The Impact of Ambient Temperature on Physical Performance and Fatigue

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ABSTRACT
Endurance of an athlete during physical exercise depends on many factors. One important factor is heat resulting from metabolic processes initiated to serve the increased energy demand during exercise. The hypothalamus in the brain is responsible for this thermoregulation aiming to transport heat from the body's core to the periphery. When the body temperature rises or when humans exercise in hot environments, the blood brain barrier becomes more permeable to neurotransmitters due to histamine release because of heat stress. This gives serotonin, dopamine and noradrenaline access to enter and leave the brain and to affect levels of fatigue. In addition, this process of thermoregulation shows a diurnal rhythm promoted by the suprachiasmatic nucleus (SCN), which also is located in the hypothalamus. It is well known that humans adapt their physiology to increased energy demands and heat production in response to regular physical exercise. Physiological adaptations can, for example, be found at the level of the muscles, heart, and the vascular and respiratory system. This thesis aims to describe the impact of a high ambient temperature on physical performance and fatigue.

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Introduction

Humans need to keep their body temperature between certain ranges independent of temperature fluctuations in their environment. During physical exercise, the body temperature rises. The process of keeping the body temperature constant is called thermoregulation and can be achieved by both behavioural and physiological mechanisms. Thermoregulation changes during an increase in ambient temperature. Histamine makes the blood brain barrier more permeable and the neurotransmitters serotonin, dopamine and noradrenaline play a role in the regulation of fatigue during exercise.

Behavioural and physiological mechanisms of temperature regulation

Behavioural addressing of thermoregulation processes involve avoidance of extreme environmental circumstances and the amount of activity of a subject at a certain point of the day. The amount of clothes is another aspect of behavioural temperature regulation, humans can put on more clothes when it is cold and less clothes when it is warm. There appears to be a role for both cultural and evolutional aspects of heat adaptation[1]. In an experiment Chinese, East Indians and Malays, all born and raised in Malaysia were tested with regard to ethnic differences in their aerobic capacity for 2 hours in the heat. All groups performed well in response to the hot environment, but the Malay group worked at a higher percentage of their maximum work capacity of the body and therefore produced more heat. However, the Malay group worked at a lower heart rate and showed reduced sweating, which indicates adaptation processes to heat strain in this group (table 1). Because the Malay group is indigenous in Malaysia, heat adaptation seems to have an evolutionary factor.

Etnic Group	Malay	East Indian	Chinese
Heart rate, beats/minute	137,8	150,3	155,0
Core temperature, in ^{o}C	38,4	38,4	38,7
Sweat loss, mL/h/m^2 body surface	322	335	380

Table 1

Physiological responses after 2 hours of exercise at a temperature of 34,9^{o}C in men from different ethnic groups all born and raised in Malaysia.

Besides certain behaviours like clothing or hiding from heat, it is primarily adaptation at the physiological level that keeps body temperature stable[1]:

1. The set point of the body temperature is regulated by the hypothalamus. The hypothalamus contains warm-sensitive and cold-sensitive neurons in the preoptic and anterior nucleus. These neurons detect temperature changes of the blood flowing to the brain and compare these with a set point, which will be 37^{o}C ±1^{o}C[2]. The body also has thermo receptors, which measure the differences in temperature in the spinal cord, abdominal viscera, bigger veins and the skin. If the temperature differs too much compared to the set point, some regulation mechanism occurs, depending on whether the body is either too hot or too cold. If the body temperature is too low, the body compensates by vasoconstriction, shivering, heat production or goose bumps to create isolation. When the body deals with a high temperature, veins dilatate, sweat increases and less heat is produced. In the hairless parts of our face and in the palms of our hands and feet special veins called arteriovenous anastomoses (AVA's) are located, which can dilate and promote heat loss. All these different actions seem to be mediated by different effector areas in the lower brain stem. The preoptic region in the hypothalamus senses the difference in temperature and

communicates by the median forebrain bundle with the lower brain stem areas, each controlling specific thermoregulatory responses. Recent experiments showed these effector areas control blood flow through the skin[3] and shivering[4]. Afferent temperature sensory input from the somatosensory system enters the preoptic nucleus by the lateral spinothalamic tract[5]. This input allows the preoptic nucleus to compare peripheral temperature from the thermo receptors in the body with the central temperature from the warm- and cold-sensitive neurons. Experiments showed the dependency of the firing rate of neurons on the temperature and on the type of neuron (figure 1). Temperature-insensitive neurons, accounting for the majority (about 60%) of the neuronal response, have the same frequency of action potentials at cool, neutral and warm temperatures, but warm-sensitive neurons, accounting for about 30% of the neuronal population, have a decrease in firing rate when temperature decreases, and an increase in firing rate when temperature increases[5]. The reason for this increase in firing rate is warmth, increasing the rate of depolarization[5]. Cold sensitive neurons, accounting for about 5% of the neuronal population, are not really cold sensitive, but they are inhibited by the warm-sensitive neurons. When the temperature drops, the warm-sensitive neuronal inhibition drops as well and the cold-sensitive neurons increase their firing rate. Consequently, warm-sensitive neurons play the major role in thermoregulatory responses[5]. The question remains what the function of the temperature insensitive neurons is, because of their non-changing firing rates at different temperatures. These neurons might function as interneurons for cold-sensitive neurons which compare excitatory and inhibitory input. Results still are inconclusive.

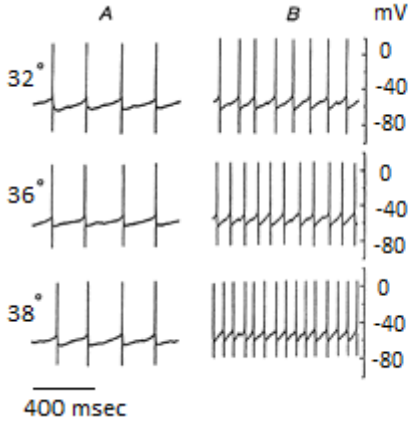

Figure 1
The effect of temperature on the activity of a temperature insensitive neuron (A) and a warm-sensitive neuron (B), in vitro in preoptic tissue of a rat. Warming increases depolarisation rate in warm-sensitive neuronds and this causes an increase in firing rate[5].

Although this feedback mechanism in the hypothalamus is primarily regulating the body temperature, there are some fluctuations in temperature throughout the day. The suprachiasmatic nucleus (SCN) in the hypothalamus is the controlling part of circadian rhythms and results from interactions between clock genes and proteins. There are different factors that influence the body temperature set point over the day with a small variation of about 1°C. These variations create fluctuations of the circadian rhythm which looks like a sinusoid (figure 2). Body temperature rises during the day, has a peak around 17:00h and drops in the night during sleep. These factors are endogenous because they are involved with the internal clock. Exogenous factors are for example the changes in ambient temperature. Most of the heat loss occurs in the late evening and the least in the morning. For that reason heat loss will be simplified during the evening[6,7].
Chronotype is the difference between individuals in the phase relationship between their internal clock and external local time. Morning types have a phase advance and probably a faster internal clock compared to the external time, which is the other way around for the

evening types[7]. Between these morning and evening groups the optimal time point for exercise is different as a result of different body temperatures at the same time of the day because of different internal rhythms.

Several other factors play a role in temperature fluctuations like the menstrual cycle of women, when the temperature rises during ovulation. Women also have more thermal discomfort compared to men in cool conditions[7]. Age is a factor for the circadian rhythm. Ageing is accompanied by a decrease in fitness, deficiencies in the thermoregulatory system and a reduction in response to melatonin, a main regulator in the circadian rhythm[7]. Children have a higher metabolic rate per body surface area. Consequently, the skin temperature for children is higher compared to adults, which increase the rate of sweating[8].

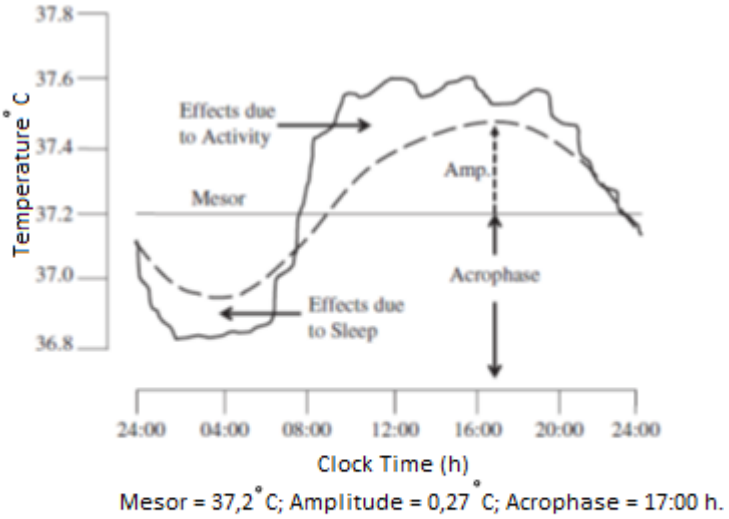

Figure 2
The circadian rhythm of core temperature during normal conditions (full line) and a constant condition (dotted line). The body temperature is dependent on external factors.

2. Muscles are composed of muscle fibers, each containing numerous protein filaments. The bundles, myofibrils, are organized in repeating segments called sarcomeres. A sarcomere is composed of a myosin filament attached to the A band, and actin filaments attached to the Z line at the end of a sarcomere. During contraction sarcomeres shorten and the myosin and actin filaments overlap. Contraction is triggered by an action potential. These action potentials activate voltage-gated sodium channels and cause calcium influx. Due to this influx, acetylcholine (ACh) vesicles fuse with the plasma membrane and are released in the extracellular space between the neuron and muscle. There, ACh activates nicotinergic acetylcholine receptors (nAChr). By binding two ACh molecules, the receptor is activated, sodium flows in and potassium flows out of the cell. Next, the electrical gradient changes and an action potential is triggered and spread through the T-tubules. The depolarisation activates L-type calcium channels in the membranes of the T-tubules, leading to the release of calcium from the sarcoplasmic reticulum. This intracellular calcium binds to troponin C located on the actin filaments of myofibrils. Tropomyosine is pushed away and expose myosin binding sites where myosin heads can bind. During this process, cross bridges are formed between myosin and actin, while phosphate and ADP are released. This release triggers myosin and actin to slide along each other and the muscle contracts. When calcium

or ATP is no longer present, intracellular calcium is pumped back into the sarcoplasmic reticulum and troponin C slides back to its original position[9] (figure 3).

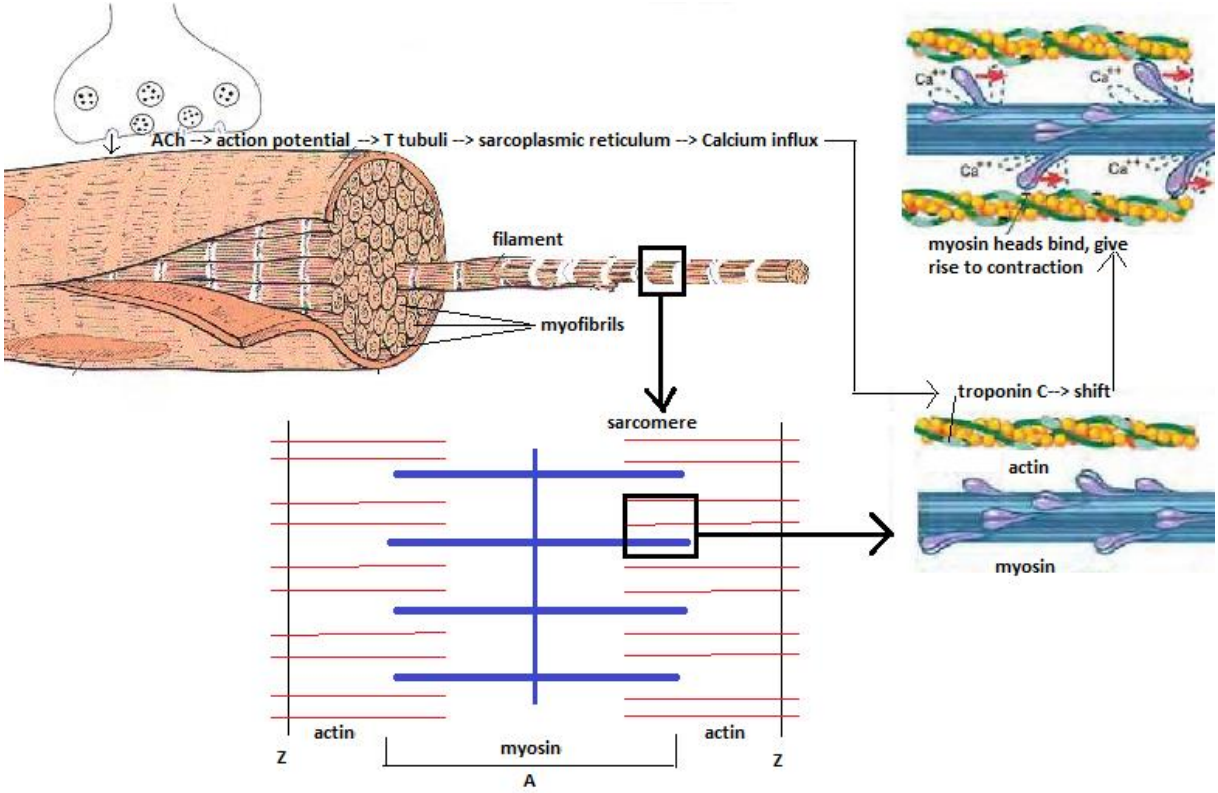

Figure 3

Acetylcholine is released in the neuromuscular junction between the synapse and the muscle fiber. The following action potential enables the release from calcium out of the sarcoplasmic reticulum. Calcium binds to troponin C and causes an allosteric shift causing the myosin heads bind to the actin filaments and the myosin and actin filament slide along each other. This gives rise to a contraction until calcium stores have run out. *Sources: http://medicfrom.com/publicpress/Massage/Structure-and-Function-of-Muscles3.html and http://www.chiro-online.com/lc/principles/module4/module4_4.html*

Heat is a by-product of energy use in the muscles. When the body is in a period of rest, energy requirements are lower. The oxygen consumption during rest is also lowered. When transition from a period of rest to exercise occurs, energy requirements increase immediately, just like the oxygen uptake. Increasing oxygen uptake needs a moment to start, a fact suggesting involvement of the anaerobic pathway in the first minutes of exercise[10]. This anaerobic pathway does not require any oxygen to create energy (ATP). The pathway principally uses the ATP stored in the muscles and when these sources are empty, creatine phosphate (CP) is used to synthesize ATP. This ATP-CP will only last a few seconds and the anaerobic pathway continues with glycolysis. Energy is released with the breakdown of carbohydrates, with lactic acid as a by-product. This breakdown continues until the threshold of lactic acid has been reached, known as muscle pain. When breathing and heart rate have increased and the oxygen is in a steady state, the energy requirement is met via the aerobic pathway. This pathway provides energy for long duration exercise. Oxygen is used in the process to convert carbohydrates, fats and proteins into energy. This process relies on the circulation to transport oxygen to the muscles and therefore is slower[11] (Table 2).

Energy System	Duration (sec.)	Classification	Energy Source
ATP + CP	1-4	Anaerobic	Muscle ATP Stores
	4-20		Muscle ATP + CP Stores
Anaerobic Lactic acid	20-40	Anaerobic	Muscle ATP, CP + Glycogen Stores
	40-120		Muscle Glycogen + Lactic acid
Aerobic	120-2400	Aerobic	
	2400-6000		Muscle Glycogen + Fatty Acids

Table 2

source http://www.elitetrack.com/faqs/answer/221

With these anaerobic and aerobic conversions of energy, heat is formed as a by-product and this buildup needs to be transported out of the muscles. An overdose of heat can have a negative effect on the regulation of metabolic processes, which have a very narrow temperature fluctuation. Cellular metabolism rises for 13% for each increase of 1 ^{o}C above 37^{o}C body temperature[1]. The loss of heat occurs at the surface of the skin. During a period of rest there is a low metabolic rate, a constant blood flow and the temperature of the muscles varies between 33^{o}C and 35^{o}C. Throughout exercise, this temperature gradient between blood and muscle turns. This gradient determines how much heat is transported. This gradient is determined by the balance of the metabolism, radiation, conduction, convection and evaporation of heat[2]:

2.1 Radiation is loss of heat by infrared heat rays. The human body emits and receives radiant heat. Depending on the difference in temperature between the body and the environment the gradient of radiation points to the coldest temperature. For naked subjects in thermal comfortable conditions radiation will encounter for about 60% of heat loss, which will decrease when the body heats up, due to the reversing of the heat gradient[2].

2.2 Conduction is the loss of heat by an object. This process is also dependent on a gradient and becomes less effective when a body is hotter compared to its environmental temperature. Conduction will account for only 3% of heat loss at room temperature[2].

2.3 Convection is the loss of heat by the air, gas or liquid. This process happens due to air warming up around the body and accounts for about 15% of the heat loss at room temperature[2].

2.4 Evaporation is losing heat by sweating. This deficiency of water and ions is only detected after a weigh loss of 2%[2]. The proportion heat loss by evaporation, normally about 25%, increases when the ambient temperature rises, due to the fact radiation, conduction and convection cannot encounter for the main percentage of heat loss if the environment is warmer than the body.

Physical adaptations of the body to exercise

Training results in various forms of body adaptations to exercise. While exercising, the body replies to an increased demand for energy and oxygen by adapting as efficiently as possible:

1. Adaption by skeletal muscles. Muscle fatigue is the decline in ability of a muscle to generate power. Due to training body muscles will increase, consequently delaying the point of fatigue. Training causes growth of muscles in both size and strength; muscles will adapt to new demand. Small damage to muscle fibers causes overcompensation of the body by replacing and increasing tissue[12]. Damaged tissue activates satellite cells which proliferate to the site of injury. Skeletal muscle tissue cannot multiply itself. Satellite cells are stem cells of the skeletal muscle tissue. At the site of injury these satellite cells will merge and as a next step multiply, differentiate and fuse to muscle fibers to form new myofibrils or fibers. As a result the myofibrils of a muscle cell increase in thickness and number. Some satellite cells form new nuclei to increase contractile myofilaments like actin and myosin. Various growth factors play a role in this process. Hepatocyte growth factor (HGF) is the main regulator of migration of the satellite cells to the damaged muscle sites. Fibroblast growth factor (FGF) plays a role in the revascularization during muscle regeneration. Growth hormone and testosterone also affects muscle growth[13].
   The size of muscle growth is a result of sarcoplasmic hypertrophy. The increase in sarcoplasmic fluid contributes for 25-30% of the size of the muscles. There is no increase in strength because the decrease in density of muscle fibers. The strength of the muscles is caused by myofibril hypertrophy, a situation in which actin and myosin contractile proteins increase in number. Due to additional myofibrils the area density increases resulting in increased muscle strength[14,15].
2. One of the cardiac adaptations is hypertrophy of the left ventricle enabling the heart to circulate blood more powerful, which is essential when muscles are contracting during exercise. Another cardiac adaption is the increase in blood volume resulting in a bigger stroke volume and an increase in cardiac output. During a period of rest the heart rate decreases.
3. Vascular adaptations are increasing distribution of blood flows to the muscles due to an increase in muscle capillarization. This blood contains higher levels of hemoglobin, transporting larger volumes of oxygen to the muscles. The additional oxygen is essential to enable extraction of the muscles. During a period of rest the blood pressure lowers.
4. Adaptations in the respiratory field are reflected by lower respiration levels in a period of rest plus an increased tidal volume. In this situation air remains in the lungs for a prolonged period, which allows more oxygen uptake. Respiratory muscles use less oxygen. The surface areas of the lungs have expanded creating more diffusion. More oxygen is extracted and absorbed.
5. At the beginning of an exercise there is a delay in the uptake of oxygen, as described previously (figure 4). The uptake of oxygen needs to increase in the transition phase from a period of rest to exercise. The following, steady state is reached in a few minutes, depending on the condition of a person. For adapted persons the period of oxygen deficit is shorter resulting in less production of lactic acid. Moreover adapted subjects will handle a higher threshold of lactic acid buildup compared to untrained subjects[10,16].

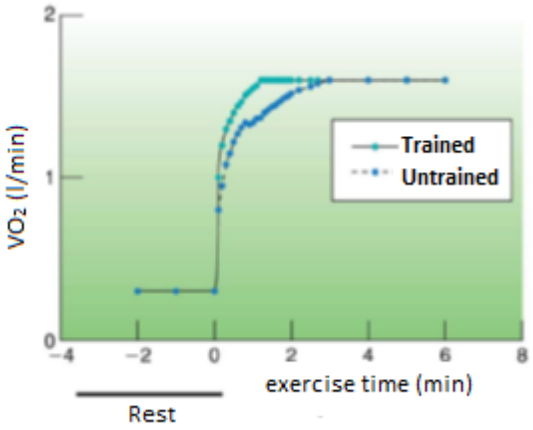

Figure 4
The lag in O_2 due to the transition from rest to exercise. Trained / adapted subjects have a shorter recover time compared to untrained subjects.

6. Mitochondria increase in size and number, which results in more energy. The rise of more oxidative enzymes causes an increased oxidative capacity. Myoglobin concentrations, muscle glycogen and intramuscular triglyceride stores increase, and fat is used more as a fuel during exercise.

Adaptation to warm environment

Humans can be adapted to exercise and perform better, but they can also adapt to a (very) warm environment. The adaptation to warm environments shows similarities with the adaptation to exercise, because in both situations there is an accumulation of metabolic heat produced by the body. Familiar processes take place when sweating or adaptations in the blood flow[8]. Humans not adapted to warm environments have a higher heart rate and limited work capacity. After exposure to a warm environment for a longer period of time, both heart rate and rise in body temperature will decrease. At the same time work capacity increases, probably due to an increase in sweat volume with lower salt concentration. Sweating takes place in the eccrine sweat glands which are enervated by sympatic cholinergic nerve fibers, depending on the intensity of the exercise. First a precursor fluid is produced with sodium and chloride, with less potassium, calcium and magnesium. Sodium and chloride are actively reabsorbed which give rise to the final sweat product. The increase in sweat volume takes 3-5 days after start of exposure to heat and keeps increasing as heat adaptation occurs. This is the period where adaptation of the sweat gland occurs, due to an increase in rate of sweating by increased secretory activities of glands. Also the latent time of the onset of sweating decreases. The adaptation of a lower salt concentration is potentially depending on the reabsorption of salt from the precursor sweat, which process is enhanced by the increased secretion of mineral corticoid during heat adaptation[8]. All of the processes are short term adaptive changes to heat exposure[8]. During long term heat acclimatization, humans still show a decrease in heart rate and rise in body temperature, but they sweat less. Perhaps this is due to the introduction of heat shock proteins, which are produced in human cells during exposure to heat. This can induce tolerance to heat in cells[17].

A lower basal metabolism is favored to keep a lower body temperature in a hot environment. In average, a rise of 10°C of the ambient temperature caused a reduction of about 2,5 till 3 kcal/m2/h in the basal metabolism of Japanese men (figure 5):

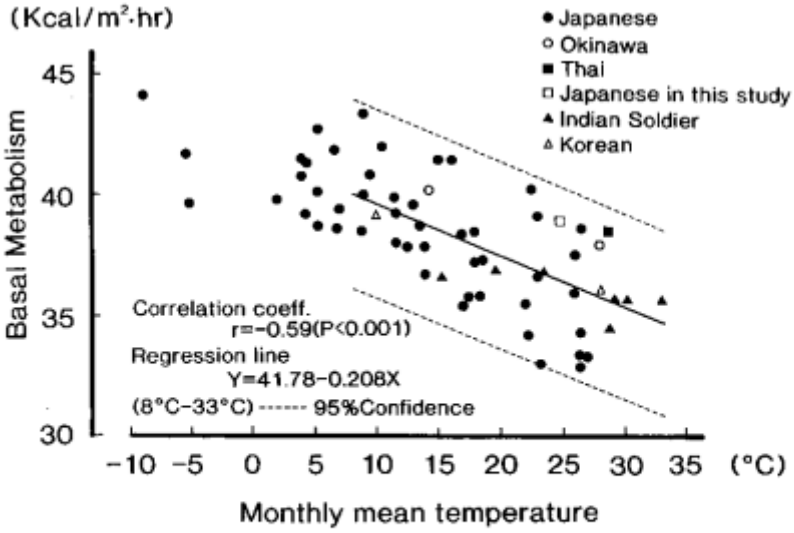

Figure 5
Climatic effects on the mean of groups of basal metabolic rate of young men in Asia. Different racial groups have different basal metabolism in the same temperature compared with other groups.

Concluding from this, basal metabolism is correlated linearly with the ambient temperature[18]. This might be a result of the reduction of thyroxin release during higher ambient temperatures[8]. A lower metabolic rate is the main adaptation in a hot climate.

Across evolution, human ancestors were unable to travel between very different climates because of distances. In our present situation humans are still not adapted to changes in climates. Using air-conditioning systems during warm summers and thick clothes and heaters during cold winter, humans try to maintain their environmental conditions constant avoiding sharp fluctuations in temperature.

However, there seems to be an effect in seasonal temperature nowadays. The thickness of the skin appears to decrease during periods of warm temperatures, whereas the subcutaneous fat deposition is also thinner in hot climates, possibly affected by a decrease in caloric intake in hot climates. Because experiments indicated athletes to have thinner skin during winter compared to non-athletes[19], there are some indications for not only warm climates but also exercises may reduce subcutaneous fat. A decrease in the subcutaneous fat layer gives rise to a higher skin temperature, which is, in combination with an increase in skin circulation, favorable for heat dissipation[20].

Combining heat and exercise

How will the body adapt when a subject exercises in a warm environment? Due to a combination of a lower core temperature plus an improvement of the blood circulation through the muscles there is a decrease in the plasma lactate production and buildup. This will lead to a reduction in ventilatory volume[21]. The reduction in ventilatory volume in combination with the smaller energy expenditure as an outcome of a lower rise in body temperature will result in a decrease in the metabolic rate. The decrease in metabolic rate is a slow adaptation process, while the decrease in ventilation, heart rate and rise in core temperature are quite rapid adaptive changes[8]. Figure 6 summarizes these changes.

Anticipation factors for exercise and heat

Next to the feedback mechanism of the hypothalamus and the adaption due to training, there are anticipation factors for exercise and heat. When preparing for exercise, subject's breathing pattern and metabolic behavior already change[13]. The breathing pattern increases, which leads to an increased ventilation at the onset of exercise. Similar results were documented from an experiment with mental tasks, suggesting a role of cortical activity in the onset of increased breathing[13]. Adrenalin, blood pressure and heart rate clearly rise in advance to the exercise already.

Behavioural processes are main factors for anticipation to heat. These factors act as a feed-forward system and are usually activated prior to the rise of body core temperature. Examples of these factors are the amount of clothes and sheltering in warm environments.

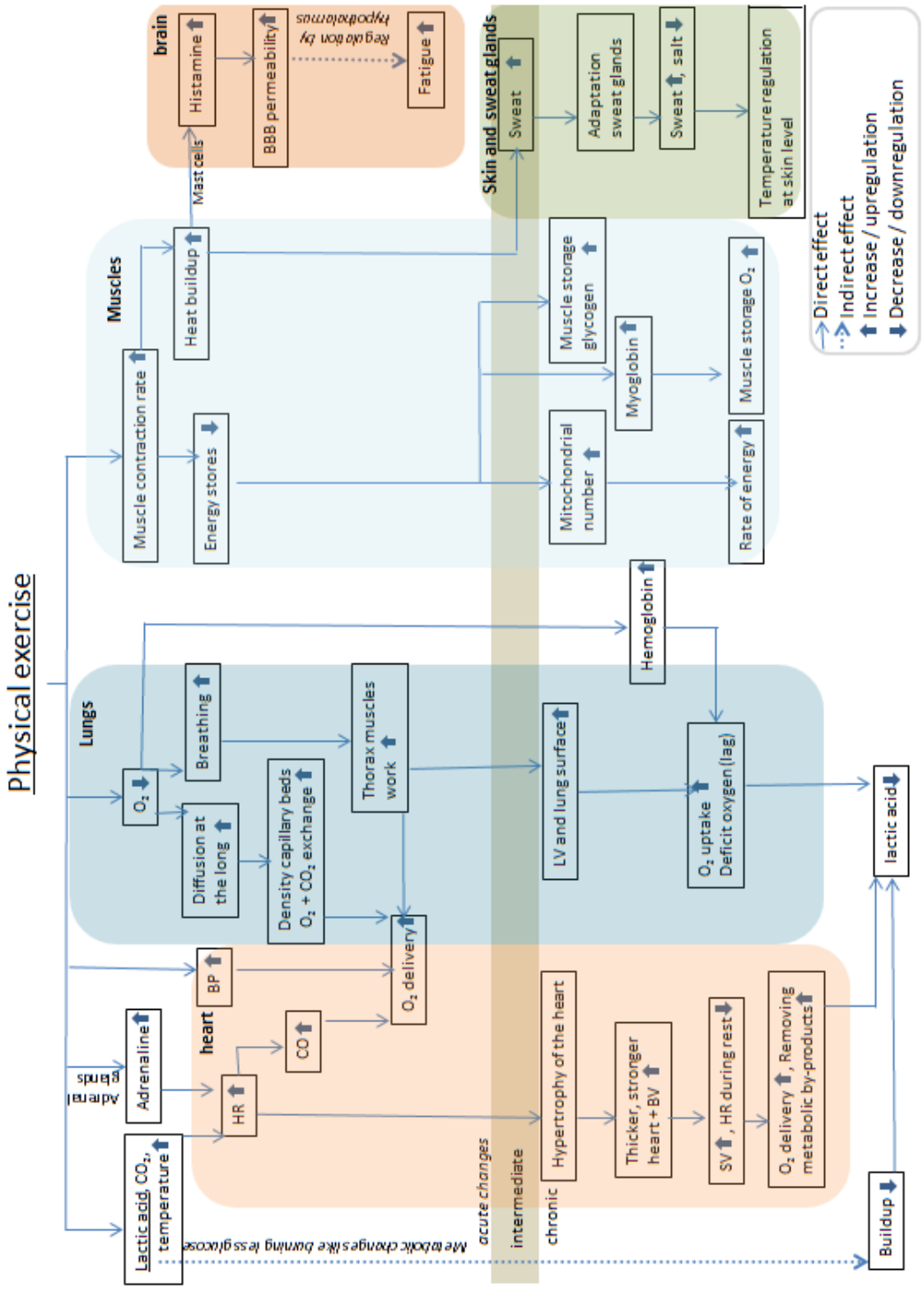

Figure 6

Immediate and chronic adaptations to physical exercise. The actions are not put in a linear chronological ranking. The decrease in oxygen (O_2) and the rise in blood pressure are almost a direct effect, while the buildup of lactic acid and temperate take a couple of minutes. The binding of histamine takes longer due to the slow G protein coupled receptor. Sweat is an intermediate adaptation, there is a lot of individual variation and it takes some time for the sweating process to start due to preceding processes. The increase in sweat is evident after 3-5 days. After very long adaptation, sweat production decreases possibly due to heat shock proteins. At the end of the processes lactic acid is decreasing, which increase the time a subject can perform exercise.

Body changes due to a rise in environmental temperature

Maximum performance in duration exercises proves to be at a temperature of 11°C, body performance decreases at both lower and higher temperatures. Temperature of the body rises faster in warm environments[22]. Changes in environmental temperature appear to have an effect on physical performance and fatigue of a human body.

There is growing evidence for the effects of high ambient temperatures being mediated by the central nervous system. The blood brain barrier prevents passage of water and polar solutes between the cerebral interstitium and the blood plasma in the periphery and is composed of tight junctions between endothelial cells[23]. The permeability of the blood brain barrier appears to differ depending on temperature. When the temperature rises, radiation, conduction and evaporation will be less effective and the body needs to adapt. A reduction in blood flow and a rise in the metabolic need are reported, which results in hypoxia in the liver and intestine. Reactive oxygen species (ROS) and NO are produced which leads to mucosal damage and hyper permeability, activation of leukocytes and the rise of the hypothalamic set point for sweating and blood flow[2,24]. This damage in combination with the heat induced stress will ensure the release of histamine from mast cells. Histamine can also be released during exercise, which has been shown in experiments with rodents[25]. Histamine appears a modulator of the changing permeability of the blood brain barrier during heat stress conditions. In an experiment with rats exposed to heat an increase in permeability was found in comparison to the control group.

Histamine interacts with the brain through histamine receptors, which are partly situated in the hypothalamus and consequently might influence thermoregulation. The effects of histamine appear to be mediated by the H_2 receptor[26]. This receptor is $G\alpha_s$ coupled. Histamine binding this H_2 receptor activates adenylyl cyclase, which catalyze the conversion of ATP to cAMP. This pathway activates protein kinase A (PKA), a cAMP dependent enzyme which phosphorylates all kinds of processes. There are indications for the phosphorylation of IP_3 [27,28], resulting in an increase of sensibility and in the rise of intracellular calcium due to the activation of ryanodine receptors situated on the sarcoplasmic membrane[28]. This process causes the increase of intracellular calcium allowing contraction of these endothelial cells of the blood brain barrier by binding to calmodulin which phosphorylates the myosin light chain (figure 7). It is also possible that histamine itself directly creates gaps between the endothelial cells of the blood brain barrier due to an increase in hydrostatic pressure[29]. There is also the option that cAMP activates GTPase Rap1 [30] which is involved in calcium regulation by activation of PLC and therefore also IP_3 [28].

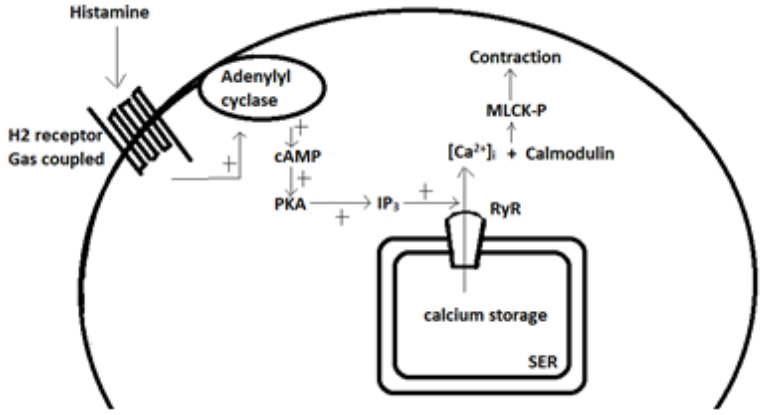

Figure 7
The pathway of histamine giving rise to a release of intracellular calcium. This enables contraction of the cells of the blood brain barrier and therefore makes it more permeable.

A longer duration of exercise in a warmer environment is associated with a raise in permeability of the blood brain barrier enabling substances to enter and leave the brain more easily. Due to the fact histamine binds to a G receptor, these processes are slow. It will take G-Protein coupled receptors some minutes before the actions are mediated. Due to hydration changes in osmotic balances occur, which normally limit the permeability of the blood brain barrier[31].

Perhaps histamine causes a decrease in the firing rate of warm-sensitive neurons in the preoptic area which removes the inhibition on cold sensitive neurons. Histamine provokes an elevation of the hypothalamic set point and suppression of heat loss responses[1]. If the buildup of heat cannot be transported, fatigue occurs more rapidly. Fatigue is the acute impairment of exercise performance that leads to an inability to produce maximal force output, possibly due to metabolite accumulation or substrate depletion. Fatigue occurs in the periphery but also at the central level. Energy depletion stored in muscles appears to be cause of peripheral fatigue. Plausibly disturbed neurotransmitter responses during exercise are cause of fatigue as is the buildup of metabolic by-products like lactic acid for instance[32].

At the central level brain neurotransmitter activity is involved in the regulation of responses during exercise. Serotonin, dopamine and noradrenaline seem to play a key role in the onset of central fatigue due to changes in concentrations during exercise[32]. Due to histamine these transmitters will penetrate the blood brain barrier more easily when the temperature is rising.

The central fatigue hypothesis is based on the monoamine serotonin involved in the feeling of tiredness, fatigue and pain[33]. Experimental results show significant higher levels of plasma volumes and serotonin when the permeability of the blood brain barrier increases (figure 8).

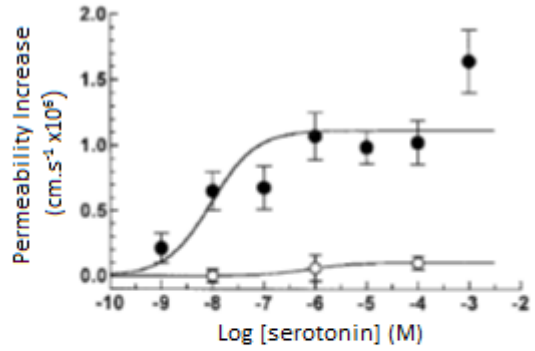

figure 8
Concentration response curves with the effect of serotonin (filled circles)on the permeability of cerebral capillaries in rats (n=4) compared to an serotonin antagonist (open circles).
Source: Abbott NJ., Inflammatory mediators and modulation of blood-brain barrier permeability. Cell Mol Neurobiol. 2000 Apr;20(2):131-47.

During exercise the amount of the precursor tryptophan crossing the blood brain barrier increases, causing higher serotonin concentrations in the brain[32]. An experiment with rats showed that increases in central serotonin activity will result in decreases in performance, while a serotonin antagonist led to improvement of performance[34]. There are indications that serotonin is involved with the onset of fatigue.

Next to serotonin the interaction between serotonin and dopamine has an impact on the fatigue at a central level[31]. Dopamine is involved with reward, the control of motor behavior and motivation[35]. Experiments showed low dopamine concentrations in interaction with serotonin when rats ended exercising due to fatigue[34]. During another experiment rats showed an increase in performance when provided with a dopamine agonist[36]. A low ratio of serotonin-dopamine interaction has a favoring effect on performance whereas a high ratio has a negative effect on performance. This ratio appears to have a significant influence on central fatigue.

Noradrenaline appears to be involved in the onset of central fatigue, however results are still inconclusive[32]. Noradrenaline is involved in consciousness and reward. Noradrenaline re-uptake inhibiters are expected to lead to a delay of fatigue, however experiments do not appear to be significant yet, probably due to negative influence on exercise during normal conditions. In normal ambient temperatures noradrenaline has a negative influence on performance[32]. There might be a more interesting role for noradrenaline during temperature changes. There are suggestions that performance in the heat is primarily regulated by the central nervous system[37]. Noradrenaline and dopamine increase appear in the preoptic area of the hypothalamus, where thermoregulation takes place[32]. An experiment showed an important role for dopamine in delaying fatigue and increased tolerance to exercise in the heat when dopamine activity in the hypothalamus is high[38]. The effects of noradrenaline come with a delay and show slower performance[32].

There are indications for the presence of a protective, fatigue mechanism, which is activated the moment a critical core and brain temperature is reached. Experiments have shown that trained subjects, each starting at different body temperatures, stop performing at a similar core body temperature[39]. In addition serotonin, dopamine and noradrenaline seems to play a role in the thermoregulation with neurons situated in the hypothalamus. Noradrenaline has effect on core temperature mediated by α-adrenoreceptors and serotonin alters the thermosensitive neurons in the preoptic area. Dopamine appears to have a positive effect on the tolerance to exercise in the heat. Unfortunately, these effects appear to vary in relation to the height of the ambient temperature[32].

In conclusion, serotonin is involved in the onset of fatigue. Dopamine has an inhibitory function for the central nervous system to stop performing exercise when the temperature of the body is high. Noradrenaline appears to lead to slower performance and a lower temperature of the body. Dopamine and noradrenaline appear to play a major role relatively to serotonin.

Conclusion

Humans have the ability to regulate their body temperature and keep it at a constant level, independently of ambient temperatures. Thermoregulation can be achieved by behavioural and physiological mechanisms. Temperature sensitive neurons in the preoptic part of the hypothalamus are the main regulators of the set point of body temperature. Depending on the kind of signal for body temperature, various mechanisms are activated like shivering, vasoconstriction, sweating and dilatation. There are variations of body temperature during the day. Because humans vary in chronotype, the ideal timing for daily exercise will differ from person to person. Also the menstrual cycle, sex and age play a role in the circadian rhythm.

During exercise, heat is a by-product produced in the muscles. This heat needs to be removed from the muscles because a heat overdose might result in a negative effect on metabolic processes. The loss of heat takes place at the surface of the skin through radiation, conduction, convection and evaporation. Evaporation plays an increasing role when temperature rises.

During exercise, action potentials enables the influx of calcium in muscle cells, which binds to troponin C and expose myosin binding sites. The myosin and actin filaments slide along each other and generate a contraction. During training, adaptation, muscles grow in size and strength. Satellite cells increase contractile myofilaments. Sarcoplasmic hypertrophy provides muscle growth in size where myofibril hypertrophy provides increase in strength of muscles.

Additionally the body attempts to keep up with the demand for energy and oxygen during exercise by adaptations in cardiac, vascular and respiratory aspects. A lower basal metabolism and thinner skin are specific adaptations to heat. Anticipation of exercise and heat appears to have an effect on breathing pattern and metabolic behavior.

When the ambient temperature is higher, stress ensures the release of histamine from mast cells. The binding of histamine results in an improved permeable blood brain barrier, a slow process due to the fact it is G protein coupled. When the blood brain barrier is permeable, serotonin levels in the brain increase. Serotonin might be involved with the onset of fatigue. Dopamine, involved with reward and motivation, decreases in the brain during exercise. The ratio of serotonin-dopamine seems to have large impact on central fatigue. Finally, involved with consciousness and reward, noradrenaline appears to play a role in the onset of fatigue. The effects of noradrenalin could be temperature dependent, more research is obligatory.

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