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ORIGINAL PAPER

Heat acclimation-induced changes in heart glycogen/glucose metabolism in rats

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Abstract Based on the observation that heat acclimation is a slowly developing response, evoked by continuous exposure to moderate heat, we investigated the time-dependent acclimatory changes of heart glycogen metabolism. Cardiac levels of key carbohydrate-related enzymes and substrates were studied in the function of the duration of short-term (STHA; 6, 12, 24 and 48 h) and long-term heat acclimation (LTHA; 7, 14, 21 and 30 days) to high environmental temperature (35 ± 1°C). The changes in heart glycogen metabolism during STHA could be separated in two phases: up to 12 h exposure, where significant decrease of the heart glycogen (Glk), glucose-6-phosphate (G6P), hexokinase (HK) activity as well as increase of heart glucose was observed; and from 24 to 48 h exposure, manifested with elevation of Glk, Glu, glycogen phosphorylase *a* (GP*a*), phosphofructokinase (PFK) and HK activities. The metabolic changes in the period of LTHA could also be seen as separate phases: in a period of 7–14 days of heat exposure there was an increase of heart Glk, Glu, G6P, HK, as well as a decrease of GP*a* and PFK, while in the period of 21–28 days there was more intensive rebound of Glk and G6P, increase of GP*a* activity and non-significant changes of Glu, HK and PFK. The results obtained have showed that acclimation to moderate hyperthermic environment has caused significant changes in examined parameters which differ depending on duration to the exposure: intensive stress-induced glycogenolytic and glycolytic processes in the period of STHA and intensive energy sparing, manifested by Glk deposition in the period of LTHA.

Keywords Heat acclimation · Enzymes · Substrates · Carbohydrate metabolism · Heart · Rats

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Introduction

Acclimation of the homeothermic organisms to heat (35 ± 1°C), briefly described as a "within lifetime phenotypic response" to environmental stress, is the process of enhancement of heat tolerance of the organism to the upper extreme of tolerable temperature and the duration of endurance in a hot environment [1, 2].

In order to obtain the enhanced energy-efficient acclimatory homeostasis, homeothermic animals manifest physiological and biochemical adaptations to the new environmental conditions, at the cellular, tissue, organ and systemic levels. Since oxygen consumption in heat-acclimated organisms is lower, metabolic adjustments designed to enhance energy reserves take place in order to guarantee long-term performance to fight the lowered oxygen supply [3]. In this sense, there is an enhancement of the metabolic machinery to elevate the energy potential of heat-acclimated

organism which is accompanied by a decrease of the rate of the whole body metabolism [4, 5]. Metabolic changes which are most evident during heat acclimation are: energy sparing, which is manifested as a rebound of liver glycogen (Glk) in rats [6–8] and hamsters [9] (as a result of increased activity of enzymes involved in a direct Glk synthesis), and decreased glucose (Glu) production [6–8]. As is the case with the liver, heat acclimation produces favorable adaptations in mechanical and metabolic aspects of the heart performance, such as: twofold greater heart Glk level, increased β-adrenergic sensibility, lowered heart rate and greater stroke volume. All these lead to increased cardiac work efficiency during long-term heat exposure [3].

It is important to stress that all these adaptations in the liver and the heart are evident when acclimation homeostasis has already been obtained (after days or weeks at continuous exposure to elevated ambient temperature of 35 ± 1°C). However, there are dynamic metabolic changes during the whole period of achieving the acclimation homeostasis. Namely, acclimation is a slowly developing response evoked by a continuous exposure to moderate heat and has characteristics of a biphasic process. It consists of an early transient, "inefficient" acclimation phase [short-term heat acclimation (STHA), up to the 2nd day of heat exposure] to an "efficient" state after acclimation homeostasis has been reached [long-term heat acclimation (LTHA), after the 2nd day of heat exposure] [2, 3]. The time-dependent changes of the hepatic carbohydrate metabolism have already been described [7], but little is known about time-dependent acclimatory changes of heart Glk metabolism in the direction of the elevation of the energy potential of the heat-acclimated organism.

Having considered the above, we estimated the effect of STHA (6, 12, 24 and 48 h) and LTHA (7, 14, 21 and 28 days) at 35 ± 1°C through the heart glycolytic/glycogenolytic potential. In this sense, we have paid special attention to the dynamics of hexokinase (HK) and phosphofructokinase (PFK), as well as to the glycogen phosphorylase *a* (GP*a*) activity, together with the changes in peripheral substrates Glk, Glu and intermediate substrate glucose-6-phosphate (G6P).

Materials and methods

The experimental study was performed on adult (3–4 months old), male Wistar rats (n = 70), with an estimated weight of 250–300 g, at 12-h (06–18 h) light regime.

The animals were divided into nine groups, comprising a control group (C), which was maintained at an ambient temperature of 20 ± 2°C, and eight heat acclimated groups. Heat acclimation was attained by continuous exposure to 35 ± 1°C for 6, 12, 24 and 48 h (STHA) and 7, 14, 21 and 28 days (LTHA), according to the heat acclimated model described in [1, 6–8, 10, 11]. Heat acclimation was attenuated in an air-flowed light-cycled (12:12-h light:dark cycle) heat chamber (4.20 m × 2.0 m × 3.0 m) by continuous exposure to regulated air temperature of 35 ± 1°C and relative humidity of 30–40%. The animals were housed 3 per cage and they received laboratory chow and water ad libitum.

All experimental animals were anesthetized with a Na-thiopental narcosis (45 mg/kg) and sacrificed using a standard laparotomic procedure. Immediately after the opening of the abdominal cavity, the isolated heart was washed with cold saline solution and immersed in liquid nitrogen. The tissues were kept at −80°C until analysis and were finally prepared into tissue powder (at liquid N_2-temperature). The tissue powder was homogenized with an ultrasonic homogenizator (Cole-Parmer Instrument 4710) in a period of 10–15 s. The whole procedure was performed at a temperature of 0–4°C (in ice).

Heart Glk, Glu and G6P concentration (assayed according to Keppler and Decker [12]) were determined in perchlorate homogenates and neutralized with 5 M K_2CO_3. We measured the production of NADPH at 340 nm in a reaction catalyzed by glucose-6-phosphate dehydrogenase. The activity of the GP*a* [13] was determined in a nuclear fraction, indirectly through the quantity of the produced inorganic phosphate [14]. We used the/a mitochondrial fraction for determination of HK [15] and PFK [16], by measuring the production of NADH at 340 nm. For the interpretation of the activity as a specific enzyme activity (nmol P_i/min/mg prot. for the GF*a* and U/mg prot. for the HK and PFK), the total quantity of the proteins was determined [17].

Statistics

Results are presented as means ± SD. To examine the statistical differences between each group, we used one-way ANOVA with Neuman–Keuls post hoc test. Correlation analyses for each parameter, depending on duration of acclimation, as well as between the parameters, were also assessed. Only significant coefficients of correlation are presented in the figures. In all tests, a probability level of $p < 0.05$ was used as a significant difference.

Results

Glycogen content and glucose concentration

The time-dependent changes of heart Glk content and Glu concentration are presented in Fig. 1, followed by the

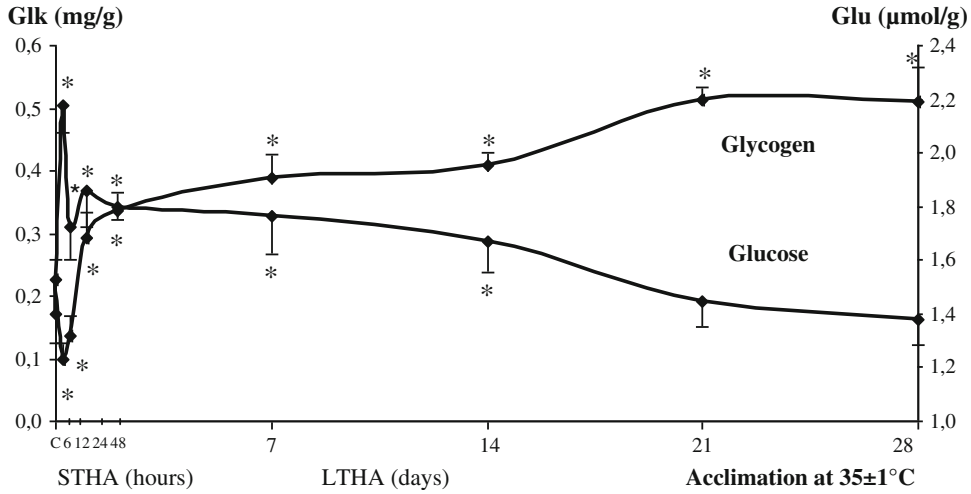

Fig. 1 Glycogen content and glucose concentration in rats during STHA (6, 12, 24 and 48 h) and LTHA (7, 14, 21 ad 28 days) heat acclimation at 35 ± 1°C. *$p < 0.05$ in comparison with control (*C*) animals. Coefficient of correlation (*r*) in a function of duration of heat exposure ($r_{Glk} = 0.859$, $r_{Glu} = -0.614$) and between Glk/Glu during the whole experimental period ($r_{Glk/Glu} = -0.627$)

Table 1 Statistical and percentage analysis of differences between experimental groups with respect to glycogen content and glucose concentration

Glycogen content (mg/g)						Glucose concentration (µmol/g)					
Group	Means ± SD	%	Group	Means ± SD	%	Group	Means ± SD	%	Group	Means ± SD	%
C	0.23 ± 0.03					C	1.40 ± 0.10				
6h	0.10 ± 0.03*	−55.86	7d	0.39 ± 0.04*	71.54	6h	2.18 ± 0.10*	55.71	7d	1.76 ± 0.14*	25.94
12h	0.14 ± 0.03*	−39.85	14d	0.41 ± 0.02*	81.56	12h	1.72 ± 0.12*	23.18	14d	1.67 ± 0.11*	19.42
24h	0.29 ± 0.04*	30.08	21d	0.51 ± 0.02*	126.86	24h	1.86 ± 0.14*	32.96	21d	1.45 ± 0.19	3.35
48h	0.34 ± 0.03*	49.02	28d	0.51 ± 0.06*	125.61	48h	1.80 ± 0.05*	28.66	28d	1.38 ± 0.09	−1.49

% ratio between control (*C*) group and heat-exposed (6, 12, 24 and 48 h, and 7, 14, 21, and 28 days) groups of animals

* $p < 0.05$ in comparison with control (*C*) animals

detailed statistical and percentage calculations (Table 1). Heart Glk content showed biphasic changes for the period of STHA: statistical significant reduction of heart Glk content in the first 12 h and significant increase up to the 48th hour. Concerning Glu concentration, there was significant increment during the whole period of STHA. It is important to stress that the lowest Glk content (C:6h, −55%, $p < 0.05$) was accompanied by the highest Glu concentration (C:6h, +55%, $p < 0.05$).

During the whole period of LTHA, there was continuous elevation of Glk, which finally resulted in 1.2-fold rebound of the heart Glk stores (C:28d, $p < 0.05$). Up to 2 weeks of heat exposure, heart Glu level attempted to maintain a relatively stable higher concentration (C:7d, C:21d, $p < 0.05$), followed by its normalization till the end of experimental period (C:21d, C:28d, n.s.).

Analyzing the overall changes in a function of duration of heat exposure, we found a relatively strong positive dependence of heart Glk content ($r_{glk} = 0.859$, $p < 0.05$) and negative dependence for the Glu concentration ($r_{glu} = -0.614$, $p < 0.05$). Also, a negative correlation between these two parameters could be seen during the whole experimental period ($r_{glk/glu} = -0.627$, $p < 0.05$).

Glucose-6-phosphate concentration and hexokinase activity

Figure 2 and Table 2 present the dynamics of the changes of G6P concentration and HK activity during STHA and LTHA. During the period of STHA, the changes in the concentration of G6P can be presented as two different phases: significant decrease (C:6 h, and C:12 h, $p < 0.05$) and tendency of normalization to the control values (C:24 h and C:48 h, n.s.). Starting from the 7th day of heat exposure, up to the end of the experimental period (28th day), there was a continuous elevation of heart G6P concentration (from 19 to 62%, $p < 0.05$).

Concerning HK activity, there was intensive and significant decrease during the first 6 h (C:6 h, $p < 0.05$) and normalization in the 12th hour of exposure. Starting from the 24th hour of heat exposure, the HK activity was significantly increased (up to 50%, $p < 0.05$), except in the

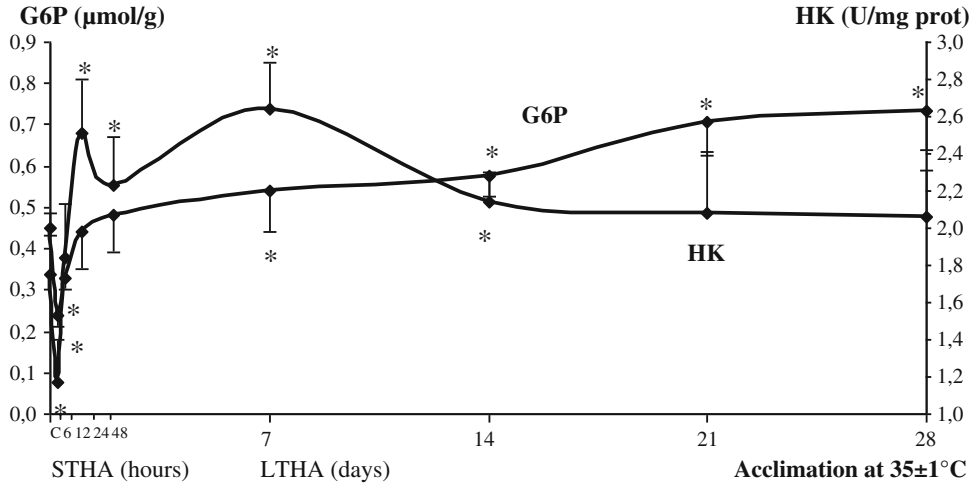

Fig. 2 Glucose-6-phosphate concentration and hexokinase activity in rats during STHA (6, 12, 24 and 48 h) and LTHA (7, 14, 21 and 28 days) heat acclimation at 35 ± 1°C. *$p < 0.05$ in comparison with control (*C*) animals. Coefficient of correlation (*r*) in a function of duration of heat exposure ($r_{G6P} = 0.892$), between G6P/HK ($r_{G6P/HK} = 0.814$) and Glk/G6P ($r_{Glk/G6P} = 0.982$).during the whole experimental period

Table 2 Statistical and percentage analysis of differences between experimental groups with respect to glucose-6-phosphate concentration and hexokinase activity

G6P concentration (µmol/g)						HK activity (U/mg prot.)					
Group	Means ± SD	%	Group	Means ± SD	%	Group	Means ± SD	%	Group	Means ± SD	%
C	0.45 ± 0.02					C	1.75 ± 0.34				
6 h	0.24 ± 0.03*	−47.20	7d	0.54 ± 0.10*	19.02	6 h	1.17 ± 0.22*	−32.82	7d	2.64 ± 0.25*	50.91
12 h	0.33 ± 0.03*	−27.47	14d	0.58 ± 0.05*	27.61	12 h	1.84 ± 0.29	5.50	14d	2.14 ± 0.15*	22.77
24 h	0.44 ± 0.09	−2.75	21d	0.71 ± 0.08*	56.01	24 h	2.51 ± 0.29*	43.61	21d	2.08 ± 0.33	19.08
48 h	0.48 ± 0.09	6.35	28d	0.73 ± 0.10*	62.57	48 h	2.23 ± 0.27*	27.46	28d	2.06 ± 0.25	18.11

% ratio between control (*C*) group and heat-exposed (6, 12, 24 and 48 h, and 7, 14, 21, and 28 days) groups of animals

* $p < 0.05$ in comparison with control (*C*) animals

last 2 weeks, where this increment was non-significant (C:21 days and C:28 days, about +19%, n.s.).

Regression analyses showed positive coefficient of correlation for G6P concentration during the whole period of heat acclimation ($r_{G6P} = 0.892$, $p < 0.05$) and a non-significant correlation for the HK activity. Both of the parameters have a significant correlation during heat exposure ($r_{G6P/HK} = 0.814$, $p < 0.05$).

Glycogen phosphorylase *a* and phosphofructokinase activity

The dynamics of the changes of GF *a* and PFK activity are presented in Fig. 3, while the statistical and percentage changes during whole period of heat acclimation for these two enzymes are presented in Table 3.

The biphasic changes were also observed for GP*a* and PFK activity for the period of STHA (up to the 12th hour and up to the 48th hour). Namely, in the first 12 h of heat exposure, GP*a* showed decreased enzyme activity, which was followed by a significant increase up to the 48th hour, reaching the peak in the 24th hour (C:24 h, 79.5%, $p < 0.05$). As for PFK activity, the non-significant changes that characterize the period until the 12th hour of STHA were followed by a significant increase of PFK activity up to the 48th hour, reaching the peak in the 24th hour (C:24 h, 102.8%, $p < 0.05$).

In the next period of heat exposure, we observed a decrease of GP*a* in the 7th and 14th days and finally, increased enzyme activity in the following period (21st and 28th days). On the other hand, the period of LTHA (7 and 14 days) is characterized by a significant reduction of PFK activity, while non-significant changes were observed at the end of the acclimation period (C:21 days, C:28 days, n.s.).

The statistical analysis showed existence of a relatively strong correlation between the activity of heart GP*a* and PFK during whole experimental period ($r_{GPa/PFK} = 0.807$, $p < 0.05$), as well as during STHA ($r_{GPa/PFK} = 0.988$, $p < 0.05$) and LTHA ($r_{GPa/PFK} = 0.706$, $p < 0.05$), separately.

Discussion

As previously described, acclimation consists of an early transient, "inefficient" acclimation phase (STHA, up to the 2nd day of heat exposure) to an "efficient" state, after

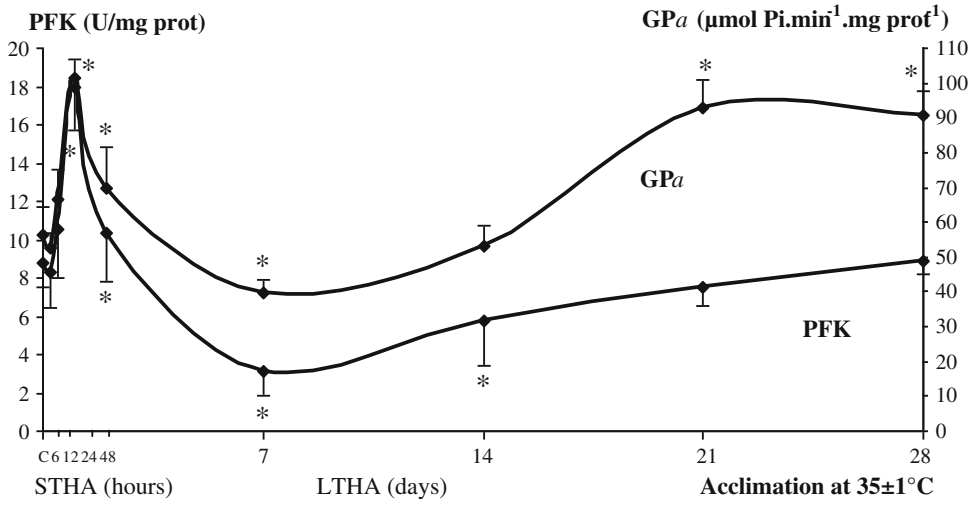

Fig. 3 Glycogen phosphorylase *a* and phosphofructokinase activity in rats during STHA (6, 12, 24 and 48 h) and LTHA (7, 14, 21 and 28 days) heat acclimation at 35 ± 1°C. *$p < 0.05$ in comparison with control (*C*) animals. Coefficient of correlation (*r*) between GP*a*/PFK during whole experimental period ($r_{G6P/HK} = 0.807$), STHA ($r_{G6P/HK} = 0.988$) and LTHA ($r_{G6P/HK} = 0.706$)

Table 3 Statistical and percentage analysis of differences between experimental groups with respect to glycogen phosphorylase *a* and phosphofructokinase activity

GP*a* activity (nmol P_i min^{-1} mg prot.$^{-1}$)						PFK activity (U/mg prot.)					
Group	Means ± SD	%	Group	Means ± SD	%	Group	Means ± SD	%	Group	Means ± SD	%
C	56.38 ± 7.7					C	8.83 ± 1.2				
6 h	52.54 ± 4.3	−6.8	7d	39.51 ± 3.9*	−29.9	6 h	8.33 ± 1.8	−9.5	7d	3.12 ± 1.2*	−64.6
12 h	66.73 ± 8.4	18.3	14d	53.27 ± 5.9	−5.5	12 h	10.54 ± 2.5	6.5	14d	5.77 ± 2.3*	−34.6
24 h	101.21 ± 5.7*	79.5	21d	93.06 ± 7.6*	65.0	24 h	17.91 ± 2.2*	102.8	21d	7.47 ± 0.9	−15.3
48 h	69.96 ± 11.4*	24.0	28d	90.69 ± 7.1*	60.8	48 h	10.35 ± 2.5*	22.4	28d	8.87 ± 0.6	0.4

% ratio between control (*C*) group and heat-exposed (6, 12, 24 and 48 h, and 7, 14, 21, and 28 days) groups of animals

* $p < 0.05$ in comparison with control (*C*) animals

acclimation homeostasis has been reached (LTHA, after the 2nd day of heat exposure) [2, 3]. The changes of the enzymes and substrates presented in this work appeared depending on the duration of heat exposure.

Short-term heat acclimation

Glk represents one of the most important energy depots in the organism as a whole [18]. Besides the well-known hepatic glycogenolysis in the STHA [6–8], we also observed intensive glycogenolysis at the level of heart Glk stores (Fig. 1). This spending of heart Glk stores in the first 12 h of heat exposure was accompanied by decrease of the GP*a* activity. Namely, depletion of Glk reserves causes inactivation of the GP*a*, which will further result in minimal glycogenolysis, with activation of glycogen synthase [19]. It could be that Glk itself is an important regulator of its own rate of catabolism [20], as well as an important determinant of GP*a* activity and rate of glycogenolysis, both in skeletal muscles and the heart [21]. Despite the difference between isoenzyme forms of GP*a* in skeletal muscles and the heart, their activation is the same [22]. In this sense, an investigation indicates that, during increased physical activity, activation of GP*a* is reduced in muscles with low Glk content [19, 23] and increased in muscles with high Glk reserves [19–21].

Spending of the heart Glk stores is followed with a decrease of G6P concentration (Fig. 2) and an increase of heart Glu level (Fig. 1) in the first 12 h of STHA. On the one hand, this situation is a reflection of the increased insulin sensitivity, followed by increased GLUT-4 transport protein redistribution in a condition of acute hyperthermic stress [3, 24]. On the other hand, it could be a result of increased epinephrine secretion and increased autonomic excitability [3, 11]. The same period of STHA is accompanied with a reduced activity of HK (Fig. 2), which is responsible for the most significant increase of heart intracellular Glu (Fig. 1). It could be observed that the activity of HK does not limit the Glu uptake, i.e. some Glu uptake exists during the maximum reduced HK activity. Concerning glycogenolytic/glycolytic enzymes (GP*a* and PFK), a relatively strong positive correlation ($r = 0.988$, $p < 0.05$) between these two parameters was found during the whole period of STHA (Fig. 3). This positive

correlation indicates an intensive glycogenolysis in the direction of production of pyruvate.

Taking into consideration the above, it could be observed that acute heat exposure (up to the 12th hour) leads to reduced spending of heart Glu and elevation of the rate of the process of glycogenolysis.

In the following period of STHA (24 and 48 h), the direction of the metabolic processes is changed. Namely, the second period of STHA is characterized with an attempt at Glk resynthesis, accompanied by increased GP*a* activity and non-significant differences of G6P, which is correlated with the Glk resynthesis. Nevertheless, this situation resulted in higher heart Glu concentration as in the first 12 h (Fig. 1). This is in accordance with the findings of Wheelock et al. [25], indicating that a greater input of Glu into cells exists in warm-exposed animals compared to those kept at room temperature.

The increased Glu level (Fig. 1) in myocardiocytes in the period of 24–48 h of heat exposure was followed by increased HK activity (Fig. 2). Compared to the group exposed to heat for 6 h, the increased HK activity reduces the intracellular (free) Glu concentration and increases concentration of intermediate substrate G6P, which most obviously is directed to Glk production. In the same period, there is increased PFK activity (Fig. 3), which also suggests increased glycolytic potential. Our results showed a positive correlation between heart GP*a* and PFK activity (Fig. 3), since they are both regulated by the concentration of G6P, i.e. GP*a* is indirectly inhibited as a result of G6P accumulation after PFK inhibition [13]. In the period of 24–48 h of heat exposure, the increased GP*a* and PFK activity were followed by insignificant changes in the G6P concentration and increased Glk pool, meaning that one part of G6P is used for Glk synthesis and another for entering glycolysis.

Generally, it could be concluded that the period of STHA might be divided into two phases (Tables 1, 2, 3). Namely, the first phase of acute hyperthermic stress (6 and 12 h) is characterized by an increased intensity of heart glycogenolysis, followed by a moderate increase of glycolytic potential. The second phase of STHA (24 and 48 h) is characterized by enhanced Glk synthesis and glycolytic potential. This leads to the assumption that the latter period (24–48 h) actually represents an intermediate period, i.e. initial phase of heart metabolic adaptation towards the new temperature condition, necessary for an easy and efficient adaptation to the newly created conditions.

Long-term heat acclimation

The obtained results show that, unlike the STHA, LTHA (7, 12, 24 and 28 days) of moderate hyperthermic environment is characterized by less dynamic, but still significant changes in the level of the examined parameters of heart carbohydrate metabolism (Tables 1, 2, 3). LTHA resulted in a further increase of heart Glk content (Fig. 1), achieving the maximum values after the 21st and 28th days at 35 ± 1°C. We found that the increased Glk and G6P in the myocardium are followed by enhanced Glu concentration, especially at the beginning of LTHA (7 and 14 days). This is probably due to the increased Glu uptake, increased insulin sensitivity and increased number of GLUT-4 transports proteins [3, 11, 24]. On the other hand, normalization of the free Glu concentration in myocardiocytes in the second period of LTHA (21st and 30th days) is a result of the previously increased HK activity (starting from the 7th to the 14th days) and Glu phosphorylation, which further reduced Glu concentration (Fig. 1) and increased G6P concentration (Fig. 2).

Increased HK activity is accompanied by further reduced activity of the GP*a* and PFK (minimum values after 7 days heat exposure). These changes indicate that the synthesized G6P is used for the production of larger pool of Glk, followed by attenuated glycogenolysis and glycolytic rate. Several other investigations suggest that the acclimation-induced augmentation of constitutive Glk is accompanied by parallel enzymatic changes which may affect the rate of glycogenolysis [11]. Some of these metabolic features, characteristic of the heart during heat acclimation are due to a sustained low thyroxin level [3, 6, 8, 11, 26–28]. Several other investigations have reported that hypothyroidism is also associated with a dramatic loss in the activity of heart PFK-1, as well as PFK-2 activity and fructose 2,6 bisphosphate level [29–31]. The sustained low level of plasma thyroid hormones, induced by heat acclimation, plays a major role in the emergence of these important cardiac acclimatory responses, apparently via the influence on the transcription of critical genes involved in cardiomyocyte contraction and relaxation [32, 33].

However, our results show that this acclimatory response is partially changed during second period of LTHA (starting from the 21st day until the end of the experimental period), when we found a further increase of heart Glk content (Fig. 1), by achieving the maximum values after the 21st and 28th days exposition at 35 ± 1°C; that is, according to Horowitz [3], the Glk level in the long-term heat acclimated heart is twofold greater. In our results, the increased Glk content is accompanied by increased G6P concentration during the whole experimental period (Fig. 2; $r_{Glk/G6P} = 0.981$). Accumulation of G6P probably enhances the glycogen synthase phosphatase reaction which resulted in elevated rate of glycogenogenesis and production of Glk [34]. There was also an increase in the activity of GP*a* in the second period of LTHA. It is important to notice that increased GP*a* activity probably represents a kind of defense mechanism which protects

cells from excessive augmentation of endogenous Glk. A larger Glk pool and elevated GP*a* activity may mediate acceleration of glycolytic potential via increased PFK.

After the 21st day of heat exposure, there was normalization of the myocardial Glu level (Fig. 1) and HK activity (Fig. 2) and resynthesis of the heart Glk pool. Some literature data [2, 3, 11] have reported that the important metabolic cardio-protective pathway developed during heat acclimation is mediated by the production of a larger pool of Glk (Glk breakdown may provide the heart with the Glu necessary for glycolysis) in conjunction with quantitatively increased glycolysis. In our results, this last was manifested with moderate increased glycolytic flux (increased activity of PFK compared to the previous period). These metabolic changes during heat acclimation represent important cardio-protective mechanisms which are necessary to ensure the continuous ATP generation needed for preservation of the cellular integrity and to maintain heart function.

Taking all these changes into consideration (our results and previous literature data), it seems that, starting from the 21st day of heat exposure, the heart muscle achieves a new and relatively stable steady-state level, i.e. the acclimated heart becomes more energetically efficient, realized through elevation of glycogenogenesis and normalization of glycolytic potential.

In summary, the results obtained have shown that acclimation to moderate hyperthermic environment can cause significant metabolic changes which differ depending on the duration to the exposure. It is important to stress that both of the STHA and LTHA showed biphasic changes, observed on the level of all examined enzymes and substrates: for STHA, the first phase up to 12 h and the second phase from 24 to 48 h of heat exposure; and for LTHA, the first phase from 7 to 14 days and the second phase from 21 to 28 days of heat exposure. Generally, an intensive stress could be seen: induced glycogenolytic and glycolytic processes in the period of STHA and intensive glycogen deposition in the period of LTHA. In the period of LTHA, a new steady-state level of energy sparing in heat-acclimated rat hearts was achieved.

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