FATIGUE DEVELOPMENT MECHANISMS DURING INCREASED INTENSITY EXERTION

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Abstract. During motor preparation, the attention is paid more and more frequently to the complex significance of fatigue in the case of the achieved sport outcome. The complexity of this process has not been utterly explained so far. It is important to acquire the profound knowledge about the central and peripheral fatigue while explaining this mechanism, because they remain in the background of the human body malfunction. It needs to be emphasized that both fatigue mechanisms should not be analyzed separately, because they are subordinated to one another. The changes mechanism in central nervous system (CNS) influenced by physical exertion leads to reticular formation impairment. This in turn results in analytic and decision making process malfunction. The proper functioning of these centers depends on appropriate neurotransmitters concentration. The short tryptophan to serotonin metabolic pathway plays a significant role in the central fatigue development. The concentration increase of this hormone leads to CNS malfunction, which causes the above mentioned changes. The purpose of this paper was to show, based on the current literature data, the predisposing mechanisms and factors in the development of fatigue.

Key words: physical exertion, peripheral fatigue, central fatigue, free tryptophan, serotonin

Introduction

The constant progress in the area of physical culture contributes to the development of technology, training means and methodological knowledge concerning a given sport discipline training. It is a fundamental and at the same time complex system of introducing new elements, that focuses on unlocking a particular competitor's potential. It is essential to pay attention to scientific studies in the case of sport and coordination abilities assessment. The knowledge integration of exercise physiology, neurophysiology and sport psychology areas may improve the contestant's proper motor development (Nunez et al. 2008).

It is common among physically active people to decrease the ability to perform intense physical exertion. It is especially important in the case of professional contestants to maintain suitable training program in order to avoid

the negative consequences of fatigue (Kokkinos 2012). The contestant's adaptation to training effort and the vast knowledge concerning human study should be one of the basic elements improving psychomotor efficiency. Talking about the last factor, it is important to put emphasis on the training efficacy or the preparatory process based on the interdisciplinarity (Andrzejewski et al. 2011).

Based on the analysis of the selected biochemical indicators level, it is possible to assess training effects. It is an easy method to assess – for assessing given parameters in various time periods, intervals and a run speed. It is also beneficial to research the correlation between other indicators and the reaction quickness (Purvis et al. 2010). The reaction quickness itself can be investigated by means of differential response time and the number of correct reactions (Andrzejewski et al. 2011).

The purpose of this paper was to show, based on the current literature data, the predisposing mechanisms and factors in the development of fatigue.

Issue description

High-powered energy levels decrease occurs in the initial physical extortion phase. ATP resources in human body amount to nearly 100 g, which cause its fast burning. Physical exertion causes ATP renewing at the expense of phosphocreatine resources, muscle, fatty acid and liver glycogen alteration. According to the literature data, with the use of phosphocreatine, the maximal speed of ATP resynthesis is about 73,3 mmol × sek^{-1} (Kokkinos 2012). As the exertion time increases, the processes utilizing glycolytique changes take place. The decreased glucose level in blood is connected with the muscle glycogen depletion. The slowdown of the glycogenolysis process accelerates unfavorable reactions, which leads to excessive metabolism products accumulation (Blomstrand et al. 1988; Herzog et al. 2008; Matsui et al. 2011).

Phosphocreatine resynthesis and the glycolysis products elimination happen partially during the exertion and also after its completion (Brooks 2009; Caruso et al.2009). Likewise, muscle anoxia results in AMP particle disintegration and uric acid concentration rise. Muscle cells are damaged and the cell membrane permeability is disturbed under the acid dissociation influence. The lactate acid increase results in the rise of hydrogen ions concentration and in some enzymes – activity limitation as well. As a consequence, lactate increase may result in the psychomotor efficiency reduction (Chmura and Nazar 2010; Mroczek et al. 2011).

The exhibited mechanism shows the most important elements of fatigue development in the human body. This process progression is conditioned by several fundamental elements. Apart from the psychomotor efficiency level, which depends on individual training extend, it is important to mention that the given kind of exertion also predisposes this process development (Meeusen et al. 2010; Nortlund 2004).

The fatigue development should be perceived as a number of changes in human energy transformation, in the processes controlling central mechanisms and human body mechanics. In 2007, Naderhof et al. presented the definition of fatigue process with reference to vast realms of human studies. According to their definition ''fatigue is a process causing muscle activity reduction and also the ability reduction to generate and elicit power during the maximum activity" (Naderhof et al. 2007).

Number of authors divide fatigue into two types: peripheral and central. The peripheral fatigue type is connected with a number of physiological and biochemical changes occurring in the muscular system, whereas the central fatigue development occurs under the influence of numerous metabolic and chemical processes in many CNS structures (Meeusen and Roelands 2010). According to a recent research analysis, peripheral and central

fatigue should not be investigated separately (Nunez et al. 2008; Nordlund et al. 2004; Place et al. 2009). Fatigue causing factors are not utterly known, and they do not explain all scientific aspects either. In order to explain fatigue development conditions, factors should be categorized into biochemical, neurochemical, physiological, genetic and cognitive-emotional. The modern measurement instruments, as well as new technologies development, proved to be useful in each component assessment (Herzog et al. 2008).

According to some authors, peripheral fatigue is caused by muscle glycogen and phosphocreatine quantity decrease, lactate acid and hydrogen ions concentration increase in the muscles, active skeletal muscle anoxia, venous outflow impediment, muscle temperature rise, excitability and resting membrane potential decrease, and muscle fiber contraction mechanism disturbance (calcium pomp impairment in the endoplasmic reticulum) (Nybo 2003).

Other authors claim, in turn, that main factors causing peripheral fatigue are the following: dominant energetic reaction type, muscle fiber type, muscle power and length (Clausen et al. 2004; Millet and Lepers 2004).

Central fatigue, on the other hand, is caused by hormones and neurotransmitters production disorder, humoral responses alteration while extortion is performed, some incorrect exploitation of energetic substrata, or non-specific CNS structure excitability decrease (Place et al. 2009). More often, modern sport training program is based on the processes happening in the CNS. However, information receiving and processing malfunction, motor slowdown, perception, prediction and decision making difficulties most often occur. In terms of professional sport, these are the most important game and success elements (Andrzejewski et al. 2011; Chmura and Nazar 2010).

In the peripheral fatigue generation process, lactate acid dissociation may be of great importance in blood pH alteration. The reduction of pH leads to skeletal muscle activity slowdown (Romer et al. 2006). The exertion, on the other hand, causes pH reduction to ~5.0. It is related to power decline and muscle contraction quickness and dependent on the physical exertion type and duration. Energy recovery is more rapid in the case of increasing intensity exertion. The energetic transformation slowdown, as the result of glycogenolysis and glycolysis enzymes influence, is another mechanism. Phosphorylase and phosphofructokinases are slowed down when pH is low, therefore, energy transport quickness may be reduced. Additionally, Ca^{2+} ions are released out of sacroplasmic reticulum. It is connected to the muscle contraction activity reduction, causing muscle power decrease. Blood pH rate is also subjected to ions release reduction out of cell membrane. Pain during the exertion may be caused by nociceptors irritation, which contributes to axons type III and IV activation under the influence of lactate acid concentration increase (Balog et al. 2000; Dahlstedt and Westerblad 2001; Place et al. 2009).

Acworth et al. and Newsholme et.al. should be mentioned first if one is to systematize all fatigue development theories. The hypothesis created in 1986 assume the 5-hydroxytryptamine (5-HT, serotonin), dopamine (DA), noradrenalin (NA) synthesis and metabolism to be the main factors during the prolonged exertion (Acworth et al. 1986; Newsholme et al. 1987). According to Meeusen's and Watson's hypothesis, one neurotransmitters system cannot be responsible for central fatigue development (Mausen and Watson 2007).

Tryptophan is one of the twenty two amino acids. Blood serum contains two tryptophan forms: free tryptophan and total tryptophan. Some scientific reports suggest tryptophan has only one ability, namely to control alteration of serotonin concentration in CNS. Therefore, it is the serotonin precursor. Due to the lack of free tryptophan and albumin affinity (Non-albumin-bound-serum tryptophan) it is able to pass through blood-brain barrier (Knott and Curzon 1972; McMenamy et al. 1957).

Serotonin is a main neurotransmitter responsible for many somatic and behavioral functions related to mood, appetite, sleep, anxiety, and endocrine regulation. At the same time, homeostasis disturbance resulted from serotonin shortage leads to mood deterioration, depression and lack of appetite. On the other hand, too high serotonin concentration, especially in CNS, results in fatigue process development, manifested in the analysis and decision making processes. According to other authors, excessive serotonin concentration increase in CNS is connected with body temperature and pulse lapse (Maeusen and Watson 2007; Matsui et al. 2011; Nybo 2003). In scientific publications one can find some understatements and the lack of particular free tryptophan metabolic pathways. Lack of this knowledge and the appearance of various hypothesis impedes unequivocal subject characteristic.

According to the atom spatial configuration, two tryptophan forms can be isolated: L-tryptophan (L-TRP) and D-tryptophan (D-TRP). L-tryptophan (L-TRP) into serotonin (5-HT) biosynthesis is a complex two-staged enzymatic process with a short metabolic pathway. Hydroxyl group and L-TRP addition happen under the tryptophan hydroxylase (TPH) influence, producing 5-Hydroxy-L-Tryptophan (5-HTP), whereas decarboxylase 5-Hydroxytryptophan enzyme decarboxylate 5-HTP occurs in the second stage. As a consequence, 5-hydroxytryptamine (5-HT) is produced (Amann et al. 2006; Nordlund et al. 2004; Yamamoto et al. 2012).

5-HT synthesis quickness depends on the free tryptophan concentration in the serum and also on the free tryptophan pass speed through blood–brain barrier. The reduction of free tryptophan permeability to CNS may be caused by the increase of free tryptophan total concentration in the serum, and also by other organic compounds increase such as BCAA, leucine, isoleucine, valine or nonesterified fatty acids (NEFA) (Blomstrand 2006; Place et al 2009; Soares et al. 2002). The reduction of transport speed to CNS is also dependent on the albumin bound to tryptophan affinity degree (Cheuvront et al. 2004).

Chaouloff's et al. research indicates that prolonged exertion influences free tryptophan increase. However, there is no free tryptophan level increase affirmation (Chaouloff et al. 1987). This kind of physical extortion is characterized by the increased muscle demand for BCAA which results in BCAA concentration reduction in the serum. Free tryptophan to BCAA ratio is significant in reference to the central fatigue development. Human subject research showed that the free tryptophan to BCAA ratio rises in time, especially after the prolonged exertion, whereas ratio decrease in favor of BCAA manifests in free tryptophan transport reduction through the blood–brain barrier. The reduction of free tryptophan permeation to CNS influences central fatigue development slowdown (Castell et al. 1999; Chaouloff et al. 1987; Cheuvront et al. 2004). Subsequently, lipolizys increases free acid fats release. As a result of bio-chemical processes, free tryptophan concentration rises. On the other hand, this mechanism causes the increase of free fat acids plasma concentration, which influences tryptophan and albumins bonding restriction and increases free tryptophan concentration rise. On the other hand, the given mechanism favors free tryptophan transport to the brain as well as the synthesis and 5-HT release (Blomstrand et al. 2009; Newsholme and Blomstrand 2006). 5-HTP shows high ability to permeate through blood–brain barrier (Jacobs 2010). It is connected with the compound structural build and relatively short serotonin half-life. Due to the monoamine oxidases, 5-HT undergoes very quick metabolism in CNS. 5-Hydroxyindoleacetic acid (5-HIAA) is the serotonin transformation end product. This metabolite, after it is removed outside the neuron, gets to the cerebrospinal fluid and blood (Burgess et al. 2006). It should be emphasized that 5-HT does not show any ability towards selective transport through blood-brain barrier (Hannon and Hoyer 2008). Its bio-synthesis process takes place in CNS, mainly in raphe nuclei neurons. Their axons, in turn, create a net where neurotransmitters are generated, including the5-HT. This dense neuronal net allows for every CNS structure accomplishment (Egeland et al. 2011).

According to Blomstrand's et al. research, free tryptophan uptake during the prolonged exertion occurs after thirty minutes and increases gradually up to two and a half hours of exertion (Blomstrand 2006; Blomstrand et al. 1988). The above mentioned research clearly proves that free tryptophan uptake increase leads to 5-HT concentration rise in various brain areas (Beguet et al. 2002; Yamamoto et al. 2012).

Having knowledge about the neurophysiological mechanisms and chemical processes in CNS during the intensity increase exertion, their effects should be discussed.

Serotonin mainly affects the nonspecific CNS structures, namely the reticular formation (Chmura and Nazar 2010). Under the intense physical exertion influence, sound-optic stimulus reaction and the analytic and decision functions reduction occur (Andrzejewski et al. 2011). Serotonin has an enormous influence over the cerebellum, spinal cord and other CNS structures via the multi-axon raphe nuclei bound (Egeland et al. 2011). Balance and motor coordination disturbance, spinal reflex impairment, posture control and tonus disturbance are the frequent fatigue development consequences. Higher 5-HT level influence also manifests in the somatic system slowdown. Frequently, bradycardia manifests under the increased intensity exertion via the blood pressure drop (Egeland et al. 2011; Watts et al. 2012).

Conclusion

Based on the scientific reports analysis, concerning mostly the influence of metabolic transformation products and the neurotransmitters, the conclusion can be drown that all of the above mentioned substances combined cause the central fatigue syndrome. The resultant changes are the most significant in peripheral processes regulation, leading to the changes within CNS. The mechanism based on the neuroendocrinological changes in the hypothalamus-hypophysis-adrenal gland axis is remarkable. Not only does this system influence the whole human body but it also affects its particular components. The neuromuscular transmission and other neurotransmitters transporters connected to this mechanism are still inscrutable. Further research in the area of neurophysiology and physical exertion physiology should be oriented on the developing activities discussed within the hypothesis and the scientific research. Verification and the theoretical knowledge extension allows for more profound investigation of these mechanisms.

Discussing the theoretical aspects of central fatigue development and their consequences, it should be emphasized that sport psychology should be widely implemented in the training process. Sport psychology is one of the most prospering areas in the branch of physical culture science. The issues treated by the psychologists are mainly connected with the particular CNS centers activity and the decision and motivation process assessment.

References

Acworth I., Nicholass J., Morgan B., Newsholme E.A. Effect of sustained exercise on concentrations of plasma aromatic and branched-chain amino acids and brain amines. Biochem. Biophys. Res. Commun. 1986; 137 (1): 149–153.

Amann M., Eldridge M.W., Lovering A.T., Stickland A.M., Pegelow M.D., Dempsey J. Arterial oxygenation influences central motor output and exercise performance via effects on peripheral locomotor muscle fatigue in humans. J. Physiol. 2006; 575 (15): 937–952.

Andrzejewski M., Chmura J., Wiacek M., Zubrzycki I.Ż. Influence of individualized training on psychomotor performance of young soccer players. J Strength Cond. Res. 2011; 22 (2): 374–378.

Balog E.M., Fruen B.R., Kane P.K., Louis C.F. Mechanisms of P_i regulation of the skeletal muscle SR Ca^{2+} release channel. Am. J. Physiol. Cell Physiol. 2000; 278: C601–C611.

Béquet F., Gomez-Merino D., Berthelot M., Guezennec C.Y. Evidence that brain glucose availability influences exercise-enhanced extracellular 5-HT level in hippocampus: a microdialysis study in exercising rats. Acta. Physiol. Scand. 2002; 176 (1): 65–69.

Blomstrand E. A Role for Branched-Chain Amino Acids in Reducing Central Fatigue J. Nutr. February. 2006; 136 (2): 544S–547S.

Blomstrand E., Celsing F., Newsholme E.A. Changes in plasma concentrations of aromatic and branched-chain amino acids during sustained exercise in man and their possible role in fatigue. Acta. Physiol. Scand. 1988; 133 (1): 115–121.

Brooks G.A. Cell–cell and intracellular lactate shuttles. J. Physiol. 2009; 587: 5591–5600.

Burgess N.K., Sweeten TL, McMahon WM, Fujinami RS. Hyperserotoninemia and altered immunity in autism. J. Austin Dev. Disord. 2006; 36 (5): 697–704.

Chaouloff F., Laude D., Merino D., Serrurrier B., Guezennec Y., Elghozi J.L. Amphetamine and alpha-methyl-p-tyrosine affect the exercise-induced imbalance between the availability of tryptophan and synthesis of serotonin in the brain of the rat. Neuropharm. 1987; 26: 1099–1106.

Cheuvront S.N., Carter R. 3rd, Kolka M.A., Lieberman H.R., Kellogg M.D., Sawka M.N. Branched-chain amino acid supplementation and human performance when hypohydrated in the heat. J. App. Physiol. 2004; 97: 1275–1282.

Calbet J.A., Boushel R., Radegran G., Sondergaard H., Wagner P.D., Saltin B. Determinants of maximal oxygen uptake in severe acute hypoxia. Am. J. Physiol. Regul. Integr. Comp. Physiol. 2003; 284: R291–R303.

Castell L.M., Yamamoto T., Phoenix J., Newsholme E.A. The role of tryptophan in fatigue in different conditions of stress. Adv. Exp. Med. Biol. 1999; 467: 697–704.

Caruso J.F., Monda J.K., Ramey E., Hastings L.P., Coday M.A., McLagan J.R., Wickel E.E. Blood lactate responses to exercise performed on a high-speed inertial device. Isokinetics and Exercise Science. 2009; 17: 1–7.

Chmura J., Nazar K. Parallel changes in the onset of blood lactate accumulation (OBLA) and threshold of psychomotor performance deterioration during incremental exercise after training in athletes. Int. J. Psychophysiol. 2010; 75 (3): 287–290.

Clausen T., Overgaard K., Nielsen O.B. Evidence that the Na^+-K^+ leak/pump ratio contributes to the difference in endurance between fast- and slow-twitch muscles. Acta. Physiol. Scand. 2004; 180: 209–216.

Dahlstedt A.J., Westerblad H. Inhibition of creatine kinase reduces the rate of fatigue-induced decrease in tetanic $[Ca^{2+}]_i$ in mouse skeletal muscle. J. Physiol. (Lond). 2001; 533: 639–649.

Egeland M., Warner-Schmidt J., Greengard P., Svenningsson P. Co-expression of serotonin 5-HT(1B) and 5-HT(4) receptors in p11 containing cells in cerebral cortex, hippocampus, caudate-putamen and cerebellum. Neuropharm. 2011; 61 (3): 442–450.

Hannon J., Hoyer D. Molecular biology of 5-HT receptors. Behav. Brain Res. 2008; 195 (1): 198–213.

Herzog R.I., Chan O., Yu S., Dziura J., McNay E.C., Sherwin R.S. Effect of acute and recurrent hypoglycemia on changes in brain glycogen concentration. Endocrinology. 2008; 149: 1499–1504.

Jacobs G., Kamerling I., de Kam M. Enhanced tolerability of the 5-hydroxytryptophane challenge test combined with granisetron. J. Psychopharm. 2010; 24 (1): 65–72.

Kokkinos P. Physical activity, health benefits, and mortality risk. ISRN Cardiol. 2012; 718-789.

Knott P.J., Curzon G. Free tryptophan in plasma and brain tryptophan metabolism. Nature. 1972; 239: 452

Matsui T., Soya1 S., Okamoto1 M., Ichitani Y., Kawanaka K. Soya S. Brain glycogen decreases during prolonged exercise. J. Physiol. 2011; 589 (13): 3383–3393.

McMenamy R.H., Lund C.C., Oncley J.L. Unbound aminoacid concentrations in human blood plasma, J. Clin. Invest. 1957; 36: 1672.

Meeusen R., Watson P. Amino Acids and the Brain: Do They Play a Roie in “Central Fatigue”? Int. J. Sport Nutr. Exerc. Metab. 2007; 17: S37–S46.

Meeusen R., Roelands B. Central fatigue and neurotransmitters, can thermoregulation be manipulated. Scand. J. Med. Sci. Sports. 2010; 20 (S3): 19–28.

Millet G.Y., Lepers R. Alterations of neuromuscular function after prolonged running, cycling and skiing exercises. Sports Med. 2004; 34: 105–116.

Mroczek D., Kawczyński A., Chmura J. Changes of Reaction Time and Blood Lactate Concentration of Elite Volleyball Players During a Game. J. Hum. Kinects. 2011; 28 (1): 73–78.

Nederhof E., Lemmink K., Zwerver J., Mulder T. The effect of high load training on psychomotor speed. Int. J. Sports Med. 2007; 28 (7): 595–601.

Newsholme P., Curi R., Gordon S., Newsholme E.A. Metabolism of glucose, glutamine, long-chain fatty acids and ketone bodies by murine macrophages. Biochem. J. 1987; 239 (1): 121–125.

Newsholme E.A., Blomstrand E. Branched-Chain Amino Acids and Central Fatigue. J. Nutr. 2006; 136 (1): 2745–2765.

Nordlund M.M., Thorstensson A., Cresswell A.G. Central and peripheral contributions to fatigue in relation to level ofactivation during repeated maximal voluntary isometric plantar flexions. J. App. Physiol. 2004; 96 (1): 218–225.

Nunez V.M., Da Silva-Grigorietto M.E., Castilo E.F., Poblador M.S., Lancho J.L. Effect of training exercise for the development of strength and endurance in soccer. Strength Cond Res. 2008; 22 (2): 518–524.

Nybo L. CNS fatigue and prolonged exercise: effect of glucose supplementation. Med. Sci. Sports Exerc. 2003; 35: 589–594.

Place N., Bruton J.D., Westerblad H. Mechanisms of fatigue induced by isometric contractions in exercising humans and in mouse isolated single muscle fibres. Clin. Exp. Pharmacol. Physiol. 2009; 36: 334–339.

Purvis D., Gonsalves S., Deuster P.A. Physiological and psychological fatigue in extreme conditions: overtraining and elite athletes. PM R. 2010; 2 (5): 442–450.

Romer L.M., Lovering A.T., Haverkamp H.C., Pegelow D.F., Dempsey J.A. Effect of inspiratory muscle work on peripheral fatigue of locomotor muscles in healthy humans. J. Physiol. 2006; 571: 425–439.

Soares D.D., Lima N.R., Coimbra C.C., Marubayashi U. Evidence that tryptophan reduces mechanical efficiency and running performance in rats. Pharmacol. Biochem. Behav. 2002; 74: 357–362.

Watts S.W., Morrison S.F., Davis R.P., Barman S.M. Serotonin and blood pressure regulation. Pharmacol. Rev. 2012; 64 (2): 359–388.

Yamamoto T., Azechi H., Board M. Essential role of excessive tryptophan and its neurometabolites in fatigue. Can. J. Neurol Sci. 2012; 39 (1): 40–47.

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