients) Exhibiting Amplitude Entrainment upon Standing.

Ratio of Amplitudes B (standing)/B (Supine)	Number of Healthy Subjects	Number of Autism Patients
<1	0	0
1-1.19	0	14
1.2-1.39	3	8
1.4-1.59	15	2
1.6-1.79	3	0
>1.8	2	0
Total	**23**	**24**

In fact, the control group exhibits high values of coherence in both coherence spectrum and Auto power Spectrum as shown in **Figures 2** and **3**. However, the Autism group shows less coherence values especially around respiration oscillation (nearly around 0.25 Hz) as illustrated in **Figure 3**. This may be attributed to dysfunction of autonomic nervous system especially parasympathetic part which normally mediated respiration signal to heart and other physiological signal in the body [9-12,15-23].

In Fact, the introduction of coherence values in this study to assess the autonomic function of Autism children patients and control healthy subjects may be helpful in using the coherence value as diagnostic medical index for autonomic function assessment [9,21-23]. Therefore one should distinguish this diagnostic index as coherence to test the autonomic function which could be performed in an ambulatory setting in every patient. The patients with diagnosed as low coherence (dysautonomia) should be carefully observed and specific drugs ordered such as beta-blockers or angiotensin-converting enzyme inhibitors to prevent morality due to autonomic dysfunction. The novelty of this study is combined different signal including HRV, PBF and respiration signals with coherence and auto power spectra compared with one signal EEG analysis using power spectra and coherence.

In summary, autonomic dysfunction revealed by coherence and posture entrainment in this pilot study is present uncommonly in patients with Autism.

The use of coherence value as medical index in diagnosis of dysfunction autonomic system in Autism need further study. We suggest that all patients with suspicion of Autism specially in children can investigated autonomic dysfunction should be under special cardio logical care.

Conclusion and Future Work

This study pointed significance of using the spectral analysis Method and Coherence index in assessing the function of autonomic nervous system for both groups.

However, further study is required to investigate more patients as well as using other quantitative methods to identify the prognosis of autonomic function with duration of Autism in children.

Acknowledgements

Estimation of Coherence Spectra

In spectra analysis, the ordinary coherence between two signals is defined as [21]

$$\text{COH}(\gamma 2) = \frac{|S_{xy}(w)2|}{|S_{yy}(w)S_{xx}(w)|}$$

Where $S_{xx}(\omega)$ and $S_{yy}(\omega)$ are the power spectral densities of two signals, $x(t)$ and $y(t)$, and $S_{xy}(\omega)$ is their cross-power spectrum at an angular frequency (ω). The coherence between two signals indicates the degree to which two signals are linearly correlated at a given frequency. In experimental modal analysis [21-22] coherence is a well-known tool for assessing the linear correlation between the structural responses $x(t)$ due to a given input excitation $y(t)$ to the structure when processing the data in the frequency domain to extract the modal parameters—natural frequencies, modal damping, and mode shapes. The following can also be inferred about the coherence:

(a) Coherence (Coh) is close to unity means the response is linearly correlated to the input excitation.

(b) In general, measurement of structural responses and input are contaminated with noises (generated due to measuring instruments or/and structures) which may cause reduction in coherence.

(c) Coherence reduces due to nonlinear relation between response and input.

(d) Coherence reduces when the response is due to extraneous inputs.

The estimation of coherence in this study was carried out in Tennessee Tech University ,MET department, using MATLab programming .

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