Increased Heart Rate Variability in Allergic and Highly Trait Anxious Individuals

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Abstract: Autonomic dysregulations were repeatedly observed in people with allergic reactions. Contradictory results of sympathetic over-activation on one hand and parasympathetic predominance on the other, were described for both atopic dermatitis and allergic rhinitis. Secondly, psychological traits of high anxiety and depression described in allergic patients are mostly associated with increased sympathetic and decreased vagal modulation. To address inconsistency in prior findings, we aim to study autonomic nervous system changes in allergic and highly anxious people via HR (heart rate) and HRV (heart rate variability) measures during stressful and relax days in day to day life. We further assess differences between allergic diagnoses and impact of acute symptom occurrence on HR and HRV. 61 subjects (26 allergic, 18 healthy high trait anxious and 17 healthy low trait anxious) took part in this study. They were repeatedly measured for HR by a portable electrocardiographic device, and assessed their subjectively experienced stress during everyday life. HRV was analyzed using time-domain, spectral and non-linear analyses. We observed increased HRV and decreased HR in allergic patients and also in healthy highly anxious subjects, when compared to controls. Both atopic dermatitis and allergic rhinitis patients exhibited parasympathetic predominance or sympathetic withdrawal, seen in increased HRV and lowered HR. Described effects of parasympathetic predominance were, however, not present during acute symptoms occurrence.

Key words: Allergy, trait anxiety, stress, heart rate variability, vagal modulation, naturalistic design.

1. Introduction

Allergic reactions are manifestations of atopy, hereditary disposition to develop hypersensitivity to environmental substances (e.g., pollen, dander, etc.) [1]. Three main manifestations of atopy are AD (atopic dermatitis), a chronic skin condition, AR (allergic rhinitis) mostly seasonal respiratory condition, and AA (allergic asthma). Psychological studies found that chronic stress plays an important role in onset and pathogenesis of allergies [2]. Based on concept of allostasis [3, 4], chronic exposure to stress leads to accumulation of allostatic load, which can be linked to physiological changes, as well as psychological states (e.g., anxiety). Allostatic load can result in various dysregulations of allostatic systems, nervous, endocrine and immune system. Studies of neuroendocrine HPA (hypothalamus-pituitary-adrenal)

axis in allergy [1, 5] found lowered levels of salivary cortisol in response to psychosocial stress in patients with AD [5] and AR [1, 6]. One of possible mechanisms of hypocortisolism is it being a result of chronic activation of HPA axis and, therefore, its inhibition through feedback regulation [7]. Similarly, autonomic nervous system dysregulation was described, however, while some studies showed sympathetic over-activation in allergy [5, 8, 9], other studies documented parasympathetic predominance [10-13].

Tran et al. [9] found constantly elevated HR (heart rate) and VLF (very low frequencies) of HRV (heart rate variability) in AD patients during scratching and also psychological stress. They also report dysfunction of parasympathetic system in acute stress, inferred from HR changes in respiratory frequencies. Higher basal HR in atopic dermatitis was also observed by Seiffert et al. [8]. However, though overall HR was higher in AD group, authors also reported lower HR

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increases during stress in AD group.

Lowered sympathetic activity or on the other hand increased parasympathetic activation in allergies was observed by another group of studies. Yokusoglu et al. [10], in a study of HRV in allergic rhinitis, found higher indices of RSA (respiratory sinus arrhythmia), associated with vagal activation in AR patients. Study was performed using 24 h ECG (electrocardiographic) measurements during everyday life of the participants. However, it was not clear whether AR patients exhibited acute symptoms at the time of HRV assessment. Similar results of autonomic changes were found in children with AR [11]. HRV increases found in atopic children also imply parasympathetic predominance and sympathetic withdrawal in AR. Boettger et al. [12] further reported increased vagal indices of HRV (e.g. high frequency HRV), during rest and controlled breathing test in atopic dermatitis patients. These results also indicate that there could be a relation between parasympathetic modulation and symptom severity in atopic dermatitis, as acute AD symptoms were positively correlated with parasympathetic HRV indices. Similarly, Lan et al. [13] described lowered HR and lowered LF (low frequency) HRV and LF/HF (low to high frequency ratio) in allergic rhinitis patients when in supine position. These data suggest lowered sympathetic modulation in AR patients.

Interpretations of these findings point out several mechanisms of autonomic dysregulations on allergy. Due to role of efferent vagus nerve in the anti-inflammatory pathway, and its inhibitory function on pro-inflammatory cytokines production [14], reported HRV changes were previously interpreted as possible effect of counter regulatory mechanism in response to allergic inflammation [12]. On the other hand, sympathetic withdrawal in atopic diseases can be according to Shahabi et al. [15] associated with allergic inflammation itself, and, therefore, increased activity of T helper 2 lymphocytes. While pro-inflammatory Th1 cytokines inhibit local sympathetic tone and

enhance systemic sympathetic tone, Th2 cytokines, that mediate atopic diseases have opposite effect, increasing local sympathetic activation in allergic reaction sites and secondary lymphoid organs, and lowering systemic sympathetic activity [16], which can be seen for example in cardiovascular psychophysiology.

From psychological and personality viewpoint, allergy reactions are largely associated with anxiety, depression emotional lability and problems in coping with stress. Factors of state and trait anxiety plays important role in etiopathogenesis of atopic dermatitis [17]. Effects of itch-scratch cycle in AD are also closely related to perceived anxiety and psychological discomfort [9]. High anxiety, social anxiety and vulnerability to stress were also described in AR [1] and AA [18]. Possible underlying mechanism can be illustrated by correlations of anxiety and Th2 immune response, as well as synthesis of IgE antibody [19]. People with allergy also exhibit higher subjective perception of stress and have higher comorbidity of anxiety disorders [20].

However, in studies when assessing HRV, anxiety and depressive symptoms are mostly associated with increase in HR and corresponding decrease in HRV [21, 22]. This is even more apparent in anxiety disorders [23] and major depressive disorder [24, 25]. Therefore, there are strong discrepancies between HRV findings in highly anxious and allergic people, although important links between both groups were described.

We would like to address this issue by assessing allergy and trait anxiety individually, comparing allergy patients with healthy highly anxious individuals and low anxious healthy controls. Other interesting issue is whether the effect observed in allergy can be attributed to acute allergic symptoms, or stable atopic disposition. When assessing this question, Buske-Kirschbaum et al. [1] found significantly blunted cortisol response in AR patients only when acute allergy symptoms were present. However, we

have not found any studies examining this issue via indices of heart rate variability.

In this study, we use naturalistic design of data collection, therefore, HRV measurements were obtained during everyday life and in response to day to day stressors. We chose repeated measurements of short term HRV instead of 24 h HRV. Shorter segments of HR are easier to avoid artifacts, which is very important when measuring HR and HRV during normal activities of a person. We can also compare repeated measurement of the same person in relation to perceived stress, allergic symptom occurrence and other within subject factors.

The aim of this study is to describe autonomic nervous system changes in allergic and non-allergic highly anxious people. We assess HR and HRV changes: (1) between allergy, high anxiety and control group; (2) between people with AD and AR, as the mentioned studies found similar effects in both diagnoses; (3) We compare changes in resting HRV and HRV during acute psychological stress. Finally, due to repeated measurements of HR in the same sample throughout one year, we can also (4) assess the impact of acute symptoms on HR and HRV and compare the same subjects during occurrence of acute symptoms and their non-occurrence.

2. Methods

2.1 Participants

26 patients suffering from allergy (of which 12 atopic dermatitis, 14 allergic rhinitis) diagnosed based on history, symptoms, and results of skin prick tests performed by an allergologist took part in this study. Trait anxiety was determined by STAI-T score, low anxiety < 39, high anxiety > 49. We chose these limits based on previous studies with Slovak sample, aiming to select only people with very high and very low anxiety [26, 27]. Within allergy group, 17 subjects had low trait anxiety and 9 subjects had high trait anxiety. In assessing the factors of allergy and anxiety, we excluded these 9 subjects from analysis. We also

excluded one subject due to missing HRV data. Therefore, 16 low anxious allergy patients were used in between group comparison.

Research sample also consisted of 18 high trait anxiety (above 49 STAI) healthy subjects and 17 low trait anxiety (below 39 STAI) healthy subjects matched for age and sex with allergy group (overall age range: 18–30 years, together 28 male, 33 female subjects). Subjects with cardiovascular, endocrine or psychiatric diseases, and subjects who took medication (e.g., antihistaminics, corticosteroids) or had other conditions that could confound with HRV measures were excluded from study. Written informed consent was obtained from all participants after explanation of all research procedures. The study was approved by ethics committee of the Trnava Self-Governing Region, Trnava, Slovakia.

2.2 Data Collection

This study is based on a naturalistic design, therefore, HRV was measured during everyday life of participants. Data were collected between January 2015 and May 2016, in separate repeated measurements. Mean gap between measurements was around 2–3 months, however, every participant selected stressful and relax measurement individually according to events in their lives. In given dates, participants recorded their ECG using FAROS 90° ECG device for 20 min in the morning (6:30–8:30), afternoon (14:00) and evening (20:00). These times were chosen because of simultaneous extraction of salivary samples, which will be analyzed in further studies. Participants were instructed how to apply the portable ECG device and how to switch it on and off. During 20-min HR measurements, participants were instructed to be seated.

For assessment of subjective perception of stress, participants filled Slovak version of perceived stress scale [28] and for this research composed checklist of adjectives, which were associated with feeling of stress, exhaustion and positive emotion.

Total number of measurement days varied among

the research sample. In this study we present results of comparison between stressful and relax days, which were chosen by each subject in advance. Stressful days were predominantly associated with heavy work load, while relax days were days with the least stress (e.g., weekends, etc.).

Measurements that could not be attributed to any of these categories were excluded from this analysis. Secondly based on repeated measurements, we also address differences between days with and without subjectively reported allergy symptoms in allergy group.

2.3 Heart Rate Variability Measures

Sampling rate for heart rate measurements was 250 Hz. For purposes of HRV analysis two 5 min windows from each dataset were selected. HR and HRV parameter values from analyzed segments were averaged. HRV was analyzed in software Kubios HRV for time-domain, spectral and non-linear analysis.

Used variables were average heart rate (in 5 min recording), expressed in bpm (beats per minute) which can be considered a good cardiovascular sympathetic marker [29]. Time domain measures were SDNN (standard deviation of all R-R intervals) as a measure of overall variability and RMSSD (the square root of mean squared successive R-R differences) as index of respiratory sinus arrhythmia, therefore, reflecting more vagal influences. Spectral analysis was performed using FFT (fast Fourier transform) algorithm. Used frequency-domain variables were VLF (under 0.04 Hz), which was previously seen as a potential indicator of sympathetic activity [9], however, there are still uncertainties in interpretation of VLF HRV. LF (0.04~0.15 Hz) as reflecting both sympathetic and vagal influences, and HF (high frequencies) (0.15~0.4 Hz) which is considered a predominant marker of RSA and vagal activation [30, 31]. From non-linear analyses, we used standard deviations SD1 and SD2 from Poincaré plot, approximate entropy and detrended fluctuations $\alpha 1$ and $\alpha 2$. SD1 is a measure of

short term variability, therefore, it strongly correlates with RMSSD and HF-HRV as indices of RSA. SD2 expresses long-term variability and correlates with SDNN and total power in spectral analysis [32]. Approximate entropy is an index of overall complexity and unpredictability of R-R interval series. Detrended fluctuations are indices of fractal attributes of given series of R-R intervals, $\alpha 1$ reflects shorter intervals (4~16 R-R series) and correlates predominantly with HF and LF, while $\alpha 2$ reflects longer series (16~64 R-R intervals) and correlates with LF and VLF [33]

2.4 Statistical Analyses

For statistical analyses, we used program IBM SPSS 20, in which we used linear repeated measures model with within subject factor—research day (stress and relax) and between subject factor—research group (allergy, high trait anxiety, control). Similarly, differences between symptomatic days and non-symptomatic days in allergy group were calculated using ANOVA. HRV differences in subjects with AD and AR were compared using independent samples t-test.

3. Results

3.1 Factors of Allergy and Anxiety in Stressful and Relax Days

16 low anxious participants with allergy, 16 high anxious subjects, and 16 controls were compared across subjectively selected stressful and relax days using repeated measures model. HR and HRV measures from 5 min windows during the same day were averaged. Subjects with missing data were excluded from this analysis. All non-normally distributed variables (HRV measures: SDNN, RMSSD, VLF, LF, HF, SD1, SD2) were adjusted by log10. Normally distributed variables (HR and non-linear ApEn, $\alpha 1$ and $\alpha 2$) were used in their raw form.

In HR, we found significant within subject differences between stress and relax day (repeated measures, within subject effect: $F = 4.827$, $p = 0.033$,

effect size $\eta^2 = 0.097$), between subject differences due to group (allergy, high anxiety, control) were ($F = 2.788, p = 0.072, \eta^2 = 0.110$), with higher mean HR in low anxious controls (bpm = 80.738) than high anxiety (bpm = 77.121) and allergy group (bpm = 72.620). In HRV, there were significant differences in SDNN within subject ($F = 5.487, p = 0.024, \eta^2 = 0.109$) and between subject ($F = 3.221, p = 0.049, \eta^2 = 0.125$), with higher SDNN in both allergy and high anxiety groups compared to controls. RMSSD shown also strong within subject effect due to stressfulness of the given day ($F = 5.435, p = 0.024, \eta^2 = 0.108$). Differences between groups were not significant overall ($F = 1.918, p = 0.159, \eta^2 = 0.079$), however, this effect was stronger when comparing them on stressful day (post hoc t-test: high anxiety and

controls: $t = 1.865, p = 0.069, \eta^2 = 0.072$, post hoc: allergy and controls: $t = 1.681, p = 0.1, \eta^2 = 0.059$). RMSSD as an indicator of RSA and vagal influences, was elevated in both allergy and high anxiety subjects, while they also shown lesser RMSSD reduction in stressful day (Fig. 1).

From spectral indices, there were significant differences in VLF between groups ($F = 3.804, p = 0.03, \eta^2 = 0.145$) however within subject effect was not significant ($p = 0.158$). In LF we found within subject differences due to stressfulness of a given day ($F = 3.937, p = 0.053, \eta^2 = 0.080$), but differences between groups were insignificant ($p = 0.299$). Similarly, in HF significant was within subject factor ($F = 2.782, p = 0.102, \eta^2 = 0.058$) and not between group difference ($p = 0.226$). All spectral indices: VLF,

Fig. 1 Estimated marginal means between groups (allergy, anxiety, control) in stressful and relax day for HRV measures: (a) SDNN; (b) RMSSD; (c) HF-HRV; (d) SD1 from Poincaré plot.

LF and HF shown similar trend of being elevated in allergy and high anxiety group when compared to controls. Besides that, all spectral indices were lower in stressful day, when compared with relax day.

From non-linear indices: SD1 had significant within subject difference ($F = 5.226, p = 0.027, \eta^2 = 0.104$), not between groups effect ($p = 0.165$). Similarly, SD2 (within subject: $F = 4.665, p = 0.036, \eta^2 = 0.094$) (between groups: $F = 2.836, p = 0.069, \eta^2 = 0.112$). There were significant differences in stressful day between anxiety group and controls (post hoc: $t = 2.306, p = 0.026, \eta^2 = 0.106$), allergy group and controls: (post hoc: $F = 2.692, p = 0.01, \eta^2 = 0.139$). Both SD1 and SD2 were higher in both allergy and anxiety group compared to controls. The difference in SD2 even grew, when SD2 in controls dropped during stress but remained elevated in allergy and anxiety. In approximate entropy, there were no differences between groups and research days. Detrended fluctuations $\alpha 1$ differences were not significant (within subject: $F = 0.777, p = 0.383, \eta^2 = 0.017$, between groups: $p = 0.555$), however $\alpha 1$ was higher in controls. $\alpha 2$ was elevated in both allergy and anxiety group, this effect was also not significant ($F = 0.624, p = 0.434, \eta^2 = 0.014$, groups: $p = 0.353, \eta^2 = 0.045$).

3.2 Comparison between AR and AD

Research groups consisted of 14 AR patients, 10 AD patients and 16 healthy controls. Trait anxiety in allergic subjects was not taken into account in this analysis. For comparison we used averaged HRV measures, within subject effect was not addressed.

We observed no significant differences between AR and AD. However, both groups similarly differ from controls in (ANOVA: bpm: $F = 5.609, p = 0.004$, SDNN: $F = 4.398, p = 0.014$, RMSSD: $F = 4.915, p = 0.009$, LF: $F = 5.075, p = 0.007$, HF: $F = 5.496, p = 0.005$, SD1: $F = 4.148, p = 0.018$, SD2: $F = 4.610, p = 0.011$). Differences between groups are shown in Table 1.

3.3 Comparison Due to Occurrence of Acute Symptoms

Allergy group was compared in days with acute allergy symptoms and days with no symptom occurrence. Independent samples t-test was used. Differences were present in HR (independent samples t-test: $t = -2.888, p = 0.006$), SDNN ($t = 2.335, p = 0.024$), RMSSD ($t = 3.301, p = 0.002$), LF ($t = 3.256, p = 0.002$), HF ($t = 2.194, p = 0.033$), SD1 ($t = 3.301, p = 0.002$), SD2 ($t = 2.147, p = 0.037$), $\alpha 2$ ($t = -2.154, p = 0.041$). HR was elevated during acute symptoms, while all HRV measures except $\alpha 2$ were lower (Fig. 2).

3.4 Subjective Stress Differences

Perceived subjective stress measured by PSS (perceived stress scale) differed between stressful and relax days significantly (repeated measures: $F = 13.935, p = 0.001, \eta^2 = 0.254$), important was also effect of group ($F = 4.459, p = 0.018, \eta^2 = 0.179$) and also interaction between these two factors ($F = 3.389, p = 0.043, \eta^2 = 0.142$) Perceived stress was overall higher in high anxiety group. Allergy group had higher values in relax days, and lower values in stressful days

Table 1 Mean HRV differences in AD, AR and healthy controls.

Variable	AD (atopic dermatitis)	AR (allergic rhinitis)	Healthy controls
Mean HR (bpm)	75.861	74.538	80.926
Mean SDNN	67.093	74.569	60.223
Mean RMSSD	48.326	51.612	40.284
Mean SD1	34.217	36.549	28.524
Mean SD2	87.938	97.625	77.983
LF-HRV (log10)	3.096	3.199	2.977
HF-HRV (log10)	2.801	2.864	2.577
$\alpha 2$	0.833	0.860	0.899

Fig. 2 Comparison of HR and HRV in allergy with and without acute symptoms.

compared to controls. When comparing symptomatic days in allergy with non-symptomatic days, subjective stress exhibited no significant differences.

4. Discussion

In this naturalistic design study of stress related HR and HRV, lowered sympathetic and predominant parasympathetic activation was observed in both allergy and high anxiety subjects. These results indicate to and hypoactive sympathetic or overactive parasympathetic branch of ANS in both groups when compared to control subjects.

Within subject factor or stressful and relax days was associated with expected cardiovascular changes of higher HR and lower HRV in stressful, compared to relax days. This effect was significant for HR and most HRV parameters with no respect to research group.

4.1 Allergy and Anxiety

Heart rate, which is often seen as cardiovascular marker of sympathetic activity was lower not only in subjects with allergy, which was observed in previous research [10, 12, 34], but also in highly anxious healthy subjects. Though similarities between highly anxious and allergic people were described earlier [8, 19], HR studies in anxiety mostly show either elevated HR or no significant effect of anxiety on HR [22, 35].

Our findings in HRV and mostly vagal indicators of HRV again show similarities between allergy and anxiety group. HRV parameters, such as SDNN, RMSSD and spectral indices VLF, LF, and HF all had higher values in both allergy and high anxiety groups than in healthy low anxious controls. While VLF, previously associated with sympathetic activity by

Tran et al. [9] was higher in our study similarly to the their study, LF and also HF, which is a predominant parasympathetic marker were all elevated, as well.

From non-linear HRV parameters used in this study, SD1 and SD2 from Poincaré plot shown corresponding patterns as time-domain and spectral analysis. While SD1 is associated to HRV at respiratory frequencies and correlates closely with RMSSD and HF-HRV, SD2 reflects more overall variability similarly to SDNN. In our results all of these HRV parameters were positively correlated in both stressful and relax measurements.

There were no significant differences in approximate entropy in relation to stressful and relax days nor to allergy and anxiety. In detrended fluctuation analysis we found higher $\alpha 1$ in healthy controls. Alpha1 reflects fractal attributes of given R-R series, therefore higher values of $\alpha 1$ should be indicator of healthy HRV. While $\alpha 1$ was higher in controls, $\alpha 2$, which assesses longer R-R series showed effect similar to time-domain and spectral variables.

Increased parasympathetic modulation in allergy observed in our data was previously repeatedly reported [34], however, the issue of increased parasympathetic or decreased sympathetic activity in anxiety is somewhat surprising. We found not only increases in vagal parameters of HRV, but also overall variability. Corresponding result was also found in our laboratory design study, using simulated public speech as stressful condition. Most studies associate high anxiety with reduced HRV and increased HR, which can also be seen in anxiety disorders studies [23]. On the other hand, close similarities between allergy and anxiety were documented [8, 19, 20]. Similar findings in allergy and anxiety were also found in HPA axis reaction to stress, where both allergy and high trait anxiety subjects exhibited lowered cortisol responses [5, 26]. In light of these results, we hypothesize, that both allergy and high trait anxiety subjects exhibit an autonomic dysregulation, which can demonstrate itself in the form of hyperreaction or hyporeaction similarly to cortisol reactivity.

When comparing atopic dermatitis and allergic rhinitis, both diagnoses were previously described with parasympathetic predominance [10, 12, 34], therefore, we tried to compare HRV in both conditions. Our results shown the same trends in both AR and AD, no significant difference between the two, just the observed effects were a little stronger in allergic rhinitis. Both AD and AR exhibited increased HRV and decreased HR when compared to non-allergic controls. So although AR and AD exhibit in a very different set of symptoms, with different severity, cardiovascular autonomic changes were comparable in both groups. We hypothesize that allergic inflammatory reaction or atopic disposition can be a general factor explaining our results. Both systemic sympathetic withdrawal described by Shahabi et al. [15], and parasympathetic predominance due to regulatory function of anti-inflammatory pathway [13], can serve as probable mechanisms of observed effect. This issue, however, needs to be further studied.

4.2 Acute Symptoms and Atopic Disposition

The data from previous HRV studies do not explain whether described autonomic dysregulation contributes to development of allergy symptoms, or is a consequence of acute allergic inflammation. Buske-Kirschbaum et al. [1] addressed this question and found dysregulated cortisol responses only during acute inflammation in seasonal AR patients. In our HRV data, we compared measurements, during which allergic subjects stated no acute symptoms with measurements during acute symptoms. Our data showed us an interesting trend. While allergic patients with both AR and AD showed increased HRV during non-symptomatic days, their HRV is lower during symptoms occurrence. Therefore, HRV of allergy patients during acute symptoms was closer to HRV of healthy controls, than to themselves during no symptom occurrence. In this analysis, we included only participants who reported allergy symptoms and took no antihistaminic nor corticosteroid medication,

therefore we can eliminate possible effect of treatment. This issue should be further addressed in a larger sample, using also different markers of parasympathetic and sympathetic activation. However, it is possible that acute inflammation and possibly related discomfort may lead to increase in sympathetic modulation, which can be serve as counterweight to observed effect of parasympathetic predominance in allergy.

4.3 Specifics of Naturalistic Design and Study Limits

The main aim of naturalistic design used in this study was to measure physiological changes during day to day stress. Building up on 24 h continuous ECG measurement studies [10], naturalistic studies in salivary cortisol [36], and our laboratory studies, we chose to analyze shorter measurements of ECG which were repeated several times during one year. Due to this design, we could also address the question of within subject development in allergy, anxiety and control subjects. In our design, participants individually selected dates of stressful and relax days based on expected stressors in their lives, most of which were work related. We used various psychological measures, such as adjectives checklist, 10-point scales of subjective stress and also widely used PSS (perceived stress scale) to assess whether given measurements could be analyzed as stressful or relax measurements.

There are, however, some limitations of used design. First we did not test the control subjects for allergy, we only assessed their self-reports and asked them about possible allergic symptoms. It may be possible some could be allergic even though they do not know about it. Another issue is less control over participants' behavior in this naturalistic design study, and also not controlling for participants breathing patterns during ECG measurement, which could affect HRV results [37]. Participants could also fail to mention any conditions or medication in their self-report and, therefore, we need to take these issues into

consideration in interpretation of the data.

5. Conclusions

We found increased HRV and decreased HR in subjects with allergy and also healthy highly anxious subjects. Highly trait anxious subjects exhibited similar pattern of HRV to allergic group, which corresponds to previously found similarities between these groups. Both atopic dermatitis and allergic rhinitis exhibited the same pattern of sympathetic withdrawal and parasympathetic predominance. However, when comparing HRV during symptomatic and non-symptomatic days, we did not find the mentioned effect during when acute symptoms were present. Future research should more thoroughly assess autonomic changes due occurrence of allergic symptoms and therefore shed more light on exact mechanisms of parasympathetic predominance and sympathetic withdrawal in allergy.

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