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THE IMPLICATIONS OF CARBOHYDRATES DURING PHYSICAL EFFORT: A COMPREHENSIVE REVIEW

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ABSTRACT. The metabolism during physical exercise changes depending on the nature of the effort in various sports, duration, intensity, environmental conditions, etc. Carbohydrates in the form of glucose and intramuscular glycogen becomes an increasingly important energy substrate during physical activity, with the muscle contraction being triggered by ATP (adenosine triphosphate). The biochemical processes that occur during muscle contraction are very complex. Degradation of glycogen to lactic acid and oxidative degradation of glycogen to carbon dioxide and water have no other role during muscle contraction but to obtain molecules of ATP. The modifications of certain biochemical parameters such as blood sugar levels depend on the exercise intensity and they, in turn, influence the speed of metabolic changes in the working capacity of the body.

Key words: *carbohydrates, ATP, physical effort*

REZUMAT. Implicaţiile carbohidraţilor în efortul fizic. Metabolismul efortului sportiv prezintă modificări în funcţie de natura efortului depus în diferite ramuri sportive, durată, intensitate, condiţii de mediu etc. Carbohidraţii, sub formă de glucoză şi glicogen reprezintă un substrat energetic important pentru activitatea fizică, contracţia musculară fiind declanşată de ATP(adenozin-trifosfat). Procesele biochimice care au loc în timpul contracţiei musculare sunt foarte complexe. Degradarea glicogenului la acid lactic precum şi degradarea oxidativă a glicogenului la dioxid de carbon şi apă nu au alt rol în procesul contracţiei musculare decât de a procura molecule de ATP. Modificările anumitor parametrii biochimici-precum glicemia, care pot influenţa gradul de efort, sunt dependente de intensitatea efortului fizic şi ele, la rândul lor, acţionează asupra vitezei de realizare a modificărilor metabolice cu rezultat direct asupra capacităţii de muncă a organismului

Cuvinte cheie: *carbohidraţi, ATP, efort fizic.*

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Introduction

In order to achieve performance, lifestyle and above all alimentation play a crucial part, both in the preparatory stages, but especially in the competition phase. For the best performance, athletes undergo a complex process of preparation during which the body is required to reach even the maximum physiological limits.

Carbohydrates during effort

Carbohydrates are organic compounds containing in their structure C, H, O and other elements found only on certain classes of compounds. The basic units of carbohydrates are the monosaccharides. Despite their similar chemical composition, carbohydrates can form an enormous number of combinations through the stereochemical variety of the hydroxyl groups that they carry many possibilities to assemble monosaccharides one to another, and through the wealth of noncarbohydrate substituents that can decorate the resulting oligo- and polysaccharides (Lombard V, 2014). Carbohydrates play primarily an energetic role, in addition to a structural and protective part.

Athletic performance is unthinkable without the involvement of carbohydrate. During prolonged muscular effort or when the external environment temperature is lowered, energy consumption is greatly increased and the need for carbohydrates increases as well. Carbohydrate oxidation accounts for 10–15% of total energy production during low intensity aerobic exercise, increasing progressively to roughly 70–80% of total energy during intense exercise (Holloszy JO, 1996).

There are two sources of glucose molecules available to the working muscle: plasma glucose and muscle glycogen. The modifications of certain biochemical parameters such as blood sugar levels depend on the exercise intensity and they, in turn, influence the speed of metabolic changes in the working capacity of the body (Crețu A, 2010). Glucose delivery to the working muscle is accelerated by a marked increase in capillary perfusion during exercise and by ingestion of carbohydrate rich meals or drinks as well as the permeability of the muscle membrane to glucose. The latter is regulated by a plethora of molecular signalling thought to include calcium, stretch and energy stress signalling and probably others. In the post-exercise recovery period, muscle glucose uptake displays an increased sensitivity to insulin in this way increasing glucose uptake after a meal in the muscles that have performed the exercise and therefore are in need of rebuilding their glycogen stores. (Thomas E Jensen, 2012). Furthermore, glucose utilization during exercise and the amount metabolized per unit of insulin plasma (used as an indicator of insulin sensitivity) increases especially when body weight loss is accompanied by physical exercise (Creţu A, 2010).

Carbohydrate in the form of glucose and intramuscular glycogen becomes an increasingly important energy substrate with rising exercise intensity (Holloszy JO, 1996). While very little net glycogen breakdown is observed at low-intensity exercise, glycogen-breakdown becomes the predominant glucose source at higher intensities (Hargreaves M, 1988), which resulted in the practice of high-carbohydrate diet regimens to increase pre-exercise glycogen levels (carbohydrate loading). However, skeletal muscle glycogen concentration exerts a regulatory effect on many cellular processes. For example, contraction-induced as well as insulin-stimulated glucose transport and glucose transporter 4 (GLUT4) translocation are inhibited by high muscle glycogen levels. (Richter EA, 2001.). A number of studies (De Bock K, 2008.), (Akerstrom TC, 2009.), (Hulston CJ, 2010), show that independent of prior training status, short-term (3–10 wk) training programs in which a portion of workouts are commenced with either low muscle glycogen and/or low exogenous glucose availability augment training adaptation to a greater extent than when all workouts are undertaken with normal or elevated glycogen stores.

Glycogen metabolisation

The two largest glycogen deposits in mammals are in the liver and skeletal muscle but many cells are capable of synthesizing glycogen. Both muscle and liver glycogen reserves are important for whole body glucose metabolism and their replenishment is linked hormonally to nutritional status. Control differs between muscle and liver in part due to the existence of different tissue-specific isoforms at key steps. Readily visualized by the electron microscope, glycogen granules appear as bead-like structures localized to specific subcellular locales. Each glycogen granule is a functional unit, not only containing carbohydrate, but also enzymes and other proteins needed for its metabolism. These proteins are not static, but rather associate and dissociate depending on the carbohydrate balance in the muscle (Shearer J, 2002).

Glycogen degradation and synthesis are relatively simple biochemical processes. Glycogenolysis is regulated by glycogen phosphorylase (GP), acting on the terminal α-1,4-glycosidic linked glucose residues, and debranching enzyme, targeting the α-1,6-branchpoints in the glycogen molecule (Roach, 2002). Therefore, glycogen degradation consists of three steps: (1) the release of glucose

1-phosphate from glycogen, (2) the remodeling of the glycogen substrate to permit further degradation, and (3) the conversion of glucose 1-phosphate into glucose 6-phosphate for further metabolism. The glucose 6-phosphate derived from the breakdown of glycogen has three fates (1) it is the initial substrate for glycolysis, (2) it can be processed by the pentose phosphate pathway to yield NADPH (nicotinamide adenine dinucleotide phosphate) and ribose derivatives; and (3) it can be converted into free glucose for release into the bloodstream. This conversion takes place mainly in the liver and to a lesser extent in the intestines and kidneys. The activity of GP is increased by allosteric binding of AMP (adenosine monophosphate) or IMP (inosine monophosphate) and competed by ATP or glucose-6-phosphate (G-6-P) (Roach, 2002).

Glycogen synthesis requires an activated form of glucose, uridine diphosphate glucose (UDP-glucose), which is formed by the reaction of UTP (uridine triphosphate) and glucose 1-phosphate. UDP-glucose is added to the nonreducing end of glycogen molecules. As is the case for glycogen degradation, the glycogen molecule must be remodeled for continued synthesis. Control of synthesis is shared between transport into the muscle and the step catalyzed by glycogen synthase (Roach, 2002).

Muscle glycogen serves only to fuel muscular activity and its utilization is controlled by muscle contraction and by catecholamines (Roach, 2002). Other studies show that after prolonged high-intensity exercise the depletion of glycogen is dependent on subcellular localization. In addition, the localization of glycogen appears to be influenced by fibre type prior to exercise, as well as carbohydrate availability during the subsequent period of recovery. These findings provide insight into the significance of fibre type-specific compartmentalization of glycogen metabolism in skeletal muscle during exerciseand subsequent recovery (Nielsen J, 2011).

Blood glucose level is kept constant by the liver glycogen reserves. When the blood glucose increases through the absorption of carbohydrates from the intestine, the excess is converted to glycogen in the liver and muscles, so that glycogenolysis that is replaced by glycogenesis. Skeletal muscle does not contribute directly to blood glucose levels, as it does not contain specific enzymes for the conversion of glucose-6-phosphate to glucose.

While certain enzymes such as glycogen synthase and glycogen phosphorylase have been extensively studied, other proteins such as the glycogen initiating and targeting proteins are just beginning to be understood. Two metabolically distinct forms of glycogen, pro- and marcoglycogen have been identified that vary in their carbohydrate complement per molecule and have different sensitivities to glycogen synthesis and degradation. The primer for glycogen synthesis is an autoglucosylating protein referred to as glycogenin.

While identifying and studying rodent muscle glycogenin, Lomako and colleagues (Lomako J, 1993) discovered that there were two forms of glycogen. These glycogen pools were shown to differ in size and protein content, with macroglycogen (MG) being the larger at 107 Da and proglycogen (PG) the smaller at 400 kDa. Both molecular forms contain only a single glycogenin but different amounts of CHO; thus they are separable via solubility in perchloric acid (PCA) because MG is soluble and PG precipitates. The literature (K. B. Adamo, 1998) demonstrates that at exhaustion, the MG store shows the greater relative depletion, and PG is the more sensitive to dietary CHO and is synthesized more rapidly after glycogen depletion. (K. B. Adamo, 1998) also demonstrated that the PG reaches a plateau at 24 h, whereas the MG pool continues to expand and is responsible for the supercompensation seen in the days after exhaustive exercise in a high CHO condition.

Gluconeogenesis (GNG)

Blood glucose is essential during prolonged periods of endurance exercise, when large changes occur in tissue oxygen delivery and use, metabolic rate, carbohydrate (CHO) oxidation, blood glucose disposal, and hepatic plus renal glucose production. Following an overnight fast, gluconeogenesis (GNG) provides 25–50% of total glucose production in resting humans, while the remainder is supported by hepatic glycogenolysis (GLY)((Bergman BC, 2000.) (Chandramouli V, 1997.) (Chen X, 1999.)). In resting humans after fasting for 40 h GNG accounts for nearly 90% of total glucose production (Staehr P, 2007). During submaximal exercise, energy demand requires muscle glucose utilization and, consequently, increases blood glucose disposal in order to prevent hypoglicemia (Brooks GA, 1994.) In contrast to rest, the relative contribution of GNG to total glucose production has been shown to decrease during hard exercise (Trimmer JK, 2002.)

Glycolysis durring effort

Glycolisis represents the enzymatic breakdown of a carbohydrate (as glucose) by way of phosphate derivatives with the production of pyruvic or lactic acid and energy stored in high-energy phosphate bonds of ATP.

The biochemical processes that occur during muscle contraction are very complex. The source of energy that triggers muscle contraction is ATP (adenosine triphosphate). There are three possible sources for ATP production: (a) *anaerobic alactacid metabolism* –the ATP-CP (phosphocreatine) or phosphagene phase, during which energy is provided from ATP stored in muscles and by phosphagene type degradation (ATP and creatine phosphate). ATP can be reconstructed by reducing phosphocreatine to creatine and inorganic phosphate, again providing energy for the ATP. This contraction stage is followed by the (b) *anaerobic lactacid metabolism*, with formation of lactic acid, given by an incompete glycogen breakdown during glycolisis. The production of lactate regenerates NAD+ (pyruvate is reduced to lactate while NADH is oxidized to NAD+), which is used up in oxidation of glyceraldehyde 3-phosphate during creation of pyruvate from glucose, and this ensures that energy production is maintained and exercise can continue. In the final stage of glycolysis (the production of pyruvate) ATP is generated. The anaerobic phase with the two components(alactacid and lactacid) is of great value as it provides the ATP energy molecules during muscle contraction in conditions of a lack of oxygen, a situation which is created after an intense physical effort. (c)*Aerobic metabolism*-oxidation or aerobic metabolism of carbohydrates and fats. In the body, muscle is continuously supplied with blood, and therefore oxygen. This causes a new phase of muscle contraction, which is more effective –the so called aerobic phase, and which provides a greater amount of energy.

Therefore, degradation of glycogen to lactic acid during the anaerobe phase and oxidative degradation of glycogen to carbon dioxide and water during the aerobe phase have no other role in muscle contraction but to obtain molecules of ATP, and creatinphosphate is used to recover the degraded ATP during muscle contraction.

Carbohydrate and fat utilization

There has been continued interest in the regulation of carbohydrate utilization in muscle tissue, as they are, together with fatty substances, the main substrates for energy production during exercise in well fed humans. The concept of a reciprocal relationship between fat and carbohydrate oxidation in muscle resulted from the work of Randle and colleagues in the 1960s (Randle PJ, 1963).

The relationship was called the "glucose–fatty acid (G–FA) cycle", and demonstrated the ability of increasing fat provision to downregulate carbohydrate metabolism in the heart and diaphragm. Furthermore, many investigations have demonstrated that increasing fat availability increases fat oxidation and decreases carbohydrate use in the whole body and skeletal muscle. By increasing the availability of free fatty acids to the working muscles, it was shown that carbohydrate downregulation during moderate and intense aerobic exercise occurred mainly at glycogen phosphorylase, the enzyme that regulates the degradation of muscle glycogen (Spriet, 2014). A main advantage of glucides over lipids is that after aerobic and anaerobic catabolism, energy is released at a rate almost three times higher in comparison with fatty substances. However, the energy released by 1 gram of carbohydrate is lower as to to the same amount of lipids.

Types of physical effort

Before classiffying physical effort, we consider necessary to define a few terms that describe different concepts: ”physical activity," "exercise," and "physical fitness". C. J. Caspersen states in his study (C J Caspersen, 1985) that physical activity is defined as any bodily movement produced by skeletal muscles that results in energy expenditure. The energy expenditure can be measured in kilocalories. Physical activity in daily life can be categorized into occupational, sports, conditioning, household, or other activities. Exercise is a subset of physical activity that is planned, structured, and repetitive and has as a final or an intermediate objective the improvement or maintenance of physical fitness. Physical fitness is a set of attributes that are either health- or skill-related.

In sport, physical effort can be classified according to several criterias: according to exercise intensity (maximum intensity effort, submaximal exercise intensity, exercise of high intensity, exercise of moderate intensity, low intensity exercise), according to the degree of oxygen supply to the body (anaerobic exercise, aerobic exercise, combined exercise), according to the type of muscle contraction (isotonic effort, isometric effort and isokinetic effort), based on energy consumption (light work, medium work, heavy work) and according to the load degree of the major systems of the body (neuromuscular effort, effort cardiopulmonary, endocrine-metabolic effort (ApostuM, 2003).

Depending on exercise intensity can be distinguished: maximum intensity effort, lasting 10-15 seconds, the energy released is from ATP, which is again created from phosphocreatine. Submaximal intensity effort, lasting up to 1 minute, the energy source used in addition to ATP is creatine-phosphate and glucose during anaerobe glycolysis which forms lactic acid. High intensity effort, lasting up to 6 minutes, releasing energy through the aerobic and anaerobic path. Moderate effort, lasting up to 60 minutes, the energy formation occurs via aerobic energy substrate -the carbohydrates. The after effort small oxygen deficiency is covered in this case by an increased oxygen consumption. Mild effort, lasting between 60 minutes and several hours, the energy formation occurs through the aerobe path using as substrate carbohydrates and fat. Fujimoto T et. al tested whether glucose uptake is enhanced in trained men during low-, moderate-, and high-intensity exercise as compared with untrained men. The results showed that skeletal muscle glucose uptake is higher in trained than in untrained men at high relative exercise intensity, although at lower relative exercise intensities no differences are observed. Thus, endurance training improves the capacity of contraction-induced glucose uptake in skeletal muscle (Fujimoto T, 2003).

Carbohydrates in skeletal muscles, heart and brain during physical exercise

Thorsten Rudroff et al. used positron emission tomography/computed tomography (PET/CT) and [18F]-FDG to test the hypothesis that glucose uptake (GU) heterogeneity in skeletal muscles as a measure of heterogeneity in muscle activity is greater in old than young men when they perform isometric contractions. The findings of the study demonstrated greater heterogeneity in GU in old men during two types of isometric contractions with the knee extensors. The GU measurements of muscle activation obtained with PET/CT imaging are consistent with age-associated differences in the modulation of muscle activation during tasks that require force or position control, but provide greater spatial information about the magnitude of the difference in muscle activity between young and old men when performing isometric contractions (Thorsten Rudroff, 2014).

Jukka Kemppainen investigated the effects of exercise on myocardial glucose uptake and whether the pattern of glucose uptake is the same as in skeletal muscle, as the heart has a greater oxygen consumption both at rest and during exercise compared to skeletal muscle (Rowell, 1986). Glucose uptake was measured using positron emission tomography (PET) and 2-[18F]fluoro-2-deoxy-D-glucose ([18F]FDG). The study demonstrated that myocardial glucose uptake is increased during mild- and moderate-intensity exercise, but is decreased during high-intensity exercise (Jukka Kemppainen, 2002).

Physiological activation increases glucose uptake locally in the brain. However, it is not known how high intensity exercise affects regional and global brain glucose uptake. Pellerin & Magistretti have introduced the astrocyte–neurone lactate shuttle hypothesis where lactate along with glucose serves as an oxidative fuel for elevated neuronal energy metabolism so that the largely glycolytic metabolism in astrocytes is linked with the largely oxidative metabolism of lactate in neurones (Pellerin L, 2003). The study of Kemppainen J demonstrated that brain glucose uptake decreases with increase in exercise intensity. Therefore substrates other than glucose, most likely lactate, are utilized by the brain in order to compensate the increased energy needed to maintain neuronal activity during high intensity exercise. Moreover, it seems that exercise training could be related to adaptive metabolic changes locally in the frontal cortical regions (Kemppainen J, 2005). The study by Kemppainen ***et al.*** provokes speculation as to the fate of the carbohydrate taken up by the brain. Secher NH states that lactate taken up by the activated brain is metabolized (Secher NH, 2005) as it does not accumulate within the brain or in the spinal fluid (Dalsgaard MK, 2004) and it is known to be a substitute for glucose metabolism (Magistretti PJ, 1999).

To conclude, during exercise the energy consumed in muscle tissue is mainly supplied by carbohydrates and fats. The use of intramuscular carbohydrate and lipid energy stores are coordinated during different types of exercise remains a subject of debate. The importance of muscle glycogen on performance during both prolonged and high intensity intermittent exercise has subsequently been confirmed in numerous studies. Furthermore, the major metabolic consequences of the adaptations of muscle to endurance exercise are a slower utilization of muscle glycogen and blood glucose, a greater reliance on fat oxidation, and less lactate production during exercise of a given intensity. These adaptations play an important role in the large increase in the ability to perform prolonged strenuous exercise that occurs in response to endurance exercise training.

REFERENCES

Akerstrom TC, F. C. (2009.). Glucose ingestion during endurance training does not alter adaptation. *J Appl Physiol,* l 106: 1771–1779. Article downloaded at the 12th October, 2014, from *http://jap. physiology. org/content/106/6/1771*

Apostu M. (2003). *Modificări biochimice induse de efortul sportiv.* Bucureşti: Arvin Press.

Bergman BC, H. M. (2000.). Endurance training increases gluconeogenesis during rest and exercise in men. *Am J Physiol Endocrinol Metab,* 278: E244–E251. Article downloaded at the 14th October, 2014, from *http://ajpendo. physiology. org/content/278/2/E244. long*

Brooks GA, M. J. (1994.). Balance of carbohydrate and lipid utilization during exercise: the “crossover” concept. *J Appl Physiol,* 76: 2253–2261.

C J Caspersen, K. E. (1985). Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep.,* 100(2): 126–131. Article downloaded at the 18th October, 2014, from *http://www. ncbi. nlm. nih. gov/pmc/articles/PMC1424733/?page=2*

Chandramouli V, E. K. (1997.). Quantifying gluconeogenesis during fasting. *Am J Physiol Endocrinol Metab,* 273: E1209–E1215.

Chen X, I.N. (1999.). The effects of free fatty acids on gluconeogenesis and glycogenolysis in normal subjects.. *J Clin Invest,* 103: 365–372. Article downloaded at the 12th October, 2014, from *http://www. jci. org/articles/view/5479*

Creţu Aurica, C. D. -I. (2010). The values of biochemical indicators in people who practice „maintenance" aerobics. *Studia Universitatis Babeş-Bolyai Chemia, nr. 2,* p. 375-380.

Dalsgaard MK et. al. (2004). A reduced cerebral metabolic ratio in exercise reflects metabolism and not accumulation of lactate within the human brain. *J Physiol.,* 554: 571–578. Article downloaded at the 22th October, 2014, from *http://www. ncbi. nlm. nih. gov/pmc/articles/PMC1664756/*

De Bock K, D.W. (2008.). Effect of training in the fasted state on metabolic responses during exercise with carbohydrate intake. *J Appl Physiol,* 104: 1045–1055. Article downloaded at the 12th October, 2014, from *http://jap. physiology. org/content/104/4/1045*

Fujimoto T, K.J. (2003). Skeletal muscle glucose uptake response to exercise in trained and untrained men. *Med Sci Sports Exerc.,* 35(5):777-83.

Hargreaves M, R. E. (1988). Regulation of skeletal muscle glycogenolysis during exercise.. *Can J Sport Sci.,* 13:197–203.

Holloszy JO, K.W. (1996). Regulation of carbohydrate and fat metabolism during and after exercise. *Annu Rev Nutr.,* 16:121–138.

Hulston CJ, V.M. (2010). Training with low muscle glycogen enhances fat metabolism in well-trained cyclists. *Med Sci Sports Exerc*, 42: 2046–2055. Article downloaded at the 16th October, 2014, from *http://www. ncbi. nlm. nih. gov/*

Jukka Kemppainen, T. F. (2002). Myocardial and skeletal muscle glucose uptake during exercise in humans. *J Physiol.,* 542(Pt 2): 403–412.

K.B. Adamo, M.A. (1998). Dietary carbohydrate and postexercise synthesis of proglycogen and macroglycogen in human skeletal muscle. *Am J Physiol. 1998 Aug*, 275(2 Pt 1):E229-34.

Kemppainen J, A.S. (2005). High intensity exercise decreases global brain glucose uptake in humans. *J Physiol.,* 568(Pt 1):323-32.

Lomako J, L.W. (1993). Glycogen synthesis in the astrocyte: from glycogenin to proglycogen to glycogen. *FASEB J.,* 7:1386–1393.

Lombard V, G.R. (2014). The carbohydrate-active enzymes database (CAZy) in 2013. *Nucleic Acids Res.,* 490-5. Article downloaded at the 19th October, 2014, from *http://www. ncbi. nlm. nih. gov/pmc/articles/PMC3965031/*

Magistretti PJ, et al. (1999). Energy on demand. *Science.,* 283:496–497.

Nielsen J, H.H. (2011). Human skeletal muscle glycogen utilization in exhaustive exercise: role of subcellular localization and fibre type. *J Physiol.,* 589(Pt 11):2871-85.

Pellerin L, M.P. (2003). How to balance the brain energy budget while spending glucose differently. *J Physiol.,* 546:325. Article downloaded at the 12th October, 2014, from *http://www. ncbi. nlm. nih. gov/pmc/articles/PMC2342533/*

Randle PJ, G.P. (1963). The glucose fatty-acid cycle. Its role in insulin sensitivity and the metabolic disturbances of diabetes mellitus. *Lancet*, 785–789.

Richter EA, D.W. (2001.). Glucose, exercise and insulin: emerging concepts. *J Physiol,* 535: 313–322.

Roach. (2002). Glycogen and its metabolis. *Curr Mol Med.,* 2:101–120.

Rowell, L. (1986). Human Circulation Regulation During Physical Stress. *New York:Oxford University Press*, pp. 96–256.

Secher NH, Q.B. (2005). Brain glucose and lactate uptake during exhaustive exercise. *J Physiol.,* 568(Pt 1):3.

Shearer J, G.T. (2002). New perspectives on the storage and organization of muscle glycogen. *Can J Appl Physiol.,* 27(2):179-203. Article downloaded at the 15th October, 2014, from *http://openurl. ebscohost. com*

Spriet, L.L. (2014). New Insights into the Interaction of Carbohydrate and Fat Metabolism During Exercise. *Sports Med.,* 87–96.

Staehr P, H. -N. O. -N. (2007). Hepatic autoregulation: response of glucose production and gluconeogenesis to increased glycogenolysis. *Am J Physiol Endocrinol Metab*, 292: E1265–E1269.

Thomas E Jensen, E.A. (2012). Regulation of glucose and glycogen metabolism during and after exercise. *J Physiol.,* 590(Pt 5): 1069–1076.

Thorsten Rudroff, J. H. -M. (2014). Greater glucose uptake heterogeneity in knee muscles of old compared to young men during isometric contractions detected by [18F]-FDG PET/CT. *Front Physiol.,* 195: 198. Article downloaded at the 12th October, 2014, from *http://www. ncbi. nlm. nih. gov/pmc/articles/PMC4035600/*

Trimmer JK, S.J. (2002.). Measurement of gluconeogenesis in exercising men by mass isotopomer distribution analysis. *J Appl Physiol,* 93: 233–241. Article downloaded at the 19th October, 2014, from *http://jap. physiology. org/content/93/1/233*