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The effect of an exam period as a stress situation on baroreflex sensitivity among healthy university students

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ABSTRACT

Purpose: Authors investigated the effect of a university exam period on blood pressure (BP) and baroreflex-sensitivity (BRS) among healthy students.

Materials and methods: Fifty-three healthy normotensive university students participated in the test. BP values and BRS were recorded once during a 14-week long semester and once during a 6-week long exam period with a Finometer device. The time-domain spontaneous BRS in lying position and after standing up was calculated with Nevrokard software. Students were divided into optimal, normal, high-normal and hypertension (HT) groups by BP values.

Results: All the BRS values calculated in the exam period were significantly lower compared to the semester period in the same positions. In supine position: (semester *vs.* exam) up-BRS was 21.9 ± 13.2 ms/mmHg *vs.* 18.5 ± 11.9 ms/mmHg ($p = .013$), down-BRS was 22.3 ± 9.3 ms/mmHg *vs.* 18.4 ± 8.2 ms/mmHg ($p = .019$). After standing up: (semester *vs.* exam) up-BRS was 9.3 ± 3.3 ms/mmHg *vs.* 7.6 ± 3.1 ms/mmHg ($p = .02$), down-BRS was 9.5 ± 3.6 ms/mmHg *vs.* 7.0 ± 2.8 ms/mmHg ($p < .0001$). The number of students decreased in optimal BP group and increased in normal and HT groups in the exam period.

Conclusions: A 6-week long exam period had enough stress effect to change cardiovascular parameters towards a higher risk even in healthy young people.

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baroreflex; exam period; healthy; student

Introduction

A primary hypertension (HT) starting at adulthood seems to begin at a younger age [1]. Some data also suggest significant correlation between HT in childhood and later atherosclerosis [2]. Blood pressure (BP) values, as well as the weight of childhood, may play an important role in the development of HT in adulthood [3].

The role of stress in the development of primary HT has been investigated for a long time. It was assumed very early that the sympathetic nervous system may be the potential link between stress and BP elevation. It was also early evaluated that norepinephrine level increases in the plasma due to every sort of stress, except emotional one [4].

The arterial baroreflex-sensitivity (BRS) is a marker of the parasympathetic activity which is responsible for the short-term cardiovascular (CV) regulation. The BRS may also be useful as a risk marker for CV diseases. Decreased BRS is suggested to be an independent predictor of poor survival following an acute myocardial infarction, according to the results of the Autonomic Tone and Reflexes After Myocardial Infarction (ATRAMI) study [5]. Decreased BRS is also suggested to be a sensitive early marker in diabetic autonomic neuropathy [6–9]. A physical stress like standing up from supine position may decrease the spontaneous BRS [10].

Physiological adaptation to a stress situation involves the activation of the autonomic nervous system. A stress situation may induce an increase in heart rate (HR) and BP [11]. BRS also can be decreased during acute physiological stress in humans [12].

At the University of Szeged, all the faculties have a 14-week long semester and a 6-week long exam period. The 4th and 5th year students in the Faculty of Medicine have 10–13 exams during a 6-week long exam period. The aim of this work was to investigate how a prolonged, as opposed to an acute, stress situation – like a 6-week long exam period – influences BP and spontaneous BRS among healthy university students.

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Patients and methods

The fifth year healthy medical students at the University of Szeged were asked to participate in the test. Their BP and BRS data were recorded once during a 14-week long semester and once during a 6-week long exam period. During the exam period it was not a criterion that data should be recorded only on the day or the day before of an exam. Students came for the measurements mostly on days between exams. It was not recorded how many days before or after an exam the measurements were carried out. During the last 2 weeks of the semester period, no measurements or data recordings were done.

Students came to the procedures without having drunk any coffee, coke or alcohol or having smoked within 30 min. They had been sitting at least for 5 minute prior the BP measurement was performed by a sphygmomanometer. The mean of three readings (with 5 minute intervals) were recorded both in the semester and the exam periods. These BP values were categorized according to the 2007 guidelines of the European Society of HT (ESH) corresponding to the year of the experiment [13]. The classification of office BP and definitions of HT grade was still the same in the 2018 European Society of Cardiology (ESC)/ESH guideline [14]. Students were divided into optimal (O), normal (N), high normal (HN) and HT groups by their SBP values. Diastolic BP (DBP), HR, body mass index (BMI) and waist-to-hip ratio (WHR) values were recorded as well.

Spontaneous BRS was calculated in a 10-min long supine and a 10-min long standing positions with a sequence (time-domain) method using a software package for BRS analysis (Nevrokard BRS 5.1.3; Medistar). The sequence method was based on the quantification of sequences of at least three heartbeats in which systolic BP (SBP) consecutively increases (up) or decreases (down), which is accompanied by changes in the same direction of the interval between ventricular depolarizations (RRI) of the subsequent beats. The Nevrokard software calculates upBRS, downBRS. The SBP and RRI files were generated *via* the beat-to-beat data acquisition system by a finger photoplethysmography (Finometer; Finapres Medical Systems B.V. Enschede, The Netherlands) at 200 Hz combined with an electrocardiogram.

From data recorded by Finometer, with the BeatScope version 1.1 software (Finapres Medical Systems BV Arnhem, Enschede, The Netherlands) at 200 Hz combined with an electrocardiogram.

Table 1. Distribution of the students according to the SBP values.

	Semester period, n (%)	Exam period, n (%)
O	44 (83)	38 (71)
N	7 (13)	12 (23)
HN	2 (4)	2 (4)
HT	0 (0)	1 (2)

The Netherlands' total peripheral ratio (TPR) could also be calculated, as the ratio of mean pressure to cardiac output, thus assuming zero venous pressure (in the right atrium).

The data were compared statistically by parametric analysis of variance (ANOVA) or non-parametric ANOVA (Kruskal–Wallis) depending on the normal distribution or rather variance identity. Relationships between variables were analysed with Pearson's correlation and a multiple linear regression test. Pairwise comparisons were made applying the Student–Newman–Keuls test. Ordinal Rank sum was also applied with Bonferroni of Dunnett corrections. A probability value of $<.05$ was considered as significant. Means ± standard deviation (SD) are reported. We used SigmaStat version 1.0 software (Jandel Scientific Software, San Rafael, CA, USA) for statistical analysis.

Results

Fifty-three medical students without any known internal disease were asked to participate (23 male and 30 female, mean age 23.0 ± 1.9 years). Twenty-eight students declared to drink coffee regularly, five of them smoked and none claimed to consume alcohol regularly. No questions were asked about their physical activity or doing sports regularly. Most enrolled students were not obese (BMI 23.8 ± 3.8 kg/m^2, WHR 0.83 ± 0.07). The mean BMI and WHR were in the normal range. BMI values of 10 students were 25.0–29.9 kg/m^2 and only in five cases $\geq$30.0 kg/m^2. WHR of 7 male students were over 0.9 and 4 female students were over 0.85.

The mean SBP of male students was significantly higher compared to that of the female students (115.4 ± 11.1 mmHg *vs.* 104.0 ± 10.6 mmHg, $p < 0.001$) but within the healthy range. The mean male and female DBP did not differ significantly (74.5 ± 8.3 *vs.* 70.4 ± 7.4, $p = .06$). Only one male student had 88 mmHg DBP, all the other students had <85 mmHg.

The distribution of students according to their BP values measured in semester and exam periods are summarized in Table 1. The number of the students during the exam period in group O decreased, in groups N and HT increased and in group HN did not

Table 2. Mean SBP, DBP and HR values during the semester and the exam period (mean ± SD).

Semester period (n = 53)			Exam period (n = 53)		
SBP (mmHg)	DBP (mmHg)	HR (beat/min)	SBP (mmHg)	DBP (mmHg)	HR (beat/min)
108.9 ± 12.1	72.2 ± 8.0	70.8 ± 7.9	112.0 ± 11.6	72.5 ± 6.9	73.1 ± 9.6

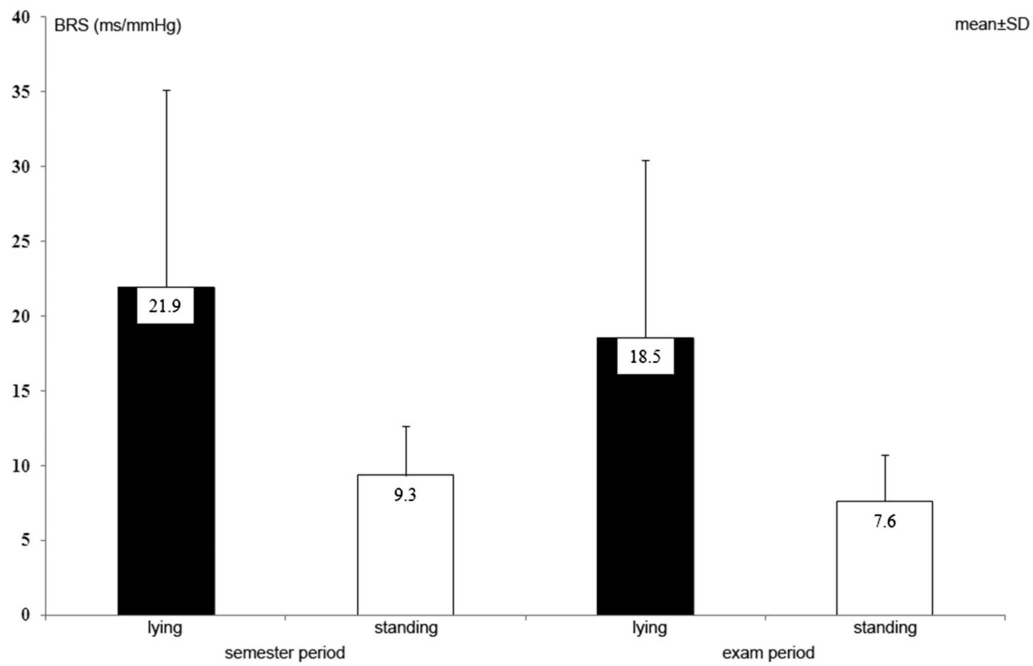

Figure 1. The upBRS in the semester and the exam period. (*p*<.001 in semester period lying *vs*. standing; *p*<.0001 in exam period lying vs. standing; *p*=.013 lying in semester period *vs*. lying in exam period; *p*=.02 standing in semester period *vs*. standing in exam period).

change. Six students' BP rose during the exam period in the group O, five of them got into the group N and one into the group HT. The number and BP of students in the group HN did not change.

Within a group, the mean BP did not change significantly in the exam period compared to semester period (group O: $p = .52$; group N: $p = .13$). The BP has significantly changed in those, whose BP elevated from optimal to normal range ($n = 5$, 108.3 ± 8.3 *vs*. 123.4 ± 2.6, $p = 0.003$).

The mean SBP, DBP and HR values during the semester and exam periods are reported in Table 2. One had DBP above 90 mmHg neither during the semester nor during the exam period. SBP and HR did not change in the exam period ($p = .12$ for SBP, $p = .12$ for HR). There was no correlation between the HR during the semester and SBP during the exam period ($p = .65$, $r = -0.06$). Neither was any correlation between HR and SBP during the semester period ($p = .74$, $r = -0.05$). The correlation between HR during the semester and the exam period was not significant ($p = .05$, $r = 0.27$). There was a positive correlation between SBP during the semester and the exam period ($p = .02$, $r = 0.32$).

All the BRS values calculated with the time-domain method decreased significantly after standing up compared to a supine position in all students not just during the semester but also in the exam period. Moreover, in both positions, all the BRS values were significantly lower in the exam period compared to the semester period (Figures 1 and 2).

The TPR was significantly higher in standing compared to the lying position in both periods involved (in the semester period: $p < .0001$ lying *vs*. standing; in the exam period: $p < .0001$ lying *vs*. standing). TPR did not change significantly in the exam period nor in lying neither in standing position ($p = .11$ for lying and $p = .29$ for standing) (Figure 3).

HR did not change in the exam period significantly ($p = .12$). During the semester period, BMI and WHR did not correlate with TPR in any position. But, in the exam period, there were positive correlations between them in both positions (BMI *vs*. TPR: $p = .002$, $r = 0.43$ for lying and $p = .002$, $r = 0.42$ for standing; WHR *vs*. TPR: $p = .002$, $r = 0.41$ for lying and $p = .006$, $r = 0.37$ for standing).

BRS did not correlate with BMI, WHR, HR, DBP or SBP, either. SBP correlated with BMI ($p = .005$,

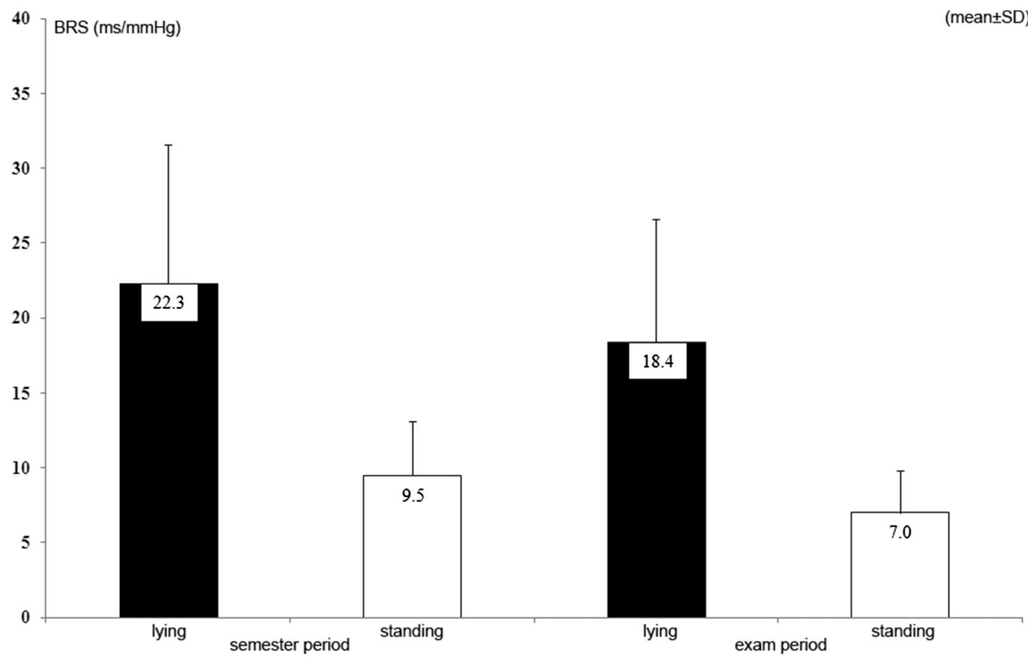

Figure 2. The downBRS in the semester and the exam period. ($p<.0001$ in semester period lying *vs.* standing and in exam period lying vs. standing; $p=.019$ lying in semester period *vs.* lying in exam period; $p<.0001$ standing in semester period *vs.* standing in exam period).

$r=0.38$) and WHR ($p=.001$, $r=0.43$) during the semester period. There was no correlation between SBP and HR in either periods ($p=.74$, $r=-0.05$ for semester period, $p=.08$, $r=0.25$ for exam period). The BMI and the resting HR did not correlate significantly in the semester period ($p=.51$, $r=-0.09$), but in the exam period there was a negative correlation between BMI and resting HR ($p=.03$, $r=-0.3$).

Discussion

It was published in 2003 that an occasional higher BP in teenage girls is an independent predictor of the development of HT when they become young adults. An occasionally elevated BP in boys correlated with a 10-year CV risk in early adulthood [14].

The role of stress in the development of HT has been well-known for a long time, however, every detail of this mechanism has not yet been discovered. There are no any data how early and how long an individual should be exposed to any kind of stress before it may elevate his BP permanently, not just occasionally.

An acute mental stress situation may increase the BP and the cardiac output in healthy individuals. Jern et al. [15] found that central type body fat distribution comes with increased systemic vascular resistance during mental stress. It is well-known that emotional stress can cause flushing and an occasional BP elevation. In such cases, plasma dopamine level increased immediately after the stress. It lasted only for a short time. Plasma samples examined later show that dopamine returns to its normal range [16]. A slight but repetitive dopamine response to emotional stress downregulates renal dopamine-2 receptors, which leads to salt retention. Salt retention is one of the risk factors of HT [17].

In clinical trials, workplace stress is defined as a combination of higher job strain with low decision latitude at the workplace. The higher is the first factor and the lower is the second one, the stress is more intense. There are relatively a small number of prospective studies investigating the association between the effects of workplace stress and BP changes in the long term and their results are not concordant. In another study, 3200 young adults (age 20–32 years) were followed for 8 years and still no correlation was found between the chronic workplace stress and the incidence of HT [18]. However, the higher job demand and the change of decision position already correlated to higher incidence of HT. In another study, 6729 white collar workers were followed for 7.5 years. During this period, a moderate rise could be observed in the incidence of HT independently of gender. Nevertheless, SBP alone elevated significantly and only among men [19].

According to a study of a 6.5-year follow-up of 448 workers, the more intense the workplace stress was,

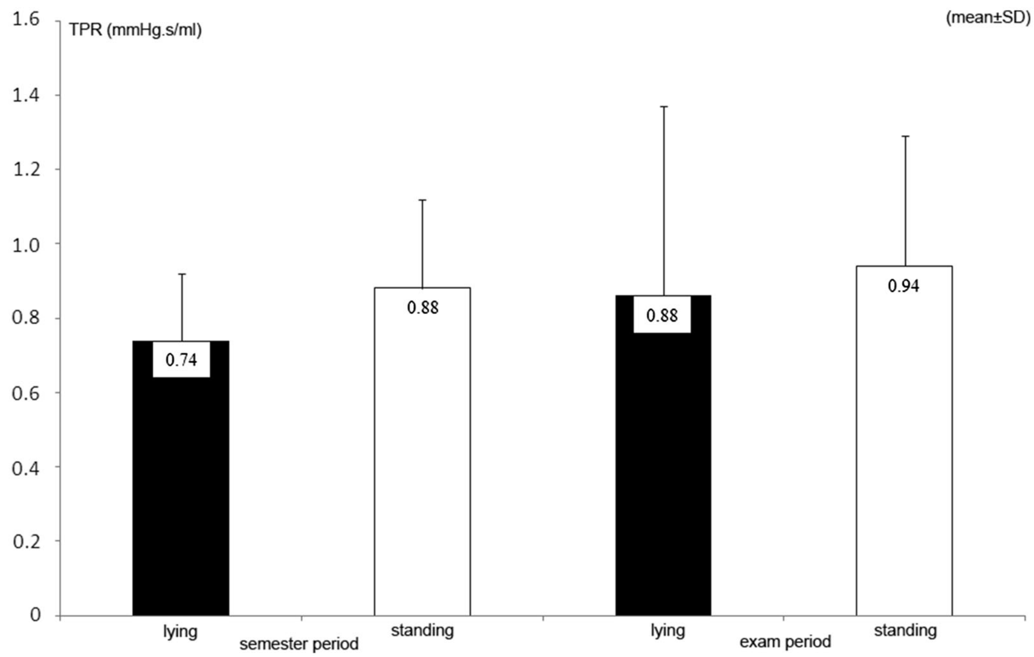

Figure 3. The TPR in the semester and the exam period. ($p<.0001$ in semester period lying *vs.* standing and in exam period lying *vs.* standing).

the BP rose higher and correlated with higher job strain [20]. The long-term implication of all this is very important because if an individual is exposed to more stress at the beginning of his working years – even at a young age –, the development of HT and greater CV risk can be foreseen. The sympathetic nervous system may play a mediator role in the development of CV complications caused by stress at work [21,22].

Flaa et al. [23] in an 18-year long follow-up study, concluded that sympathetic activity during the process of mental arithmetic predicts future BP and possible HT independently from the initial BP. In another work of Flaa et al. [24], 19-year old men only with high BP showed a CV and catecholamine hyperreactivity to mental stress. Hassellund et al. [25] in an 18-year long follow-up study, found that CV reaction to mental stress, constitute relatively stable individual characteristics that, only to a slight extent, changed as years went by.

Anxiety could be a precursor to HT development [26]. Zhang et al. [27] investigated the relationship between anxiety, BP and HR increase in peri-exam period among 64 college students. They found that the smoking group and the family HT group had high anxiety score with high BP and HR in the peri-exam period in young medical students, and their amplitudes of increase showed positive connection with the extent of anxiety. In our work, there was no significant difference between the mean SBP, DBP and HR values during the semester and the exam period. Only six students' SBP increased significantly. The number of smoking students was small for a statistical analysis. Family history was not examined.

In a study published last year, involving 364 participants (4th year general medicine students, 207 females and 157 males) authors found that almost over 50% of the participants experienced stress during their university years without any gender difference. The prevalence of BP $>$ 120/80 mmHg among participants was 11.0% [28]. In our work, the prevalence of SBP $>$ 120 mmHg was 16.9% and DBP $>$ 80 mmHg was 20.8%.

Zeller et al. [29] found, investigating 121 medical students taking the final licencing exam that only their DBP increased slightly. SBP did not change significantly and interestingly HR decreased during the exam. Pramanik et al. [30] found, among 55 normotensive medical students, that DBP significantly increased during the preparation period for the final exam compared to DBP measured during a stress-free period. There was no significant alteration in the SBP and HR. Their possible explanation was that the head down and the neck flexed posture – reading books – is known to increase the peripheral vascular resistance due to stimulation of the vestibular system through the vestibulo-sympathetic reflex.

In our work, all the students' DBP was under 90 mmHg except for one, whose DBP was over 85 mmHg.

TPR and HR did not change in the exam period and did not correlate with BRS. Therefore, TPR and HR cannot explain the increase of BRS during the exam period.

In our work, SBP increased during the 6-week long exam period, which could be associated to stress. Increased sympathetic activity may be at the background of decreased spontaneous BRS and increased TPR in our tests.

Conclusions

BRS decreases and SBP increases during the exposition to 6-week long exam periods among university students in Szeged. This prolonged but transient stress situation repeats a minimum of 12 times during the 6 years at the Faculty of Medicine for students between 18 and 24 years old. Future studies are required to verify if this stressful situation affects their BP and CV risks in their later age.

Ethics committee approval

Approved by the Human Investigation Review Board, University of Szeged, Albert Szent-Györgyi Medical and Pharmaceutical Centre (3/2007).

Disclosure statement

No potential conflict of interest was reported by the authors.

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