Pain and physiological adaptation in women presenting fibromyalgia.

Kerstin Wentz[1]*, Trevor Archer[2]

[1]Occupational and Environmental Medicine, Sahlgrenska University Hospital, Göteborg, Sweden
[2]Department of Psychology, University of Gothenburg, Gothenburg, Sweden

Abstract

Objective: The aim of the present analysis was to examine physiological adaptation to a sub-maximal test by measuring heart rate (HR) and heart rate variability (HRV) from the perspective of the fibromyalgia (FM) pain experience. Method: Twenty-five women presenting FM and healthy women were education- and age-matched. In their homes, all women completed questionnaires regarding health related quality of life and physical activity. All the women performed a stepwise load increment submaximal exercise test on a cycle ergometer to the severe perceived exertion level. HR and HRV were recorded before, during and after the test. Current pain was recorded before and after the test upon the FM women.

Result: Correlational analysis over all the pain ratings and adaptation measures of HR and HRV showed that higher HR on two or three levels of workload were linked to greater clinical pain in women presenting FM. Pain at baseline related to clinical everyday pain. Both these pain measures correlated with the intersection between HR and workload and pain after the test. Reactivity through increase in pain from the test did not relate to everyday pain or baseline pain. Pain reactivity instead related to more adaptive HRV from the test, similar to the HRV adaptation of healthy women. In FM, the pain measures were neither related to HR at baseline, maximal workload during the test nor to physical exertion during the test.

Conclusion: FM implies everyday clinical pain that is related to the intersection between HR and workload. In contrast to clinical pain, pain reactivity from the test related to a more physiologically adaptive pattern in terms of HRV. Clinical pain and pain reactivity seem to mobilize separate physiological processes via separate mechanisms.

Introduction

From naturalistic examination is learned that fibromyalgia (FM) pain increases from being very active [1]. Also from naturalistic perspective Okifuji et al. [2], recorded that fibromyalgia (FM) symptoms were exacerbated from poor sleep, stress, exercise and cold in turn ameliorated from rest, warm bath, heat and relaxation. Yet another study group with fibromyalgia pictured aggravation of fibromyalgia pain in connection to cold, noise, stress and changes in weather [3].

Pain and mental load

In healthy individuals a potent acute stress response may be associated with a decrease in sensitivity to pain, so-called stress-induced autoanalgesia. Moreover, among healthy individuals there is a variation regarding pain modulation that is linked to the cardiovascular system. This implies that amongst other effects that recordings from healthy individuals presenting hypotensive blood pressure show comparatively intensified signaling in the neurological pathways during the pain experience as opposed to the comparatively suppressed signaling of hypertensive healthy individuals [2]. In a review on interactions between the cardiovascular and the pain regulatory systems, Bruehl et al. describe the functional role of blood pressure in the endogenous regulation of pain whereby the blood pressure

versus pain sensitivity relationship may be proposed to "reflect a homeostatic feedback loop helping restore arousal levels in the presence of painful stimuli" [4]. Similarly, post-exercise (stress arousal) blood pressure is associated with a generalized inhibitory pain mechanism [5]. Following the arousal phase, the pain regulatory mechanisms instead shift from inhibition to facilitation in order to make self-care possible. The review by Bruehl et al. indicated also the significance of endogenous cardiovascular regulation for chronic pain mechanisms.

Events, e.g. stress or exercise, as above, justify that mental load, autonomous nervous system (ANS) measurements and pain are examined together and also applies to study groups with FM as compared with healthy controls. For example, Thieme et al. observed a significantly higher heart rate before the mental load condition in a study group with FM. Within the load condition, the study group with FM reported increases in pain corresponding to a blunted ANS reactivity. Moreover, the levels of stress-induced pain thresholds were related statistically to a lower level of heart rate reactivity and to lower levels of blood pressure reactivity [6].

La Rovere, has described how the arterial baroreceptor reflex system prevents short-term extensive fluctuations of arterial blood pressure and how ANS control of the cardiovascular system may be evaluated through that (barorepceptor) system

[7]. Accordingly, Reyes del Paso et al. examined ANS responses to mental stress in FM patients and observed a blunted reactivity of the cardiovascular system to the stressor that included a reduced resting baroreflex sensitivity and the lack of a baroreflex sensitivity to a mental load condition [8].

Pain and physical load

Koseck et al., compared FM patients with healthy controls as regards the effect of physical exercise on sensitivity to experimental pressure pain. Pain sensitivity was registered during and after physical load in terms of isometric contractions of the quadriceps thigh muscle. During and shortly after the exercise a decrease in pain sensitivity was observed in the healthy controls. In contrast to the healthy controls, among FM patients pressure sensitivity increased instead during and after the exercise [9]. Vierck et al., compared FM patients with healthy controls and found a contrasting lack of any ameliorating effect from exercise (on a treadmill) in the patients regarding thermal pain sensations applied to the hand [10]. This upside-down effect from exercise in FM was evident also from a study using a bicycle ergometer test wherein FM patients, unlike healthy controls, reacted with an increase in pains but also stiffness, fatigue, paresthesia and sleep disturbances (van Denderen et al.,). From this specific situation, the baseline values for HR were unreported but FM patient delivered a lower quantity of work and lower heart rate levels during the later stages of the test. The differences in HR were only statistically different at workloads of 80 and 110 Watts. This latter finding was discussed in terms of that low physical fitness in the FM study group would mean a relatively higher HR under a physical load suggesting instead a lower sympathetic activity in FM [11]. Based on the above experimental design Reyes del Paso et al. suggests both reduced sympathetic and parasympathetic cardiac influences in fibromyalgia [8].

Heart Rate Variability

Besides recordings of different measures related to blood pressure regulation or HR from individuals diagnosed with FM, several studies have examined ANS functioning in FM in terms of adaptation of inter-heartbeat-intervals. This measurement is based on the time between the R waves (RR-intervals) in the electrocardiogram) termed heart rate variability (HRV). This technique offers a measurement of flexibility of the HR has been analyzed and presented for several different parameters [12]. Consequently, HRV measures may be interpreted as successive adaptive changes in the parasympathetic branch of ANS and in the balance between sympathetic and parasympathetic activity. In an article on HRV measurements and fibromyalgia. Staud described the two major components of the HRV spectrum as a high-frequency (HF) band and a low-frequency (LF) band. The LF and HF measures should be presented as normalized units (LFnu or Hfnu) in order to represent the relative value of each power component from the perspective of the total power (the total modulation of the beat-to-beat signals). The balance of the sympathetic and parasympathetic components of the ANS is mirrored through normalized units [13]. According to Kulshreshtha and Lerma, sympathetic hyperactivity and parasympathetic hypoactivity have been detected in FM. Essentially, HRV parameters have been found also to relate to pain severity [14,15].

Lange et al. investigated the baseline values and the response of HRV to an incremental, aerobic submaximal exercise test in female patients presenting FM and to compare the result to a gender- and age-matched healthy control group. The R-R-intervals, the standard deviation of RR-intervals (SDNN) and the square root of the mean of the sum of the squares of the difference between adjacent intervals (RMSSD) were selected for statistical analysis together with the power specter of the total power for HR, divided into HF (0.15-0.4 Hz) and LF (0.04-0.15 Hz). The result regarding HF and LF was recalculated in normalized units (n.u.) [16]. An ancillary purpose was to study HR before, during and after the exercise exertion test.

The procedure, characteristics, sub maximal test and the data analysis including psychometrics, are described in Lange et al. In short, Lange et al. observed that HRV values at baseline and the HRV values after an incremental, aerobic submaximal exercise test showed no difference between the groups. Instead, a discrepancy between the groups was observed in HR adaptation to the ergometer sub maximal test wherein the HRV of the healthy reference had been altered significantly compared with the test. The HRV of women presenting FM showed only one statistically significant alteration of HRV measurements in terms of a reduction in RMSSD. Consequently, the proportion of LF power was not increased from the test in women presenting FM but remained virtually the same as compared to rising from 56 to 73 LFn.u. in the control group. Similarly, the proportion of HF n.u. power was not decreased as in that group. The study group presenting FM also adapted more heterogeneously since the standard deviations of both LFnu and HFnu measures rose from 15nu to 20nu from baseline to the post-test situation. Alternatively among the controls, these measurements showed the opposite pattern for the standard deviation decreasing from the test (from 20 to 15nu).

Concerning HR at baseline and during the first three levels of workload, women presenting fibromyalgia showed a statistically significantly higher HR than the healthy women. The mean HR at rest in the former was 70 (sd 10) and in controls 63 (sd 8). At work load level 25 W the corresponding values were 95 (sd10) and 87 (sd 9), at 50 W 111 (sd 13) and 98 (sd10), at 75 W 129 (sd 17) and W 115 (sd 15) and at 87.5 W 140 (sd17) and 130 (sd16). After the work load level 50 W, the group presenting fibromyalgia decreased in a stepwise manner from 23 to 13 at 87.5 W at which point HR was also no longer statistically different between the groups.

In the Lange et al. study, pain recordings from the test were not included in the analysis of collected physiological measures from women presenting FM. Collected data on clinical pain in terms of the Body Pain (BP) covered both Pain magnitude and Pain interference over 4 weeks from SF-36 but was not part of the analysis.

Aim

The aim of the present analysis was to examine physiological adaptation to a sub maximal test in terms of HR and HRV from the perspective of fibromyalgia pain experience. Fibromyalgia pain was registered as a health-related quality of life attributes with regard to pain during the last 4 weeks BP and recorded before and after the sub maximal test.

Methods

Participants

Twenty-five women presenting FM who expressed an interest in participating were recruited from primary health care and rehabilitation centers in the region of Västra Götaland (Sweden). Inclusion criteria were female gender, with the participants aged 20-60 years showing a registered FM diagnosis within the last 7 years. Exclusion criteria were prior trauma to the head, brain damage, severe somatic disease, muscular disease, heart disease or anemia, dependent in personal activities of daily life as well as drugs affecting HR. The healthy control group was age-matched, pairwise ±3 years, and recruited from employees (volunteers) within the health care service and education-matched with the FM patients. The healthy control group was required to confirm their healthy status, and the same exclusion criteria as for the FM patients were used, with one addition: prolonged pain.

Study Design

Ethics

The cross sectional study was approved by the Regional Ethical Review Boards at the University of Gothenburg as a part of a larger project "Affective, cognitive and defensive interplay in fibromyalgia: from premorbid strain to treatment of somatic manifestations". Informed consent was obtained from all the participants prior to the study.

Procedure

The attending physician for each woman presenting FM either referred the participant to the study or were contacted by the first author to confirm the FM diagnosis and to certify their appropriateness for inclusion in the study. Demographic data were collected through questionnaires sent to the home of each participant together with questionnaires about quality of life and physical activity. Participants were assigned to a rehabilitation center to perform a submaximal exercise test. In conjunction with the test, body weight and height were registered (Table 1).

Measurements

Current pain, using a visual analog scale (VAS) 100 mm, was measured before and after the test to characterize the women with FM, together with the questionnaires regarding quality of life and physical activity levels.

To assess health related quality of life in the dimension of pain the Short-Form 36 (SF 36) was used. All the scales range between 0 and 100 where a higher value represents a higher estimated quality of life (Ware et al.,) implying that concerning the sub-scale Bodily Pain (BP) a low level of pain is indicated by a higher value and vice versa [17]; The sub-scale, BP, is composed by two items concerning pain during the last four weeks reflecting level of pain and interference from pain, respectively. The SF-36 has been showed to be an appropriate instrument for assessing quality of life in women with FM [18]. Physical activity was measured through the Saltin-Grimby Physical Activity Level Scale [19].

The submaximal exercise test including the variety of measurements is described in detail in Lange et al. In short, the participants performed a stepwise load increment submaximal exercise test on an electronically-braked cycle ergometer to the very hard exertion level. The testing was conducted in the afternoon at least 3 hours after the last meal or coffee and the participants were asked to avoid smoking prior to the test. Before the exercise test, HRVwas recorded over 5 minutes during a supine rest. HRV was recorded using a Polar RS 800CX heart rate monitor (Polar electro, Kempele, Finland) that performs HRV recordings [20]. HR and blood pressure were measured after 10 minutes of supine rest. HR was registered from the heart rate monitor and blood pressure was taken manually with stethoscope (Littmann Classic II S.E., 3M, St. Paul, Minnesota) and sphygmomanometer (Welch Allyn, Inc., Skaneateles Falls, New York, USA). HR, blood pressure and rating on the Borg RPE scale (rating of perceived exertion) was collected during the submaximal test that started at a workload of 25 W and was increased with 25 W each 4 minutes. When the subject responded with a score of 17 (very hard exertion) on the Borg RPE scale, she was asked to carry out the remaining minutes at the present workload if possible [21]. Directly after the test, the subjects had 20 minutes of supine rest during which HR and blood pressure were measured repeatedly during 20 minutes and HRV was recorded for the last 5 minutes.

Table 1. Demographic characteristics among FM patients and healthy controls.

	FM (n=24)	Reference group (n=26)	p-value
	mean ± SD	mean ± SD	
Age (years)	49.4 ± 9.8	48.7 ± 9.0	0.799
BMI (kg/m^2)	27.3 ± 6.0	25.1 ± 3.0	0.113
Pain duration (years)	12.7 ± 9.6	NA	
Education (n=22/25)			0.967
≤ 9 years	1 (4.5%)	1 (4%)	
9-12 years	5 (22.7%)	6 (24%)	
>12 years	16 (72.7%)	18 (72%)	
Saltin-Grimby physical activity (n= 22/24)			0.019
Inactive	7 (31.8%)	2 (8.3%)	
Light physical activity	11 (50%)	11 (45.8%)	
Moderate physical activity	3 (13.6%)	9 (37.5%)	
Vigorous physical activity	1 (4.5%)	2 (8.3%)	

Values are given as mean ± standard deviation (SD), median (range) and number (percentages).
BMI: Body Mass Index; VAS: Visual Analog Scale; NA: not applicable; SF36: short form 36 health survey.

Analysis of data

The pain index of SF-36 BP concerned both women presenting FM and healthy women. The differences between women presenting FM and healthy controls regarding BP from SF-36 and regarding difference in HR from the incremental, aerobic submaximal exercise test compared to baseline was examined using one-way ANOVA. In a next step, the collected pain measures before and after the aerobic submaximal exercise test that only concerned women presenting FM were correlated together with the BP measure.

The amount of physiological variables was restricted through formation of sum variables concerning HR during successive levels of workload. Two levels of workload (25 W and 50 W) formed the variable HR2N and three levels of workload (25 W, 50 W and 75 W) formed the variable HR3N. A correlation concerning pain measures from SF-36 and from the sub maximal test, HR from two and three levels of workload HR2N and HR3N together with HRV after the test was carried out. In first subsequent regression analysis, clinical pain represented by BP was predicted from the HR3N values. In a second regression analysis, pain after the sub maximal test (VASpost) was predicted from BP and the difference between pain at baseline and pain after the test (VASdiff). In all the calculations, the level of significance was 0.05 two-tailed.

Results

Recording through the Body Pain scale from Health related quality of life Short Form (SF-36) regarding pain during 4 weeks (were a low value represents a low quality of life (consequently high pain). In women presenting FM, the test result indicated a mean value of 24 (SD=13.7) with a minimum value of 0 and a maximum value of 51 on a scale ranging from 0-100. The difference in heart rate (HRdiff) resulting from the test ranged from 25-128 with M=51, SD=21. The corresponding figures concerning healthy controls regarding BP were M=82, SD=16.7, whereas HRdiff was M=64.8, SD=12.1. A between-groups ANOVA regarding BP and HRdiff from the incremental, aerobic submaximal exercise test compared to baseline showed a significant effect Groups effect with regard to the difference in HR at peak and at baseline (F (1, 46)=7.687, p=0.008, where FM women increased HR from the test to a lesser degree than controls. The estimations of clinical pain, BP, revealed the corresponding results wherein F (1, 40)=150.709, p<0.0001, where the FM women reported significantly more pain during 4 weeks.

The study group presenting FM recorded their pain response before and after the incremental, aerobic submaximal exercise test using a visual analog scale (VAS). Pain before the test (VASpre) ranged from 0-100 with M=42.65, whereas VASpost ranged from 0-100 with M=55.39. VASdiff ranged from -38-60 with M=12.74 and an absolute value M=19.

Table 2 indicates that there was a significant relationship between all pain measures except for the increase in pain from the test VASdiff in relation to both pain at baseline VASpre and clinical pain BP.

Table 2. *Correlational analyses between pain measures in the group presenting FM (N= 21-23). The magnitude and pain-interference during 4 weeks in terms of Body Pain index of SF-36 (BP) (reflecting pain related level of health and inversely level of pain), pain at baseline (VASpre), pain after the aerobic submaximal exercise test (VASpost), the difference between pain at baseline and after the test (VASdiff).*

	BP	VASpre	VASpost	VASdiff
BP		-0.499*	-0.576**	ns
VASpre	-0.499*		0.571**	ns
VASpost	-0.576**	0.571**		0.543**
VASdiff	ns	ns	0.543** 0.007	

** Correlation is significant at the 0.01 level (2-tailed)
* Correlation is significant at the 0.05 level (2-tailed)

Table 3 indicates discontinuous relationships between the different pain measures on one hand and between pain measures and physiological measures on the other. These relationships are described below.

Table 3. *Correlation between pain measures and physiological adaptation measures in women presenting FM as indicated by pain at baseline (VASpre), pain after the aerobic submaximal exercise test (VASpost), the difference between pain at baseline and after the test (VASdiff), the magnitude and interference from pain during 4 weeks in terms of Body Pain index of SF-36 (BP) (reflecting pain related level of health and inversely level of pain) together with HRV after the test measures in terms of low frequency normalized units LFnupost, high frequency normalized units HFnupost and sum variables mirroring, HR at two levels of workload (25W and 50W) HR2N and three levels of workload (25W, 50W and 75 W) HR3N .*

	BP	Vaspre	VASpost	VASdiff	LFnupost	HFnupost	HR2N	HR3N
BP N	1 22	-0.499* 21	-0.576** 21	ns	ns	ns	-0.495* 20	-0.674* 13
VASpre	-0.499* 21	1 23	0.571** 23	ns	0.144 20	ns	ns	0.559* 14
VASpost	-0.576** 21	0.571** 23	1 23	0.543** 23	0.577** 20	-0.577** 20	0.459* 21	0.458 14
VASdiff	Ns	ns	0.543** 23	1 23	0.491* 20	-0.491* 20	ns	ns
LFnupost	Ns	ns	0.557** 20	0.491* 20	1 20	-1.000** 20	ns	ns
HFnupost	Ns	ns	-0.577** 20	-0.491* 20	-0.1000** 20	1 20	ns	ns
HR2N	-0.495* 20	ns	0.459* 21	ns	ns	ns	1 21	0.976** 14
HR3N	-0.674* 13	0.559* 14	0.458 14	ns	ns	ns	0.976** 14	1 14

** Correlation is significant at the 0.01 level (2-tailed)
* Correlation is significant at the 0.05 level (2-tailed)

Pain over 4 weeks or clinical pain (BP)

The level of pain over 4 weeks in terms of the BP value of health related quality of life regarding interference from pain or clinical pain during 4 weeks. A higher value means less interference from pain. Accordingly, the clinical level of pain (BP) corresponded positively with VASpre and VASpost and with sum variables concerning heart rate at two 2HRN or three levels HR3N of work load. Higher HR on two or three levels of workload meant worse clinical pain (Tables 2 and 3).

VASpre

The base line pain measure, VASpre, corresponded positively to the level of pain over 4 weeks, BP (the value requesting an inverse interpretation regarding interference from pain during 4 weeks). VASpre correlated significantly with the pain rating after the test VASpost. VASpre correlated positively also with HR during three different levels of workload in terms of sum variable HR3N.

VASdiff

The difference between the pain ratings before and after the test VASdiff did not correlate with interference from pain over 4 weeks measure BP or with VASpre. Taken together, VAS diff correlated with HRVpost measures implying that a higher LFnu post corresponded to a higher VASdiff from the test. A lower HFnu post value corresponded to a higher VASdiff. In all these aspects, the VAS diff measure seems to mimic the "after the test physiological patterns" of healthy women where LFnupost value increased and the HFnupost value decreased whereas women presenting fibromyalgia produced a higher increase in pain from the test from this "healthier" pattern. A positive correlation between the VASpost the VAS diff was identified.

VASpost

VASpost correlated positively with VASpre, VASdiff and level of clinical pain BP. VASpost correlated with HRVpost measures and a higher LFnu post corresponded to a higher level of pain after the test. A lower HFnu post value corresponded to a higher pain after the test. In all these regard the VAS post measure mimics the "after the test" physiological patterns of healthy women where LFnupost and the HFnupost value decreased whereas in women presenting fibromyalgia implying a higher level of pain after the test.

A linear regression analysis using the enter method was performed regarding the study group presenting FM with BP as the criterion variable. A significant regression equation was obtained: $F_{(1, 11)}=9{,}154$ p=0.0012. An adjusted R square explained 0.405 of the variance in BP from HR3N as predictor with a Beta=-0.674 (p=0.012). The level of health related quality of life in terms of everyday pain BP (less pain and less interference from pain) during 4 weeks corresponded to a lower heart rate during three levels of work load (HR3N) and inversely higher pain during four weeks corresponded to higher heart rate at three levels of work load (Table 4).

A linear regression analysis using the enter method was performed regarding the study group presenting FM with VASpost as the criterion variable. A significant regression equation was found $F_{(2, 18)}=11{,}031$ p=0.001. An adjusted R square explained 0.501 of the variance in VASpost from BP as a predictor with a Beta=-0.511 (p=0.005) together with VASdiff with a Beta 0.472 (p=0.008) (Table 5).

VASpost, as in pain after the sub maximal test, correlated with all the other pain measures but was best predicted by pain over 4 weeks BP and pain reactivity to the test VASdiff. The predictors together accounted for 50% of variance in pain after the test indicating almost equal importance from the clinical everyday pain component and the reactivity component of the VASpost measure. The reactivity measure of VASdiff is also without a correlative connection to pain measures other than VASpost.

Discussion

Women presenting FM reported significantly more clinical pain during 4 weeks and less ability to mobilize HR during a submaximal test as mirrored by the HRdiff than healthy women value.

The correlational analysis over all the different pain ratings and physiological adaptation measures in terms of HR and HRV indicated that pain at baseline, i.e. VASpre, was a measure that mirrored clinical pain or 'stable' pain together with BP. As with BP, VASpre correlated with HR3N and VASpost. This situation presents a contrast between a "being in pain" condition as in the VASpre or BP and the reactivity measure of VASdiff, which became noticeable since the VASdiff did not correlate with clinical pain BP or VASpre. Contrastingly, there was rather the opposite relationship in terms of a markedly insignificant value of r=-0.139 between VASdiff and BP. This relationship ought not to be assigned to a ceiling effect since the mean of VASdiff was 12.7 with a slight correlation to the BP value. Moreover, to react with pain in terms of VASdiff also appeared as a condition healthier than "being in pain" (BP) since the VASdiff value increased when the HRV measurements were more similar to the patterns of healthy women in terms of a shift in balance towards the sympathetic component at the expense of the parasympathetic component of the ANS from the test as documented by Lange et al.. For this interpretation also speaks that VASpre correlated, indeed insignificantly, but negatively with VASdiff (r=-0. 329).

Mobilization of the sympathetic system is linked to increased pain but parallel higher values of VASdiff and VASpost both signal to a "healthier" increase in LFnu and likewise the decrease in HFnu from the test. Reactivity through increase in pain does

Table 4. *Linear regression analysis using the enter method with the level of pain over 4 weeks Body Pain (BP) value as the criterion variable. BP reflects health related quality of life and requests an inverse interpretation regarding interference from pain or clinical pain. A variable from physiological testing (aerobic submaximal exercise) HR3N (sum variable 25+50W+75W) served as predictor variable for the FM patients. Model summary below.*

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	0.674	0.454	0.405	10.7329

Table 5. *A linear regression analysis using the enter method with the level of pain after an incremental, aerobic submaximal exercise test (VASpost) as the criterion variable. A variable reflecting health related quality of life during 4 weeks (BP) that also requests an inverse interpretation regarding interference from pain or clinical pain served as predictor together with a variable reflecting increase in pain from the test as compared to a baseline rating (VASdiff). Model summary below.*

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	0.742	0.551	0.501	19.047

not relate to everyday pain or baseline pain also. According to the findings of Lange et al., the study group presenting FM became more heterogenic from the test regarding both LFnupost and HFnupost measures with standard deviations rising from 15nu to 20nu. This finding may confirm that of Thieme et al. on identifiable subgroups in FM regarding physiological responses to mental load [22]. The study group of healthy controls became more homogeneic regarding physiological adaptation to the test seeing that the standard deviation decreased from 20 nu to 15 nu [16].

VASpost correlated with all pain measures. A higher level of pain from the test implied a greater increase in pain but also a higher level of pain over the 4 weeks as represented by BP. These two latter measures also accounted for over 50% of the variance in pain after the test, which indicates both clinical pain and a pain reactivity element in the outbursts of pain.

The present experimental design also included observations on breaks from clinical pain (pain gaps) in everyday life (including the return of pain). The phenomenon of intermittent clinical pain in FM is reported recurrently by approximately one third of patients with FM [23-26]. In the present study, clinical pain was best predicted by an intersection between workload and HR. Regarding clinical pain being intermittent, the intersection between workload and HR also appears as a physiological "hub" (manuscript submitted for publication).

There were no correlative links between HR at baseline, the level of the work load of peak performance, the HR of peak performance or to any of the pain measures. Therefore, it may be suggested that the pain recordings were neither influenced in the main by HR at baseline nor by the level of effort in terms nor of HR at the peak nor maximal work load during the test. They were, as documented by Lange et al., also not related to rated physical exertion during the test. Instead, in the present result the HRV measures after the test were related to VASdiff and VASpost in a manner implying that healthier patterns in terms of increase in LFnu and decrease in HFnu gave rise to more pain after the test and more pain from the test. A higher level of pain after the test and a higher level of interference from pain over 4 weeks were related to a higher level of HR at two levels of work load or two and three levels of work load respectively. In parallel, Reyes del Paso et al. reported that the level of every day clinical pain in FM is inversely related to baroreflex sensitivity recorded during induced mental stress.

With regard to the physiological adaptations that occur in FM, Lange et al. recorded a higher resting HR in women presenting FM and thereby confirmed the result from Thieme et al. who found a comparatively increased HR from experimental baseline measurements in a study group presenting FM. In addition, Riva et al. recorded HR during relaxation, sleep, daily activity and stress and documented a comparatively higher resting heart rate and suggested a reduced influence from the parasympathetic branch of the ANS. In tandem, Riva et al. compared women presenting FM and healthy women regarding stress hormones during 24 hours and documented significantly lower adrenaline and dopamine levels among women presenting FM [27]. In parallel to the findings of Lange et al., the result on HR in women with FM was unrelated to exercise habits.

Limitations

As described in more detail by Lange et al. the study group presenting FM and healthy controls, were matched with each other only with regard to age and education. In parallel, the reference groups used for comparison with FM may be matched for reported levels of pain, fatigue and depressiveness. As opposed to this kind of rigorous matching, the SF-36 instrument recorded significant differences between the two groups regarding physical and psychological health. From the perspective of examining the physiological and psychological interplay of psychobiology in fibromyalgia the representativeness of the sample is instead of greatest value. As described by Lange et al. the SF-36 recording confirmed that the current sample studied was representative for women presenting FM in the western region of Sweden.

In conclusion, pain in fibromyalgia may be regarded as multidimensional wherein the clinical level of the pain experience is not related directly to pain reactivity arising from the workload but instead to the intersection between HR and workload where the higher HR on two or three levels of workload means worse clinical pain. An increase in pain from the test and pain level post-test both corresponded to a healthy adaptive pattern expressed through an increase in LFnu and decrease in HFnu. Clinical pain and pain reactivity mobilize separate physiological processes pertaining to sympathetic expressions of "jump and play" via separate mechanisms.

Acknowledgement

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*Correspondence to:

Kerstin Wentz
Occupational and Environmental Medicine
Sahlgrenska Academy and University Hospital
Göteborg
Sweden
Tel: +46 (0)31 786 3219
E-mail: kerstin.wentz@amm.gu.se