Cardiovascular neurometrics of the hyperactive child

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Abstract

With the advent of powerful minicomputers, the assessment of hyperactivity may shift from heuristic evaluations based on psychometric data to neurometric analyses of the relationship between central and autonomic nervous system activity and behavior. Neurometrics refers to algorithmic extraction of salient features of electrophysiological data. A neurometric assessment of hyperactivity is proposed, based on the extraction of rhythmic features of the heart rate pattern. Specifically, we will concentrate on spectral measures of respiratory sinus arrhythmia, i.e. a neurally mediated periodicity associated with respiration and cognitive processes like attention. The computation of spectral measures requires a heart rate series that is stationary. Consequently the algorithm is augmented with suitable tests. It is shown by means of a simple simulation experiment that the presence of non-stationary mean trends is harmless. The occurrence of non-stationary autocorrelation is a nuisance, however, and we will discuss a pertinent test based on evolutionary spectral analysis.

1. Introduction

The concept of the Hyperactive Behavior Syndrome in children has been introduced in the 1950s (Laufer & Denhoff, 1957). The clinical symptoms included hyperactive motor behavior, short attention span, variability in performance, impulsiveness, irritability, explosiveness and poor school-performance. Although variants of the term "hyperactivity" have been used throughout the literature, there has been increasing recognition that the problem these children have, is not well characterized in terms of motor overactivity. In 1980, the official diagnostic manual of the American Psychiatric Association DSM 111 adopted a new label "attention deficit disorder" (ADD). While this new label refers only to attentional problems, research findings indicate that attentional problems represent one of a constellation of closely related deficits.

Historically, the hyperactive syndrome evolved from follow-up of children with known insults to the CNS. The assumption of underlying organicity is evidenced by the frequent interchangeable use of the label 'MBD'. Consequently, ADD/hyperactivity has been conceptualized in terms of brain function. Moreover, the past decade has shown a rapid growth of psychophysiological techniques which have been applied to clinical problems such as ADD/hyperactivity (Halliday, 1985).

With the advent of powerful and economical minicomputers, many investigators have turned their attention to the problem of devising methods to extract and quantify features of diagnostic utility from electrophysiological data. The most ambitious and consistent approach to this issue has been that of 'neurometrics' as developed by John (1977) and his associates. Neurometrics is a technology that is intended to increase the sensitivity of electrophysiological assessment and to extend its utility in the domain of sensory, perceptual, and cognitive functions. This assessment quantifies features objectively extracted from the EEG and multimodal ERPs elicited in a variety of standardized test conditions, and describes brain dysfunctions in terms of statistically significant deviations from age related normative values (e.g. John, 1977; Pricep, John, Ahn & Kaye, 1984).

The central idea underlying the neurometric approach is the emphasis on quantitative evaluation of brain function as opposed to reliance upon qualitative interpretation of behavioral and psychometric data. The quantitative evaluation of brain function, however, is not limited to salient features extracted from the surface EEG or ERPs. In this paper we will present a neurometric approach based upon quantitative measurement of features extracted from the heart rate pattern reflecting various aspects of brain function related to attention and motor behavior.

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1.1. Cardiovascular neurometrics

The prevalence of heart rate in cardiovascular psychophysiology is based upon the assumption of a relationship between heart rate and the CNS. That is, heart rate is assumed to index cognitive processes. Before the arrival of sophisticated measurement equipment and new methodology, heart rate was viewed as a global measure of arousal or emotion. With the introduction of new technology, however, the role of monitoring heart rate shifted from a crude measure of arousal to a sensitive index of cognitive processes.

There are two basic approaches in extracting salient features of heart rate: (1) description of the directional trend in heart rate (see van der Molen, Somsen & Orlebeke, 1985, for a review); and (2) description of heart rate variability. Heart rate variability has been used as an estimate of neural control over the heart, and thus, indirectly as a measure of CNS integrity (e.g. Porges, 1986). Heart rate variability has also been related to perceptual-cognitive performance. Porges and Humphrey (1977), for example, found that subjects with greater baseline heart rate variability had faster reaction times and were better able to focus attention.

Heart rate variability represents the sum of many influences and is, therefore, not the optimal measure of the neural mediation of the heart. One of the oscillations in the heart rate pattern is associated with respiration (i.e., respiratory sinus arrhythmia, RSA). This rhythm is particularly important because the changing amplitude of RSA parallels psychological constructs such as attention and vigilance.

1.2. RSA and Hyperactivity

It has been widely accepted that respiration influences phasic modulation of vagal efferent output to the heart. Research on neural pathways of vagal cardio-inhibitory neurons has demonstrated that these neurons show a respiratory-related pattern of discharge with the primary efferent action on the heart during expiration (cf. Spyer, 1981). Moreover, it is long known that exaggerated amplitudes in RSA are associated with high levels of vagal tone and low levels of motor activity. Porges, assuming a parallel between spontaneous motor activity and vagal tone, hypothesized that hyperactivity, which clinically has been characterized by a lack of control and inhibition of spontaneous motor behavior, may have an autonomic correlate of low vagal tone. It was found that the administration of methylphenidate improved the performance of hyperactive children on attention demanding tasks, and shifted the pattern of heart rate response toward greater parasympathetic mediation. These findings were taken to suggest that the hyperactive child is deficient in levels of parasympathetic activity and is dominated by activity of the sympathetic system (Porges, 1976).

2. Quantification

2.1. Spectral analysis

If heart rate variability were only influenced by respiration, heart rate variability would be equivalent to RSA and would covary with vagal tone. However, heart rate variability is influenced by other factors, including changes in blood pressure and in the thermoregulatory system. Therefore, it is necessary to partition from the total heart rate variability, a measure of RSA by quantifying the component mediated by breathing. Spectral analysis is the proper tool to study fluctuations in heart period. It can be used to study rhythmic activity of heart rate by decomposing the time series into constituent sinusoidal functions of different frequencies. The frequencies of interest in the study of RSA are the frequencies associated with normal breathing. In adults this is about 10 - 25 breaths per minute; in children approximately 15 - 30. To calculate the component of heart rate variability associated with breathing, the spectral densities for each frequency within this band are summed. The accumulation of spectral density estimates of heart rate activity associated with the respiratory frequency band provides an estimate of RSA (Porges, 1986).

2.2. Preliminary steps

The first and most important step is to determine the condition under which the psychophysiological measures will be taken. It is common practice to measure heart rate variability from a treatment condition and pre/post treatment conditions. The treatment condition may consist of attention demanding tasks, specifically tailored to detect the attentional deficits in hyperactive children (e.g. Porges & Coles, 1982; van der Molen, Somsen & Orlebeke, 1985). The next step is the recording of the EKG and the identification of a relevant phenomenon in the EKG. For our purposes, the QRS complex in the EKG can be used. R-R intervals can easily be detected with a 1 ms resolution (e.g. Rompelman, 1985).

Having converted the EKG into an event series, the next question that arises is how to process the cardiac event series, if possible, in relation to other signals (e.g. respiration). The beating of the heart may be operationalized as a point event detected by the occurrence of the R-wave. Many spectral methods require preprocessing, because they need a regular signal instead of signal estimates of R-wave occurrence. There are a variety of methods that may be used to generate an estimate of a point process at equal time intervals (e.g. de Boer, Karemaker & Strackee, 1984). Weighting is a suitable method that allows time-indexed comparisons with other physiological systems (e.g. respiration, blood pressure). Heart period is converted to time-based data by estimating heart period for successive time windows. For each window, the weighted heart period is calculated as the sum of each heart period occupying the window, multiplied by the proportion of the window that it occupies. It is necessary to estimate the heart period at sequential intervals of approximately one-half of the duration of the shortest heart period (Porges, 1986). The next step to spectral analysis is the application of a Fourier transform to the signal. At this point it is important to note that spectral analysis provides reliable and interpretable estimates of the amplitude of a periodic oscillation, only if the data are at least weakly stationary.

Porges (1986) suggests that the time series of heart period activity is usually not stationary. In most situations RSA is superimposed on a complex baseline trend. This baseline trend tends to exhibit large shifts over time relative to the amplitude of RSA. This shift in mean and variance of the HR often violates the stationarity assumption. Porges argues that traditional methods of detrending and filtering do not effectively remove the variance of the baseline trend to make the processed heart period pattern stationary. His solution to this problem is to model the complex baseline trend with a series of localized polynomials. These short duration polynomials are stepped through the data set, providing residuals that are free from trends and slow sinusoidal changes. The residuals are analyzed with spectral analysis and the sum of the spectral density estimates are compared across the respiratory frequency band.

2.3. Evolutionary spectral analysis

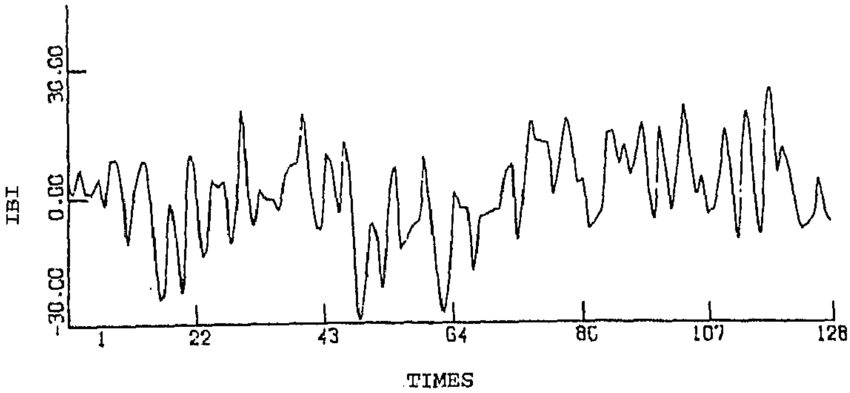
Porges' procedure of preprocessing the heart period signal can be criticized for at least three reasons. First, Porges' conception of 'stationarity' is incongruous with definitions that can be found in leading time-series texts (e.g. Brillinger, 1975). This is particularly clear when he points to the Traube-Hering-Mayer wave as one of the main sources of non-stationarity. This wave occurs with a periodicity of approximately 10 to 15 s per cycle and has been implicated in blood pressure control. Conceptually, this slower oscillation is not different from RSA. Secondly, Porges assumes that the time-series of heart period activity is not stationary; his procedure, however, does not include a test for this assumption. Moreover, even after preprocessing there is no way of knowing whether the residual rhythmic heart period pattern is stationary. Thirdly, Porges' preprocessing procedure functions as a high-pass filter in which the cut-off frequency is dependent upon signal characteristics. Thus, all frequencies slower than the filter's cut-off are lost. Hence, the residual spectrum does not provide potential relevant information concerning the 0.1 Hz component in the heart rhythm that has been associated with mental effort (e.g. Mulder, 1985). Finally, it can be shown that the characteristics of the residual spectrum are not different from the characteristics of the spectrum computed on the 'raw' data, as far as the higher frequencies are concerned.

In the remainder of this paper we will present the outline of a spectral technique that includes a test for the stationarity of time-series. This technique is labeled 'evolutionary spectral analysis' (Priestley, 1981). After presenting the basic notions of evolutionary spectral analysis, we will illustrate this technique with simulated and experimental data.

Testing stationarity

For the sake of conciseness, we will henceforth concentrate on sequences of inter-beat intervals (IBIs), because a consideration of alternative measures of cardiac activity would not seriously affect the present discussion (cf. de Boer *et al.*, 1984). An application of spectral analysis then, requires that a sequence of IBIs is weakly stationary. This means that the sequence has to have both a

1 a



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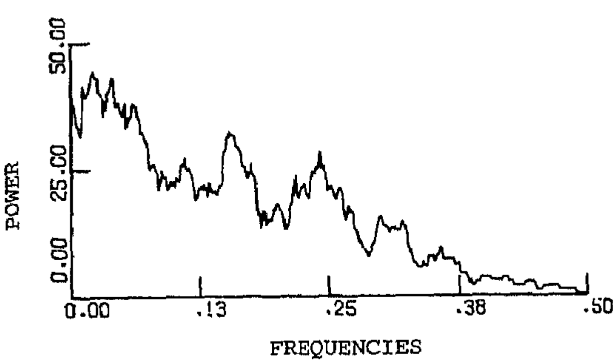

constant mean function:

$$E(IBI(t)) = m$$

for all t, as well as an autocorrelation function that is invariant under translations along the time axis:

$$cor(IBI(t), IBI(t+u)) = cor(IBI(t + t''), IBI(t + t'' + u)) = c(u)$$

for all t, t'' and u. We will first consider the requirement of a constant mean function.

By definition, a non-stationary mean function or trend consists of low-frequency oscillatory components (cf. Hannan, 1970). In case one would prefer to define a trend as a polynomial function of sufficiently low order, or otherwise, this would be immaterial to our present concerns, i.e., the spectrum of a trend is always concentrated in a neighborhood of zero frequency. The reason is, that in a formal sense cosinusoids, orthogonal polynomials, and the like, constitute interchangeable basic functions for the linear space spanned by a signal (Ahmed & Rao, 1975). We already indicated, however, that a natural spectral measure of RSA is given by the power in a frequency band centered at 0.25 Hz. As spectral values at sufficiently separated frequencies are mutually uncorrelated (Brillinger, 1975), it therefore can be expected that spectral RSA measures (centered at 0.25 Hz) will not be affected by the eventual presence of trends (centered at 0 Hz). Hence, it can be expected that there is no need to detrend an IBI sequence (e.g., by means of some form of high-pass filtering procedure) in order to obtain an unbiased spectral measure of RSA. Only if one is also interested in the low frequency part of the spectrum, the removal of a non-stationary mean function is desired if apparent trends can be separated from other fluctuations to be studied.

All this can easily be demonstrated by means of a simple simulation experiment. An IBI sequence (total length 1024 intervals) with non-stationary mean function (exponentially damped 0.005 Hz sinusoid) and substantial low-frequency components has been generated, the initial part of which is shown in Figure 1a. The estimated spectrum of this sequence is shown in Figure 1b, revealing the presence of various peaks, e.g. in the neighborhood of 0, 0.1, and 0.25 Hz. Next, following Porges' procedure, the low frequency components

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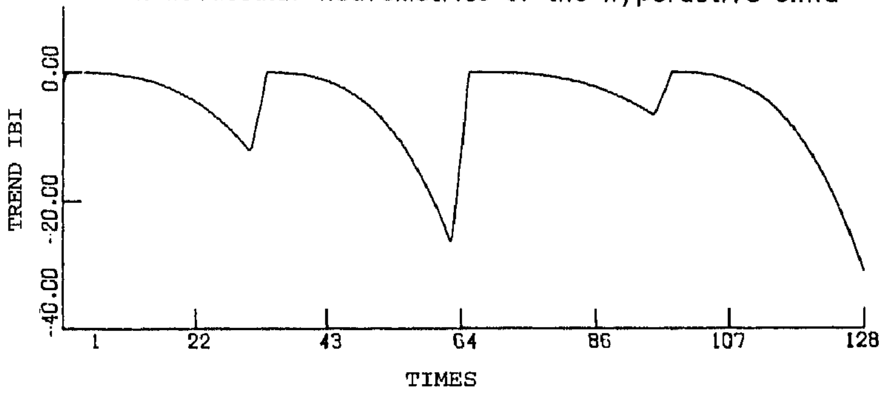

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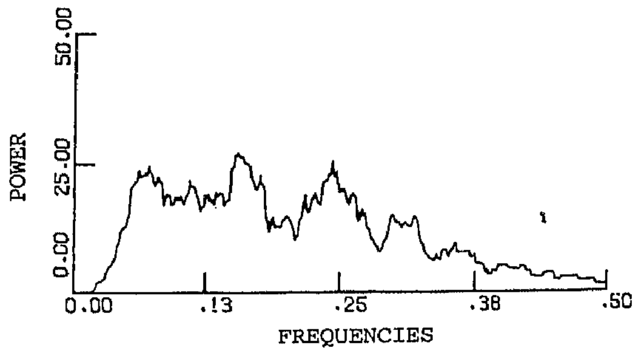

Figure 1. Initial part of simulated IBI sequence (1a), estimated interval spectrum of the sequence (1b), initial part of polynomial trend removed by means of high-pass filtering (1c) and estimated interval spectrum of filtered sequence.

of the original IBI sequence are removed by means of high-pass filtering (a third-order polynomial is fitted to each consecutive epoch of 32 intervals, yielding a filter with cut-off frequency at 0.0625 Hz). Figure 1c shows part of the trend which has thus been removed. Finally, Figure 1d depicts the estimated spectrum of the filtered IBI sequence: clearly, the spectral values at frequencies above 0.1 Hz. are equal to those of the original series shown in Figure 1b, the latter could have been used directly in order to compute a spectral RSA measure. The situation is entirely different if one turns to the case in which the autocorrelation function is non-stationary. The spectrum will then also be time-varying as it corresponds with the Fourier transform of the autocorrelation function, and one should proceed by forming spectral estimates based on segments of the data, rather than all the data, for which the concerning assumption of stationarity does not appear to be too seriously violated (Brillinger, 1975, p. 176).

Let the non-stationary spectrum P(f,t) be represented by:

$$P(f,t) = |A(f,t)|^2 \, P(f)$$

where A(f,t) is a time- and frequency-dependent function that modulates the spectral representation of an IBI sequence. If A(f,t) is slowly varying with time - i.e., for each fixed f, A(f,t) (considered as a function of t) has a Fourier transform whose absolute maximum occurs at zero-frequency - then P(f,t) is called an evolutionary spectrum. Priestley and Subba Rao (1969) present a test for evolutionary spectra which is based on a double window technique. First, a Bartlett window covering a relatively small time interval is used in order to compute local Fourier transforms of the IBI sequence at each time point. This yields a time-dependent sequence of transforms IBI(f,t), where f belongs to a given set of F frenquencies. Second, a Daniell window covering a relatively large time interval is applied to the IBI(f,t) sequence in order to compute estimates of P(f,t) at a set of T well-separated time points. Simultaneous resolution in the time and frequency domain is limited because the product of T and F has an upper bound. In this way, a two-way array of spectral estimates at different times (first factor) and frequencies (second factor) is obtained. Using a logarithmic transformation, the test then amounts to a two-factor analysis of variance in which the residual variance is a known function of the bandwidth of both windows. If only the main effects of time and frequencies are significant, i.e., $\log P(f,t) = 2\log|A(t)| + \log P(f)$, then $P(f,t)$ is called uniformly modulated because $A(f,t)$ is now constant across frequencies:

$$P(f,t) = |A(t)|^2 \, P(f)$$

An IBI sequence with uniformly modulated spectrum can be conceived of as the output of a weakly time-dependent filter $A(t)$, the input of which is a stationary sequence with spectrum $P(f)$.

As Priestley and Subba Rao already illustrated the validity of the test by means of a simulation experiment, we will confine ourselves to a presentation of some typical outcomes with real data. IBI sequences comprising 450 intervals were obtained with 8 subjects while they were resting, carrying out a reaction-time task, or doing mental arithmetic. An application of the test to each of the 24 IBI sequences indicates that only four sequences have a significantly time-varying spectrum. Each of these non-stationary sequences has been obtained with a different subject. Two sequences have been obtained while a subject was doing mental arithmetic, one sequence while a subject was resting, and one while a subject carried out a reaction-time task. All significant outcomes only pertain to the main effect between times, hence the concerning spectra are uniformly modulated.

It turns out that in this sample significant results appear to be arbitrarily distributed across subjects and experimental conditions. As to this, one should bear in mind that the test focuses on evolutionary spectra or, equivalently, non-stationary autocorrelation, and hence is insensitive to differences in mean level. Moreover, frequencies in the neighborhood of 0 Hz do not enter the test, consequently the outcomes are not affected by the presence of trends. Given the unsystematic occurrence of non-stationary autocorrelation, then, a regular application of the test is called for. As soon as an IBI sequence with non-stationary autocorrelation is thus detected, one should proceed by forming separate spectral estimates based on stationary segments of the data. These segments can be determined by means of a suitable iterative procedure, where at each step the test is again used in order to ascertain stationarity.

3. Conclusion

This paper presented the outlines of a cardiovascular neurometric approach that has the potential to be used in the assessment of hyperactivity. A lot of work has to be done, however. To date a lack of normative data prevents the inclusion of this technique in current diagnostic procedures. Even more important, RSA should be measured under carefully controlled experimental conditions. These conditions should be derived from a psychophysiological model of hyperactivity that relates physiological indices and cognitive processing. In a more general sense, it should be established more firmly that developmental trends in vagal control over the heart parallel the trends in behavior.

Spectral analysis is a basic tool in cardiovascular neurometrics of, e.g., hyperactivity. That is, the use of spectral techniques in this context can be very profitable if the necessary precautions have been made in order to ascertain second-order stationarity. As to this, the presence of non-stationary trends can almost always be handled satisfactorily by means of filtering techniques. On the other hand, the usual filtering techniques do not correct for non-stationarity of the entire spectrum. Therefore one needs a suitable test in order to 1) detect non-stationarity of spectral values in, e.g., the RSA frequency band and 2) to invoke suitable corrective measures. We proposed one such test and illustrated its use with an application to real data. A more definite evaluation of the characteristics of this test will be determined from an extensive application to simulated and real data. The results of this study, including a consideration of alternative corrective procedures for non-stationarities in the high-frequency band, will be presented in a forthcoming publication.

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