Fear induced complexity loss in the electrocardiogram of flight phobics: A multiscale entropy analysis

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Abstract

In this study we explored the changes in the variability and complexity of the electrocardiogram (ECG) of flight phobics ($N = 61$) and a matched non-phobic control group ($N = 58$) when they performed a paced breathing task and were exposed to flight related stimuli. Lower complexity/entropy values were expected in phobics as compared to controls. The phobic system complexity as well as the heart rate variability (HRV) were expected to be reduced by the exposure to fearful stimuli. The multiscale entropy (MSE) analysis revealed lower entropy values in phobics during paced breathing and exposure, and a complexity loss was observed in phobics during exposure to threatening situations. The expected HRV decreases were not found in this study. The discussion is focused on the distinction between variability and complexity measures of the cardiac output, and on the usefulness of the MSE analysis in the field of anxiety disorders.

The study of the cardiovascular system's complexity is important since the output from healthy dynamic systems is characterized by a greater irregularity (Bhattacharya, 2000; Goldberger et al., 2002; Penttilä et al., 2003; Pikkujämsä et al., 1999; Vigo et al., 2004). The general principle is that the organism is a complex adaptive system and that the turbulence or complexity in its behavior allows for the broadest range of adaptive responses (Guastello, 2004, p. 6). Therefore, diminished complexity should be found in non-healthy systems, and complexity measures can be useful diagnostic tools in some cardiac disorders (Costa et al., 2002). Although anxious patients probably cannot be labeled as cardiac non-healthy patients, and big differences between their heart functioning and the healthy heart system are not foreseeable, subtle differences can be found in some nonlinear characteristics

(e.g., entropy) of their cardiovascular system. In this case, complexity measures should be useful diagnostic tools also in the anxiety disorders field.

Multiscale entropy (MSE) was recently introduced by Costa et al. (2002) as an enhanced method to evaluate the regularity of complex time series. Traditional measures like Approximate Entropy (ApEn; Pincus, 1995) or Sample Entropy (SampEn; Richman and Moorman, 2000), which have been used in some studies on anxiety disorders (Bornas et al., 2006a; Caldirola et al., 2004; Perna et al., 2004), are based on single-scale analysis. This means that they do not take into account the complex temporal fluctuations inherent in healthy physiologic control systems. Because fractal properties have been found in many healthy biological systems including the human cardiovascular system (Deering and West, 1992; Ivanov et al., 1999; Peng et al., 1995; Small et al., 2002) a meaningful measure of complexity should take into account multiple time scales (Costa et al., 2003, p. 54). Briefly, the MSE analysis constructs consecutive coarse-grained time series by averaging a successively increasing number of data points in non-overlapping windows. For scale 1, the coarse-grained time series is the original time series. For scale 2, the time

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series is made up of the average of consecutive pairs of data points, so that its length is the length of the original time series divided by the scale factor (in this case 2), and so on. Then, SampEn is calculated for each of the coarse-grained time series. SampEn (m, r, N) is the negative natural logarithm of the conditional probability that two sequences similar for m points remain similar at the next point. SampEn(m, r, N) = $-\ln [A^m(r)/B^m(r)]$, where $B^m(r)$ is the probability that two sequences will match for m points, whereas $A^m(r)$ is the probability that two sequences will match for $m + 1$ points.

To the best of our knowledge, MSE has not been used in any study on anxiety disorders. The heart system's complexity, however, has been the focus of some research during the last decade. Based on several studies on generalized anxiety disorder (Lyonfields et al., 1995; Thayer et al., 1996), panic disorder (Friedman and Thayer, 1998a), and specific phobias (Friedman and Thayer, 1998b), Thayer and Lane (2000) presented a dynamical systems model of emotion regulation which integrates autonomic, attentional, and affective systems into a functional (as well as structural) network, although their measures belong to the linear research tradition (usually the interbeat variability in the time domain and the spectral power in the frequency domain). According to this model, inhibition plays a key role as far as it keeps sufficient levels of variability shown in the healthy human heart beating. Inhibition is mediated by the parasympathetic system (specifically through the vagus nerve) following the "instructions" given by the brain. Therefore a decrease in the activity of the parasympathetic system will be reflected in a decrease of the vagally mediated heart rate variability (i.e., diminished high frequency band power). Unlike the more traditional hypothesis according to which the cardiac changes seen in several anxiety disorders (e.g., the heart rate increases) are the effect of an overactivity of the sympathetic nervous system (SNS) (e.g., Sarlo et al., 2002), Thayer and colleagues argue that these changes are due to the relaxation of the inhibitory function of the parasympathetic system. Since the high frequency band (HF:0.15–0.4 Hz, in accordance with the Task Force on Heart Rate Variability, Camm et al., 1996) power is exclusively or overwhelmingly mediated by the parasympathetic nervous system (PNS), and sympathetic influences predominate in the low frequency band (LF:0.04–0.15 Hz), spectral analysis of power changes in the HF and LF bands can help to find out the specific contribution of the PNS and the SNS to emotion regulation.

There is a problem, however, in the use of HF power decreases as indexes of the system complexity losses. Variability and complexity might not be the same. For variability measures, the order of the input is irrelevant –the focus is to quantify the degree of spread about a central value. In contrast, discerning changes in order from apparently random to very regular is the primary statistical focus for complexity measures like ApEn (Pincus, 2000, p. 142). Therefore a signal might be highly variable but very regular. Approximate entropy, like sample entropy and MSE, are complexity measures based on the regularity of any system's output (e.g., heart rate). The HRV decreases found in some studies (e.g., Johnsen et al., 2003) cannot be interpreted as complexity losses unless a complexity measure corroborates

those findings. In other words, the variability of the system under stressful conditions has been repeatedly found to be lower than in normal conditions, but it is not clear if the system's complexity diminishes also under stress.

Another problem with the use of HF power is the strong influence that respiration has on it. Because the power spectral amplitude of the HF component is influenced by unstable respiration cycles, these cycles should be constantly regulated. In a recent review, Tripathi (2004) states that "no worthwhile interpretation can be made of analysis of HRV unless these respiratory confounders are controlled" (p. 66) after saying that respiratory rate is one of these confounders. The need for respiratory control was yet emphasized by Grossman et al. (1991). HF power values obtained during a free breathing baseline show great intraindividual variability, making it difficult to assert that further power decreases are due to exposure (i.e., they can be related to changes in the respiration rate of the patient instead of stimuli-evoked). In the same way, the absence of significant decreases can be due to the intrinsic variability of the measure during free breathing. Further, as Beauchaine (2001) points out, the use of the term vagal tone in the literature on HRV has been a source of confusion because the validity of measures taken without respiratory control is moderate (p. 188) and they could reflect vagal reactivity instead of vagal tone. Sarlo et al. (2002) used a 1-minute paced breathing condition to evaluate vagal tone at rest in the blood/injury phobics and spider phobics who participated in their study. They found greater vagal tone at rest in blood phobics compared with spider phobics.

The first aim of this study was to evaluate changes in the heart rate variability (including vagal reactivity) and ECG complexity of flight phobics when confronting feared simulated situations. A matched healthy non-fearful control group was included in order to corroborate that changes were due to fear, i.e., to the emotional meaning of stimuli and not just to their cognitive meaning. Secondly, the study explored vagal tone and complexity differences between flight phobics and matched healthy non-fearful controls, during a paced breathing task for vagal tone but also during free breathing and exposure conditions for complexity.

Variability was assessed by spectral as well as by a time domain measure (the root mean of the squared successive interbeat intervals differences, RMSSD). RMSSD was expected to decrease during exposure, as reported in other studies on specific phobias (e.g., fear of flying, Bornas et al., 2005; dental phobia, Johnsen et al., 2003). HF power decreases during exposure were also predicted to the extent that HF power (like RMSSD) measures the vagally mediated HRV. We should add, however, that Sarlo et al. (2002) did not find changes in respiratory sinus arrhythmia when blood phobics and spider phobics were exposed to threatening films. On the contrary, they found increased sympathetic activity during exposure, so we measured LF power changes to test the additional hypothesis that fear induces the SNS overactivation.

Complexity was evaluated by the MSE analysis of the ECG time series. In accordance with the general principle that healthy systems are more complex than non-healthy systems,