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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.

Keywords: Flight phobia; Heart rate variability; Complexity; Multiscale entropy analysis

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,

reduced entropy was expected in flight phobics compared to healthy controls. Entropy decreases were also predicted for phobics during exposure to fearful conditions. Regarding the effects of paced breathing on HRV, breathing at 0.2 Hz should be reflected by a clear peak at this frequency in the HF spectral band. The total HF band power was expected to increase also during paced breathing because of the increased parasympathetic activity. On the other hand, we expected no effects of paced breathing on the system's complexity.

1. Method

1.1. Participants

Sixty-one flight phobics (40 women) with a mean age of 36.59 years (S.D. = 10.2) and 58 non-phobic healthy controls (38 women) with a mean age of 42.16 years (S.D. = 9.3) participated in the study. All of them were older than 18, and signed a written consent form. Exclusion criteria were: being in psychological treatment, taking psychotropic medication, suffering from any other psychopathological disorder requiring immediate treatment, having a history of psychotic symptoms or current psychotic disorder, suffering from cardiovascular or respiratory illness, or being pregnant. Phobic participants met DSM-IV (American Psychiatric Association, 1994) criteria for specific phobia (flying) as the main diagnosis, and showed elevated levels of fear of flying, closed to the ones reported in other studies on flight phobia (e.g., Bornas et al., in press; Öst et al., 1997).

1.2. Procedure

Phobic participants were recruited through advertisements in local newspapers. Seventy-two subjects asked for treatment, and they attended the first session at the Clinical Laboratory of the University of the Balearic Islands. Healthy controls were sixty-six university workers who voluntarily decided to participate in the study, which was announced through the university e-mail service. None of them reported a current respiratory, cardiac or mental disease (including fear of flying). Upon arrival, they were given general information about the study and signed a written consent form. Each subject was then seated approximately 1 m from a 17-in. monitor and sensors were attached for psychophysiological recording. A 3-min adaptation phase was followed by a 5-min resting baseline period (BL), a 5-min paced breathing (0.2 Hz) task (PB), and a 5-min period of exposure to a threatening flying sequence (E). The whole experiment was controlled by a computer (Pentium IV 1.6 GHz). Short text messages appeared on the screen before the beginning of each task. During baseline the subject was asked to look at the computer's screen and be relaxed. Five minutes later, the paced breathing task began. The breathing phase was paced by means of a picture of a human face with arrows pointing to the mouth when inspiring and going out from the mouth when expiring; a scrolling bar on the bottom of the screen also indicated the inspiration and expiration phases, which had the same duration. The message ''now we need to evaluate your responses to some flying stimuli'' came up on the screen before the 5 min. exposure phase. It should be stressed that subjects did not know that feared stimuli would be presented to them until this moment. A modified version of the take-off sequence of the Computer Assisted Fear of Flying Treatment (CAFFT, see Bornas et al., 2002 for a description) was used as the threatening stimulus. We chose this sequence because take-off is usually the most feared moment among flight phobics. After exposure, actual fear was assessed using a 1–9 point scale (1 = no fear, 9 = extreme fear) and the subject was invited to go to an adjacent room for a clinical interview.

The Anxiety Disorders Interview Schedule for DSM-IV (ADIS-IV; Brown et al., 1994) was used to individually assess all phobics. They completed the Fear of Flying Questionnaire (FFQ; Bornas et al., 1999), and the Fear of Flying Scale (FFS; Haug et al., 1987). Eleven flight phobics and eight controls were excluded from the study for clinical reasons (i.e., flight phobia was not the main problem) or physiological reasons (i.e., anomalous ECG signals).

1.3. Stimuli and Apparatus

The modified take-off sequence of the CAFFT was shown on a 17-in. screen and sounds were played through speakers. The length of the sequence was 5 min. Twenty still pictures with their corresponding sounds (recorded in a real environment) were included. Sessions were conducted in a dimly lit and sound-attenuated room. ECG was recorded in a Lead II configuration (a positive electrode on the left ankle, a negative electrode on the right wrist, and the ground electrode on the right ankle) using 10 mm Ag/AgCl electrodes. Instructions were given to subjects in order to avoid arms movements during the experiment. The signal was recorded on a BIOPAC MP150 monitoring system and the sample rate was set to 200 Hz.

1.4. Data reduction and analysis

After visual inspection of the ECG recordings to detect anomalous signals, five subjects in the phobic group and eight subjects in the control group were excluded from further analysis. An automatic R-wave detector was used to identify the interbeat intervals (IBI) in milliseconds, from which the RMSSD was calculated. Instantaneous HR was obtained from the ECG recordings using the algorithm developed by (Berger et al., 1986) with a sampling rate of 4 Hz, and the high frequency band (0.15–0.4 Hz) as well as the low frequency band (0.04–0.15 Hz) power was calculated with the Fast Fourier Transformation method on these HR time series ($N = 1100$). The HRV analysis software (version 1.1; Niskanen et al., 2004) developed by the Biosignal Analysis and Medical Imaging Group at the University of Kuopio was used to detect the HF spectral peak during free breathing and paced breathing conditions.

Before conducting the MSE analysis, the ECGs were nonlinearly filtered with the *nrlazy* program of the TISEAN software package (Hegger et al., 1999). This program performs a simple nonlinear noise reduction: each embedded point is replaced by the average vector calculated in its neighbourhood with a given size (interval of the data/1000). We set embedding dimension $m = 5$, and delay for the embedding $d = 1$. MSE was calculated using the software available in Physionet (Goldberger et al., 2000) developed by Costa. The length of each time series was approximately 60000 points (5 min), r was set to 20% of the standard deviation and m was set to 2. Following Costa et al. (2002) the series were coarse-grained up to scale 40, so that the shortest time series had 1500 points.

1.5. Statistics

A two-way repeated measures group (phobic/control) condition (BL/PB/E) analysis of variance (ANOVA) was computed on each physiological measure. Measures with highly skewed distributions were ln transformed before conducting statistical analysis. Alpha level was set to .05 and adjusted (Bonferroni) for multiple comparisons. When sphericity cannot be assumed, ε values are reported. All the analyses were computed using SPSS 12.0S for Windows (SPSS Inc. 1989–2003).

2. Results

2.1. Self-reported fear

Only the phobic participants rated on a 1–9 point scale the level of fear they had experienced during E, giving a mean $M = 4.82$ (S.D. = 2.37). To know if they really experienced more fear than the control group we can take into account a previous study that used the same fearful stimuli (Bornas et al., 2005). Fifteen fearful flyers and 15 non-fearful flyers confronted the take-off sequence and rated the experienced fear. The means and standard deviations were $M = 4.28$ (S.D. = 1.50) for the phobic group, and $M = 1.65$ (S.D. = 0.68) for the control group. Though moderate, the level of fear of the phobic group was significantly higher, $t(28) = 6.18$, $p < .01$, and this group's mean is very closed to the mean of the phobics who participated in the current study.

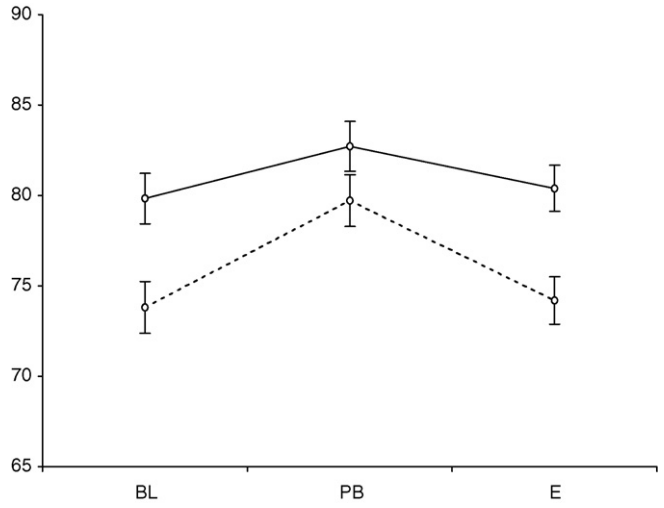

Fig. 1. Mean HR during baseline, paced breathing, and exposure conditions for phobics (solid line) and controls (dashed line). Error bars represent standard errors of the mean.

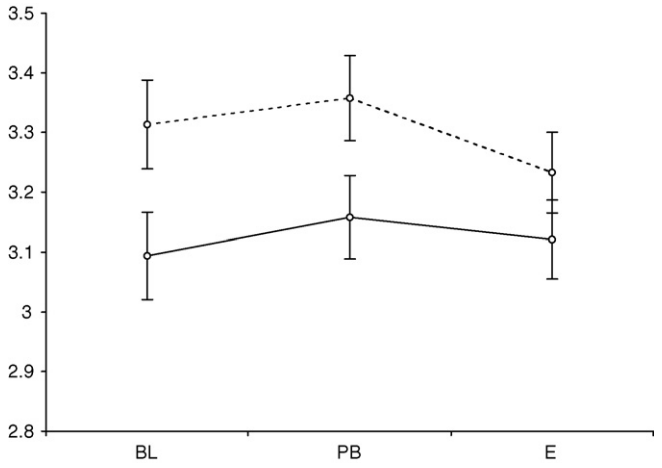

Fig. 2. Mean RMSSD values (ln transformed) during baseline, paced breathing, and exposure conditions for phobics (solid line) and controls (dashed line). Error bars represent standard errors of the mean.

2.2. Heart rate

The repeated-measures ANOVA revealed significant main effects for condition, $F(2,234) = 66.27$, $p < .001$, $\epsilon = .857$, group condition, $F(2,234) = 9.20$, $p < .001$, $\epsilon = .857$, and group, $F(1,117) = 7.29$, $p < .05$. Both groups showed the same pattern of change (see Fig. 1): significant HR increases from BL to PB, $t(60) = 4.33$, $p < .001$ for the phobic group, and $t(57) = 8.63$, $p < .001$ for the control group, and significant decreases from PB to E, $t(60) = 3.79$, $p < .01$ for the phobic group, and $t(57) = 8.80$, $p < .001$ for the control group. The HR of the phobic group was higher than the HR of the control group at BL, $t(117) = 3.00$, $p < .01$, and E, $t(117) = 3.40$, $p < .01$ (see Table 1).

2.3. RMSSD

The repeated-measures ANOVA revealed a main effect for condition, $F(2,234) = 4.086$, $p < .05$, $\epsilon = .927$. The group - condition interaction was not significant. The main effect for group was marginally significant, $F(1,117) = 3.57$, $p = .061$. A significant variability decrease was found only for the control group from PB to E, $t(57) = 2.96$, $p < .05$. As can be seen from Fig. 2, the RMSSD of the phobic group was lower than the RMSSD of the control group at BL, $t(117) = 2.11$, $p < .05$, and PB, $t(117) = 2.00$, $p < .05$ (see Table 1).

Table 1
Mean scores and standard deviations for flight phobics and healthy controls in baseline (BL), paced breathing (PB) and exposure (E) conditions

	Condition					
	BL		PB		E	
	M	S.D.	*M*	S.D.	*M*	S.D.
HR phobic	79.82	11.52	82.71	11.04	80.38	10.82
HR control	73.81	10.25	79.71	10.55	74.18	8.94
ln RMSSD phobic	3.09	0.56	3.16	0.56	3.12	0.51
ln RMSSD control	3.31	0.58	3.36	0.52	3.23	0.52
ln LF phobic	6.38	0.98	6.61	1.03	6.79	0.88
ln LF control	6.43	0.99	6.46	0.83	6.67	0.89
ln HF phobic	5.61	0.92	6.39	1.00	5.67	0.87
ln HF control	5.66	1.07	6.58	1.07	5.54	1.05

HR: heart rate; RMSSD: root mean of the squared successive differences; LF: low fequency; HF: high frequency.

2.4. HF power

The repeated-measures ANOVA revealed a main effect for condition, $F(2,234) = 118.63$, $p < .001$, $\epsilon = .851$. Neither the main effect for group nor the group condition interaction was significant. Both groups showed the same pattern of change (see Fig. 3): significant HF power increases from BL to PB, $t(60) = 7.73$, $p < .001$ for the phobic group, and $t(57) = 8.93$, $p < .001$ for the control group, and significant decreases from PB to E, $t(60) = 7.36$, $p < .001$ for the phobic group, and

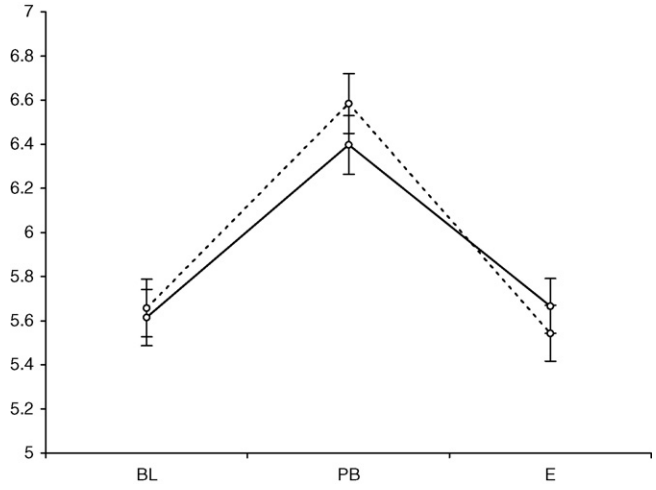

Fig. 3. Mean HF band power values (ln transformed) during baseline, paced breathing, and exposure conditions for phobics (solid line) and controls (dashed line). Error bars represent standard errors of the mean.

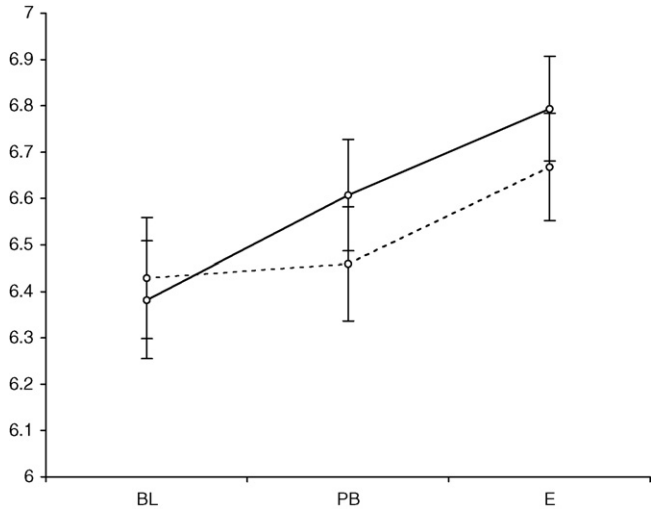

Fig. 4. Mean LF band power values (ln transformed) during baseline, paced breathing, and exposure conditions for phobics (solid line) and controls (dashed line). Error bars represent standard errors of the mean.

Table 2
Main effects revealed by the two-way repeated measures group condition ANOVAs computed on SampEn values obtained with the MSE analysis for scale factors 30–40

	Condition		group condition		Group	
	F	*p*	*F*	*p*	*F*	*p*
sf30	3.018	.054	1.551	.215	4.159	.044
sf31	3.674	.030 e= .929	1.147	.319	4.193	.043
sf32	3.392	.038 e= .942	1.477	.230	4.111	.045
sf33	4.207	.018 e= .932	1.129	.322	4.119	.045
sf34	4.146	.020 e= .915	1.152	.315	3.920	.050
sf35	4.855	.010 e= .926	1.217	.296	4.099	.045
sf36	4.529	.014 e= .923	.990	.368	4.013	.047
sf37	5.058	.009 e= .913	.592	.554	4.101	.045
sf38	4.771	.011 e= .925	.980	.377	4.024	.047
sf39	4.447	.015 e= .910	.494	.593	4.032	.047
sf40	4.816	.011 e= .921	.497	.594	4.302	.040

sf, scale factor.

$t(57) = 10.24$, $p < .001$ for the control group. A clear peak was found at 0.1998 Hz in the HF band during paced breathing.

2.5. LF power

The repeated-measures ANOVA revealed a main effect for condition, $F(2,234) = 11.477$, $p < .001$. Neither the main effect for group nor the group condition interaction was significant. LF power increased from PB to E in the phobic group, $t(60) = 4.83$, $p < .001$, as well as in the control group, $t(57) = 2.73$, $p < .05$ (see Fig. 4).

2.6. Complexity, MSE

As can be seen in Fig. 5 the SampEn values of both groups increase from scale factor 1 to 20 in all conditions and then they remain stable. In the phobic group, the differences between the means also show an increasing trend so that they reach statistical significance at scale factor 30, being the values from condition E lower than the values from BL. SampEn means obtained during the PB phase are in the middle. The ANOVAs revealed several significant main effects for condition and/or for group when the scale factor was set to a value 30 (see Table 2).

The ANOVA computed on the SampEn values obtained for scale factor 35 revealed significant main effects for condition, $F(2,234) = 4.855$, $p < .01$, e= .926, and group, $F(2,234) = 4.099$, $p < .05$ (very similar results were found for scale factors 30 to 40). As shown in Fig. 6, the entropy values of the phobic group were lower than those of the control group at PB, $t(117) = 2.08$, $p < .05$, and E, $t(117) = 2.12$, $p < .05$. An entropy decrease was also observed for the phobic group from BL to E, $t(60) = 2.56$, $p < .05$.

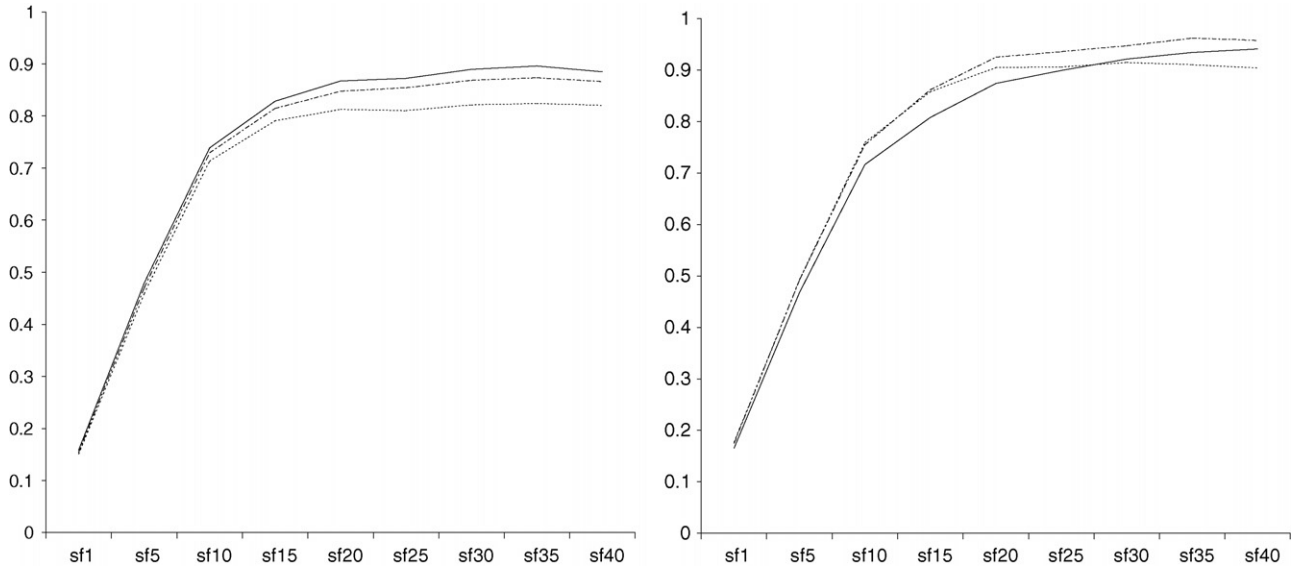

Fig. 5. Mean SampEn values for scale factors 1, 5, 10, 15, 20, 25, 30, 35, and 40 during baseline (solid line), paced breathing (semi-dashed line) and exposure to fearful stimuli (dashed line) conditions for the phobic group (left panel) and control group (right panel).

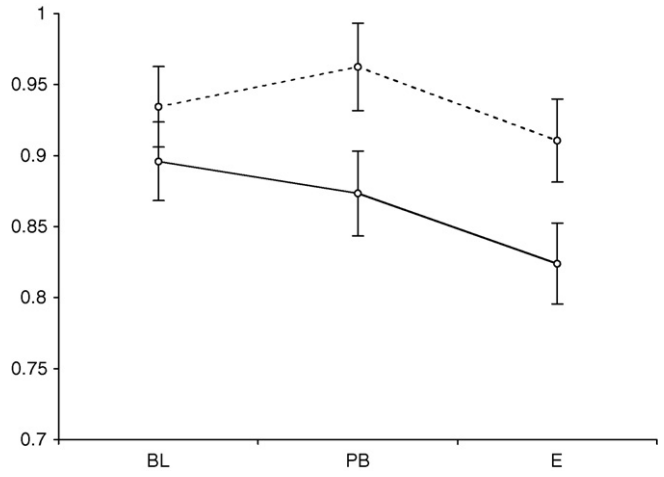

Fig. 6. Mean SampEn values (scale factor = 35) during baseline, paced breathing, and exposure conditions for phobics (solid line) and controls (dashed line). Error bars represent standard errors of the mean.

3. Discussion

In this study we explored the changes in the variability and complexity of the ECG of flight phobics when they performed a paced breathing task and were exposed to threatening stimuli. The RMSSD was used as the time domain measure of HRV and the HF spectral power was taken as the frequency domain measure of HRV. To evaluate complexity changes we performed a multiscale entropy analysis of the nonlinearly filtered ECG mV time series with scale factors varying from 1 to 40.

First of all, we have to say that phobic participants reported a moderate level of fear after exposure to the threatening stimuli. Based on previous studies (Bornas et al., 2005) we assume that non-phobics experienced less fear, but the fact that the stimuli did not evoke high fear can be seen as a limitation of the study (see below).

The flight phobics heart rate (HR) was higher than the non-phobics HR during exposure, and this could confirm that phobics were more anxious when confronting fearful stimuli. However, the phobics HR was higher also during BL. On the other hand, while the non-phobics HR decreased very clearly from PB to E, the corresponding decrease in the phobic group was much smaller (though still significant). In our opinion these facts (a) corroborate the idea that the stimuli did not generate very high anxiety, and (b) prevent to conclude that phobics were not anxious during exposure.

No differences from baseline to exposure were found in the HRV of flight phobics. Contrary to previous research (e.g., Bornas et al., 2005; Johnsen et al., 2003), the RMSSD values were almost identical in each condition. It should be noticed, however, that the mean values found in this study during baseline were extremely low, and therefore a floor effect could account for the lack of a RMSSD decrease during exposure. In fact, the RMSSD values found for the control group during BL were significantly higher and more similar to the values reported in previous studies (Bornas et al., 2005). Surprisingly, however, the RMSSD values of this non-phobic group decreased when they were confronted with the flying stimuli.

Regarding HF power, we did not find a statistically significant difference from BL to exposure. A possible explanation has to do with the paced breathing phase we placed between the baseline and the exposure conditions (a detailed discussion on the seemingly therapeutic effect of paced breathing can be found in Bornas et al., 2006b, in press). As expected, the HF power increased clearly during PB, and decreased during exposure. If we consider the PB phase as a kind of baseline, then the exposure to feared stimuli had the expected effect and reduced the vagally mediated HRV. The problem, however, is that the pattern of changes of the HF power in the control group is very similar to the phobic pattern. We can hardly attribute the HF decrease to fear as the control participants had no fear of flying. It seems more feasible that it was due to the completion of the paced breathing procedure.

The LF band power has been considered as a measure of sympathetic activation in other studies on anxiety disorders (e.g., Piccirillo et al., 1997). The observed increases in the LF power of the flight phobics during exposure to fearful stimuli are in agreement with the sympathetic activation found in blood phobics by Sarlo et al. (2002) who, nevertheless, did not found the same pattern in spider phobics. According to these authors, specific phobias may have specific autonomic reaction patterns, and the flight phobia pattern seems to be more similar to blood phobia than to animal phobia. Once again, however, the results of the control group make it difficult to accept that fear evoked the observed sympathetic activation. Since phobics and non-phobics showed LF band power increases from baseline to exposure, we have to conclude that exposure induced sympathetic activation, but this effect did not depend upon the emotional meaning of the stimuli.

The MSE analysis revealed a complexity loss from baseline to exposure in the phobic group, although it could not be seen until the scale factor was 20 or higher, and that loss was probably caused by the experienced fear. The observed complexity loss is rather small but this is not surprising if we remember that subjects did not suffer from any cardiac disease. Since they were cardiacally healthy we think that having found some decrease is very important as it confirms the sensitivity of the MSE analysis beyond the field of cardiac illness, in the study of anxiety disorders. This finding is in accordance with the complexity loss hypothesis derived from the Thayer and Lane's model of emotion regulation. To the best of our knowledge this model has always been tested using variability measures instead of complexity measures, even though the model was built up within a dynamical systems theoretical framework. Our findings on variability do not lend support to that hypothesis (see above) but the results on complexity confirm the model's prediction. In other words, according to our results fear induced a system's complexity loss while keeping variability unchanged. We think that future studies should elucidate the conceptual confusion that exists around the term variability, when it refers to nonlinear complexity.

Regarding differences between groups, we expected phobics complexity to be lower than non-phobics complexity, since the

cardiac output from healthy systems has been consistently found to be more complex (Guastello, 2004). Our results partially confirm this prediction. Phobics complexity was not lower than non-phobics complexity during free breathing. However, both during paced breathing and exposure to fearful stimuli the MSE analysis revealed lower entropy values for the phobic group. The baseline conditions in this study did not involve any pressure. Participants could breathe freely and they did not have to attend to any stimuli or to perform any task. On the other hand, the paced breathing condition and the exposure to fearful stimuli condition share the fact that they impose some constraint to the system. Our results seem to indicate that the heart rate complexity of the phobics is lower than the complexity of non-phobics only when they are under some pressure.

Finally, our results agree with one of the findings reported by Costa et al. (2002, p. 068102-2): ''The entropy measures for time series derived from healthy subjects increases on small time scales and then stabilizes to a constant value''. It should be said that these authors studied heart beat time series while we analyzed the original mV time series from which heart beat series can be extracted. In fact the ECG mV time series have been analysed in more basic research studies on predictability (Govindan et al., 1998), and nonlinearity in the cardiac output (Small et al., 2002). It may be interesting also from an applied point of view. Long interbeat intervals time series require much more ECG recording time than mV time series. In one minute, for example, we can get 60–80 intervals depending on the subject's heart rate. However we have 12000 mV values with the 200 Hz sampling rate we used in this study. To our knowledge MSE has not been used with mV time series in any previous study. Therefore, we can only speculate about the clinical usefulness of analyzing mV time series instead of interbeat intervals series.

One of the limitations of this study is that no control, non-fearful stimuli were presented. The complexity loss could be due, therefore, to global arousal or even to the information processing disregarding its emotional meaning. The fact that controls behaved like phobics in some cases (e.g., HF power) seems to lend support to this hypothesis, though differences between groups were also found in the study.

Another limitation of the study has to do with the evaluation of the control subjects fear of flying. Though it was required that control subjects had no fear of flying to participate in the study, it would have been better to evaluate their level of fear using the same questionnaires we administered to phobic participants (FFQ and FFS), and we could ask them to rate the discomfort they could have experienced during exposure using the 1–9 point scale. In this way we could be sure that the fear of flying level of the control group was significantly lower and that none of the control participants felt fear when confronting flight-related stimuli.

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