CHRONOBIOLOGY FROM THEORY TO SPORTS PRACTICE

Ľudmila Jančoková et al.

Towarzystwo Slowaków w Polsce
Krakow 2013

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The monograph is published with the financial support of *VEGA 1/0757/12 Reactive and Adaptation Indicators of Changes in Motor and Mental Abilities of Sportsmen in Relation to Bio-rhythms of Different Lengths*.

ISBN 978-83-7490-701-9

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PREFACE

The nature and its laws belong to key principles of the existence of the Universe as well as of the existence of us. They reflect constant changes in our solar system varying in forms and shapes. Everything unable to adapt to changed living conditions dies. Human being, nature, and their rhythmicity constitute the trinity of dynamic components contributing to qualitative and quantitative (de)synchronization of our world and existence. Their power and presence are indisputably proven by scientific statements dating back to 17th century that serve as the evidence for the basic theory of biorhythms even today.

Rhythmicity and rhythms as a part of the scientific discipline called chronobiology represent the wide range of contrasts whereas in context of a human being they are a portmanteau of their physical, intellectual, emotional, intuitive, aesthetic and spiritual features. In nature, they are manifested by the alternation of night and day, low and high tide, seasonal rhythm, week and lunar cycles. They symbolize brutal energy comparable to the power of our inner sea or inner clock whose ticking emerges and vanishes with us in the closed cycle of positive and negative sinusoids. Nowadays, chronobiology, biorhythms and health are discussed and talked over at various levels of social life, including medicine and sports, and this monograph “Chronobiology from theory to practice” proves it right. Team of prominent authors offers a wide range of local, as well as foreign theoretical knowledge and findings enriched by experimental verification of the biorhythms influence on physical, motoric and psychical level of a human being. The authors also extend and highlight the chronobiological approaches, applications and methods of researches to biorhythmical influence on sports performance and the applying of biorhythms to practice, as well as their mental and practical platforms of employing the biorhythms in the prevention, people's (sportsmen's) health and sportsmen's longevity.

The monograph is intended for a broad range of experts, particularly those interested in sports, since it represents the contribution to readers forethoughtful understanding of the importance of chronobiological approaches and dexterity not only within its theoretical background but mainly within the sport practice that will boost the sports performance leading to sportsmen's longevity.

My sincere thanks go to foreign and local authors who took part in creative process of the monograph and contributed to increase knowledge and possibilities of the application of chronobiology in the sport practice.

Ľudmila Jančoková

CONTENT

INTRODUCTION

Movement as a fundamental manifestation of life is an expression of the way of human existence and, at the same time, a tool for communication with oneself and one's surroundings. For thousands of years, it has been determined mostly by biological factors. It has become an integral part of preparation for life and a means of survival, as we can see by looking at the history, differing opinions and theoretical grounds of chronobiology in connection with movement and human health. This manifests itself in the efficiency of movement and in the importance of rhythmicity that determines qualitative and quantitative cyclic changes. If we aim at ideal performance and ideal response of the organism we should respect the principles of rhythmicity. Our physical activity, mental freshness and intellectual capacities oscillate between the top and the bottom of the sine waves representing daily, monthly, annual and multiannual rhythms. It has been proven that violation of these rhythms leads to various functional and structural health issues (depression, accelerated cell ageing, increased risk of cardiovascular diseases, etc.) and to a decrease in physical and mental performance. Although rhythms are independent from our will, they can be influenced in certain ways, what creates appropriate conditions for natural renewal of human biorhythms. They constitute one of the primary factors with an impact on our longevity and health.

The monograph is divided into five chapters providing the reader with general information on chronobiology and biological rhythms and on the most important starting points for potential practical application of this knowledge into the field of sports. At the same time, it serves as a generalized summary of daily, multi-daily, annual and multiannual biorhythms in association with their relationship with sport performance and their practical applicability. Visualisation and activational aspects of biorhythms offer the benefits of making practical use of the impact of time on neuromuscular performance and adaptation to time-specific training.
Ramadan and its impact on sport performance with the possibility of synchronization of circadian rhythms at difficult circumstances negate

and disprove some opinions on heliogeophysical processes and human metabolism determined by the Earth and Sun movement. The last part deals with the desynchronization of circadian rhythms in sportsmen - jet lag syndrome.

1 HISTORICAL AND PRESENT BACKGROUND OF CHRONOBIOLOGY AS A SCIENTIFIC DISCIPLINE

Ľudmila Jančoková

Chronobiology **–** "C*hronos*" (meaning time in Greek), "*biology*" (*bios* – life, *logos* – science) is a scientific discipline that objectively examines and quantifies mechanisms of biological time structure including important periodic signs of life from molecular level through unicellular organisms to a complex organism (human being). It also analyses periodic variations of biochemical, physiological and behavioural indicators called ***biological rhythms***.

Influenced by the existence of periodic rhythms in the environment, our civilisation has been developing for hundreds of millions of years. The development of life on Earth has been affected by cyclic interaction of the Sun, Moon and Earth since time immemorial. Therefore, it is necessary to look at the existence of the rhythmical variations in living organisms as well as at an adaptation to the planetary system. The basic biological periodicity was stored and preserved in the genomes of all organisms (Halberg, 2006; Homolka et al., 2010).

As early as prehistoric times, in order to preserve their existence our ancestors were observing planetary cycles and their changes within a day, within months and seasons. The then analogical observations of rhythmicity followed the needs of hunters, breeders or cultivators.

The man was watching the sky to measure his lifetime from one sunrise to another, from one new moon to the next one. The awareness of "**time**" is what distinguishes human beings from other living organisms. Only the man acquired the ability to perceive the time as a continuum of the past, present and future what made him conscious of the fact that his days are limited.

At the beginning of the civilisation, even before Christ, **the actual observation took place and was** documented in writing and published.

The author of the first written reference to the periodic signs of life especially in plants was ***Androthenus*** who wrote it 300 years BC (Pittendrigh, 1960; Reinberg and Smolensky, 1983; Pittendrigh and Harold, 1993; Arendt, 1998, 2006).

Scientific interest in periodic phenomena was increasing in the course of centuries but the recognition of chronobiology as a scientific discipline was a result of a lengthy process despite many significant discoveries achieved during its formation that later contributed to the current understanding of chronobiology.

Therefore, it is not surprising that ancient Greek and Roman scientists were already aware of certain bioperiodic phenomena. One of the most influential contributions in the historic and cultural context was ***Aristotle's*** physics. Until the 16th century, Aristotle*'s system was considered to be a reliable understanding of nature. According to his theory, the world consists of two spheres* – supralunar and sublunar. The supralunar sphere comprises the realm of the eternal order and ideal constitutions; the sublunar realm depends on the perpetual cycle of birth and death. Aristotle sought and found the empirical basis for the understanding of these changes in direct observation of periodic changes of anatomical structures of marine animals during the full moon (Jančoková, 2000, Homolka et al., 2010; Jančoková et. al, 2011; Wikipedia, 2013).

Cicero described the changes in oyster*s'* and other molluscs′ behaviour according to the moon phases. ***Pliny*** confirmed these observations. In his encyclopedia of natural history "*Historia naturalis",* he described low and high tide. The rhythmicity and its dependence on phenomena occurring in the external environment was the subject of research of ***Bacon*** and ***Kepler*** in the Middle Ages, as well as of other scientists in later periods (Aschoff, 1960, 1974; Agadžaňan, 1976; Agadžaňan et al., 1997, 2004).

The first findings about circadian and seasonal variations in physiological and pathological functions of a human organism are dated back as early as the 2nd century. They can be found in the writings of

Soranus of Ephesus, a physician working in Alexandria and later in Rome. His findings and notes were elaborated in the work "*De Morbis Acutis & Chronicis*" (Concerning Acute and Chronic Diseases) written by ***Caelius Aurelianus*** who, in the 5th century, was one of the first to state that: "...heavy breath and wheeze called asthma by the Greeks is an illness and a great burden, men suffer from it more than women, and the elderly more than the young ... more in winter and at night than in spring and during the day…" (Aurelianus, 1722, pp. 429 in Lemmer, 2009).

For centuries, people believed that periodic phenomena in a living organism represent simultaneous effects of cyclic changes in the environment (e.g. light-dark cycle, succession of the seasons, temperature fluctuations etc.). Until 1729, the doctrine of an endogenous origin of circadian rhythms, especially in plants, was generally acknowledged. In the same year, a French astronomer *Jean-Jacques d´Ortous* ***de Mairan*** conducted the first known experiment in the field of biological rhythms. He was observing the movement of leaves of some heliotrope plants throughout the day and night. When he placed plants into constant darkness, he noticed that their leaves continued to move at the same intervals (Romanov, 1980; Reinberg and Smolensky, 1983; Foster and Kreitzman, 2005, 2011; Daan, 2010). De Mairan came to the conclusion that heliotrope plants have their own internal clock. His observations would have passed unnoticed, if his colleague ***Marchant*** had not published his findings. The results of these observations were presented at the Academy in Paris. However, it was not de Mairan who presented them, but Marchant, who was a member of the Academy at the time. He pronounced the hypothesis that similar regular variations occur in human beings as well (Berger, 1980, 1995; Wikipedia, 2011). Thirty years later, in 1758, a French biologist *Duhamel* ***du Monceau*** verified the observations of de Mairan. Similar observations are also described in the works of *Georg Christoph* ***Lichtenberg***, *Carl von* ***Linné*** and *Charles* ***Darwin*** (Pittendrigh, 1960; Pittendrigh and Harold, 1993, Homolka et al., 2010). And it was a Swedish taxonomist ***Carl von Linné (Carolus Linnaeus),*** who pointed out that different plants open and close their flowers at exactly the same time. Therefore, in 1751, he made use of this knowledge to build a "*flower clock*" with which it was possible to determine the time of the day with a relative precision (Figure 1.1). It was mainly biologists who paid attention to cyclic motions of plants and who verified them by simple experiments (Ibarra, 2010).

Figure 1.1 Flower clock
(by Záhorská, 2013)

In 1832, almost 100 years later, Swiss biologist *Auguste Pyramus* ***de Candolle*** became the first scientist to give a well-founded explanation of how some factors of the external environment affect plants. He proved that a biological rhythm could be reoriented by which he discovered the inversion.

Botanist *Erwin* ***Bünning*** (1936) was another scientist who articulated the thesis on the existence of biological clock in organism that is able to differentiate time units and organize basic life functions accordingly.

First research related to the periodicity in human beings usually dealt with health conditions. In his works and memoirs, *Franz* ***Halberg*** states that his first encounter with timing in disease was related to circaseptan periodicity known even to ***Hippocrates*** in Greece, ***Galen*** in Rome and ***Avicenna*** in Persia. Based on his own practical experience, he claimed that, in most cases, the disease lasted for 7 days (Halberg, 2006).

According to the research he carried out, Franz Halberg discovered that a disease manifests itself by a circaseptan periodicity, even before taking sulphonamide and penicillin. (Halberg et al., 1965, 1974;

Hildebrandt et al., 1992; Cornélissen and Halberg, 1994; Halberg et al., 2003, 2012).

In 1614, ***Sanctorius*** of Padua***,*** an Italian physician and physiologist, published results of his long-term research in his work *De medicina STATIC aphorismi.* As a physician, he was concentrating on the development and improvement of instruments and devices designed to quantify the manifests of particular vital functions in a human organism. For thirty years, he was observing his metabolism by weighing himself and examining the divergences in his body weight throughout the day considering various metabolic processes (digestion, sleep and diet).

Furthermore, Sanctorius was also weighing all the food he ate, as well as his faeces. He discovered that his body weight fluctuated in a monthly rhythm similar to a 30-day cycle. To carry out his measurements and observations, he used a set of specially constructed devices including those designed for weighing (he built a huge weighing machine with a chair Figure 1.2), a thermometer (1612), a hygrometer, a trocar (to remove excess water from the abdomen and the chest), a catheter to remove kidney stones.

Figure 1.2 Sanctorius sitting in the weighing machine (1664)

In 1602, he invented the first machine system to measure heart rate and he named it the pulsilogium.

It is also worth mentioning his documentation of psychological changes reffering to Ecclesiastes: “To everything there is a season...” (Reinberg and Smolensky, 1983; Halberg et al., 1986; Lemer, 2009). For his pioneering and detailed studies, Sanctorius is considered to be the founding father of basal metabolism (Eknoyan, 1999).

Gradually, but yet sporadically, the first observations and documentations of other physiological functions and their changes in human body started to appear. Body temperature was among the first subjects of these observations. In 1782, German physicist *Christoph Friedrich* ***Elsner*** described in his book the variations of body temperature during the day with periodic changes in environment, sleep, wakefulness and diet. In 1806, *Paul Joseph* ***Barthez*** observed the fluctuation of body temperature during the day and night and found out that while sleeping, human body temperature is lower than after waking up. In 1845, *John* ***Davy*** was another scientist who described the variations in daily rhythm of the body temperature. In 1868, *Carl Reinhold Augusta* ***Wunderlich*** described in detail his observations of a 24-hour rhythm of body temperature during the night and day, in health and during illness. In 1887, an Italian physiologist *Angelo* ***Mosso*** envisaged the existence of oscillation in body temperature within the context of its today's understanding as an endogenous rhythm with attributes such as stability and plasticity.

General descriptions, as well as detailed measurements of other human biological rhythms can be found in numerous texts from ancient times. The first significant report was written by a German physician *Christoph Wilhelm* ***Hufeland*** more than 200 years ago**.** In his book "Die Kunst das menschliche Leben zu verlängern (1797)" (*The Art of Prolonging Human Life)* he says: "... period of twenty-four hours, formed by the regular revolution of the Earth, in which all its inhabitants partake,. . ., that is related to diseases too. This regular period is apparent in all diseases; and all the other small periods, so wonderful in our physical history, are by it in reality determined. It is as it were, „the unity of our natural chronology" (Mikeska and Petrásek, 1973; Mleztko and Mleztko, 1985; Lemmer, 2009). Aschoff (1991, 1998) remarked that considering ***Hufeland's*** theories, he may be considered as "the patron saint" of modern chronobiologists.

The dissertation on the importance of chronobiology and the research of biological rhythms in human beings by *Julien-Joseph* ***Virey*** (1814) is regarded as a strategic work in this field (Reinberg, et al, 2001; Lemmer, 2009; Ibarra, 2010). In his dissertation, Virey described the history of human life, as well as research on the circadian physiological functions indicating either health or illness. He not only characterized their periodic changes and the impact of drug dosage but he also paid attention to the basic mechanism of physiological functions. Virey referred to *Thomas* ***Sydenham***, who was considered to be one of the founders of clinical medicine and epidemiology at the time. Sydenham recommended administering of drugs in the evening to enhance their impact. Virey suggested that the biological clock is "entrained by the rapid movement of the Sun." He is considered to be the first chronopharmacologist since it was him who stated that "… no medication is equally indicated at all clock hours" (Reinberg, Lewy, Smolensky, 2001).

In 1806, a French physicist *Jean Arnaud* ***Murat*** described periodic phenomena in physiology developing Virey's thesis. His observations were based on constant and periodic motion of the Earth rotating on its axis that is ca. a 24-hour cycle and on the revolution of the Earth around the Sun that represents a 365-day-5-hour-49-minute cycle. His work is grounded in the findings concerning the phenomenon of periodicity of physiological functions that corresponds with the constant succession of night and day, which is represented by the alternation of sleep and wakefulness. Murat did not discover any correlation between menstrual and moon cycles during his observations. In this context, it is necessary to point out other facts related to physiological functions that did not pass unnoticed either.

The heart rate (pulse rate) is one of the physiological functions that do not remain constant throughout 24 hours. First findings about the heart rate fluctuation during night and day appeared at the beginning of the 17th century in the documents of Struthius (1602), Sanctorius (1631) and Targiri (1698). Elevated heart rate after waking up was documented and described as well (Lemmer, 2006, 2009).

In the 18th and 19th centuries and at the beginning of the 20th century, daily variations of the heart rate were generally observed and described in detail by several scientists: Bordenave (1787), Zimmermann (1793), Reil (1796), Falconer and Hufeland (1797), Autenrieth (1801), Barthez and Wilhelm (1806), Knox (1815), Grützman (1831), Howell (1897), Hill (1898), Hensen and Jellinek (1990), Weysse and Lutz (1915) (Lemer, 2009).

Polish physician *Josephus* ***Struthius***, was probably the first person who ever tried to synchronize different frequencies with quality of impulses using music. Struthius stated that variations in heart rate differ between men and women, sleep and wakefulness, health and illness and the seasons of the year. Struthius is one of the first scientists who claimed that the heart rate is regulated by internal and external factors. He also knew that aging may influence the heart rate. A few months later, the impact of these factors was confirmed by other authors whom we have already mentioned.

In 1767, *Le* ***Cat*** agreed on the influence of music on human psyche in his publication. He highlighted the fact that the power of music affects human mind and, by means of its own mechanisms, it has influence on human health too. Considering this, it is easy to understand the connection between two parts of a human being: the body and the soul. He also wrote about the elevated heart rate and blood pressure caused at the sight of doctors what he called the “white-coat syndrome”. The same had been stated by ***Targiri*** in his book Medicina Compendaria more than 300 years before where he had written that the heart rate and the blood pressure elevation may be caused not only by internal and external factors, but also by the presence of a doctor. Targiri also mentioned the fact that movement itself can increase the heart rate several times (Targiri, 1698, pp. 662 in Lemmer, 2009).

Johann Caspar ***Hellwig*** (pseudonym: Valentin Kräutermann) described similar observations and pointed out the importance of bedside manners. In 1756, *Théophil* ***de Bordeu*** came to similar conclusions concerning the necessity to measure the pulse several times and the phenomenon caused by presence of a doctor that he called “pulse of the doctor”.

However, back then it was difficult to measure the heart rate exactly, since there was no clock with minute accuracy. It was Sanctorius who became aware of this problem and, therefore, he invented the first apparatus for pulse rate measurement called pulsometer. He also added that it is possible to use pulsometer to observe how and when the pulse changes and that the change of the length of the pulsometer's pendulum could be later used for comparison (Figure 1.3).

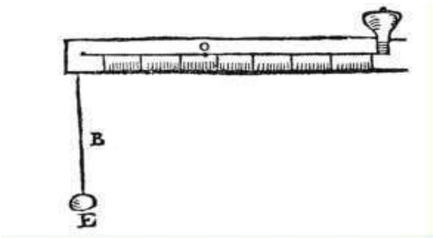

Figure 1.3 The apparatus for pulse rate measuring
(by Sanctorius, 1631)

The following years brought a good few documents on the heart rate rhythms of the healthy as well as the ill.

In 1776, *Carlo* ***Gandini*** suggested very precise recommendations on how to take the pulse rate – that is by applying pressure with fingers to the artery (Figure 1.4).

Figure 1.4 Pulse rate measurement
(by Carlo Gandini, 1776)

Other scientists also studied the pulse rate, for example *M.* ***Bordenave*** described the pulse rate in sleep and wakefulness in 1787. Furthermore, in 1793, a Swiss physician *Johann Georg* ***Zimmermann*** wrote that the pulse rate of human beings depends on the time of the day, mood, age and sex. He also noticed that the pulse rate increases when the fever occurs and suggested that the most effective way to take the pulse is to use the other hand.

From what was stated above, it is clear that the changes of the pulse rate throughout the night and day represented one of the most significant observations at the time. In 1796, *Johann Christian* ***Reil,*** a professor at the University of Halle, mentioned that the pulse rate increases towards the evening, but not because of some stimuli – it happens on account of the increased sensitivity of organism during the day (from morning to evening).

Description of heart rate was also included into physiology textbook in 1801. *Johann Heinrich Ferdinand* ***von Autenrieth***, teacher of anatomy, physiology and pharmacology at the University of Tűbingen in Germany, submitted accurate data for the heart rate according to the time of the day (1801). In adulthood, the heart rate is 65-70 bpm in the morning and 75-80 bpm in the evening. Furthermore, in his dissertation, Virey claims that the heart rate is at its lowest at 2-3 a.m.

It is interesting that *Gottlieb Wilhelm* ***Tobias*****,** an evangelic priest and a member of physicians and biologists association in Berlin and Halle, claimed in his book that the heart rate depends on a respiratory rate that is different for inhalation and exhalation. In 1806, a French encyclopaedist *Paul-Joseph* ***Barthez*** noticed the variations in vasodilatation throughout the day. In his book, he mentioned that dilatation of small vessels is more considerable in the evening and at night. Relative dilatation that occurs in vessels during sleep is more significant in veins than in arteries.

The observations of the period influenced the development of devices for the heart rhythm monitoring, measuring of heart rate became a part of diagnostic procedures and dilatation of blood vessels at night was documented (Lemmer and Portaluppi 1997; Lemmer, 2006; Portaluppi and Hermida, 2007).

As early as 1845, ***Bergman*** held an opinion that the origins and causes of rhythmicity are rooted in the organism itself (Mletzko and Mletzko, 1985). In the same year, *John* ***Davy*** was the first man who mentioned the existence of two rhythms: circadian and circa annual**.** The following decades also brought new findings about rhythmic processes in a human organism. *Angelo* ***Mosso*** (1892) and *John A.* ***Bergström*** (1894) focused on oscillations of physical and psychical performance of a human being throughout the day. *Ernst* ***Graffenberg*** (1893) observed the impact of light and dark on the amount of erythrocytes in blood.

The teaching of *Claude* ***Bernand*** (1845) played a major role in chronobiology (Poupa, 1961; Schreiber, 2005; Marduel, 2006). *Claude* Bernard is considered to be not only a founder of modern physiology, but also the author of the concept "***the environment within***" (milieu intérieur). He stood out thanks to his understanding of the stable internal environment and also to the discovery of the principle of homeostasis (Arendt, 2006; Den, 2013).

In the 17th and 18th centuries, the theoretical base of the experimental method was not well structured yet. The physiologists of the period were trying to prove their assumptions (hypotheses) by doing experiments. However, they had difficulties to interconnect their experience into a meaningful system**.** Only thanks to the Bernard's theory of the physicochemical stability of the internal environment of organisms the experiments were put in order. It was possible to measure and observe individual physicochemical parameters and their variability or invariability under various circumstances. The experiments became unified and gained certain continuity. Today, the homeostasis is considered to be one of the fundamental aspects of life possessing a biological clock.

The 19th century also brought great progress in natural sciences and increased interest in observation of various natural phenomena including periodic changes, as well as enriched methodological and diagnostic possibilities (e.g. with an exact thermometer), which enabled scientists to observe the variations in activities and reproduction (and similar phenomena e.g. change in colour or body temperature).

In the 20th century, publications dealing with considerably significant spectrum of oscillations in animal and human organism were published. The first scientific works with the objective of proving or influencing the functioning of the biological clock appeared. There were still numerous sceptics but more and more scientists understood that biological rhythms are one of the most important qualities of biological systems, as well as a significant feature of their singularity.

The beginning of the 1920s became a turning point in the research on rhythmic processes. At the time, studies of American physiologists *Wightman Wells* ***Garner*** and *Harry Ardell* ***Allard*** iscussing photoperiodism (the concept is still in use) came out. In 1923 – 1928, *Nathaniel* ***Kleitman*** published his observations of biorhythms of body temperature. In 1923, ***Jonson*** made a very interesting discovery, too. He found out that circadian rhythm does not last exactly 24 hours. In 1927, a Swedish physician *Eric* ***Forsgren*** described the 24-hour periodicity of some metabolic parameters (e.g. hepatic glycogen, biliary excretion) for the first time. *Jacob* ***Möllerström*** (1929) proved the existence of circadian rhythm in a decrease of certain blood values. From then on, the research on a wide spectrum of hormones, minerals, vitamins and other biologically important substances expanded, especially in relation to a 24-hour rhythm. *Erwin* ***Bünning*** (1936) pointed out that the photoperiodic time measurement could depend on internal circadian rhythms of sensitivity to light. In 1938, researchers Nathaniel Kleitman and Bruce Richardson spent 32 days in the Mammoth cave in Kentucky and observed their own physiological functions. Nathaniel Kleitman, who is considered to be a father of sleep research, published a book called "Sleep and Wakefulness" (1939). Together with his follower, Eugen Aserinsky, he described the REM sleep (Rapid eyes movement). Alongside with another of his followers, William Dement, they found the connection between the REM sleep and dreaming (Aserinsky and Kleitman, 1953; Dement and Kleitman, 1957; Dement, 2001).

Erich von ***Holst's*** publications (1937 and 1939) offer profound understandings of the interaction among various rhythms in an organism that has become an issue of great interest nowadays. That was probably the milestone that permitted the comprehension of the concept of "*biological clock*" (Reinberg and Smolensky, 1983; Chandrashekaran, 1998).

The idea that there is an "internal clock" affecting the organism was expressed by *Hudson* ***Hoagland*** in 1935 when he assumed the chemical character of time measurement and supposed that the physiologic time depends on the rate of certain chemical processes. In 1938 and 1940, mechanisms of biological rhythms were examined by *Hans Albrecht* ***Bethe***, who regarded the rhythmicity to be one of the basic characteristic of animate matter (Mletzko and Mletzková, 1985; Lee and Brown, 2007).

Eminent scientist and academician *Vladimir Ivanovich* ***Vernadsky*** scientifically proved the concept of biosphere. In his book "The Biosphere" (the first print in 1926), Vernadsky smartly supposed on the principle of empirical generalizations, that the Earth is a self-regulating system. He thought that life was and is a geological force shaping our planet Vernadskij, 1997). *Nikolai Evgenevich* ***Vedensky*** (1953) highlighted the issue of time factor with regard to physiological functions of particular tissues and organs.

In 1943, *Gregor* ***Pincus*** detected the fluctuation in excretion of 17-ketosteroids. The principle of long-term blood pressure fluctuations was first understood among others by an American professor *Franz* ***Halberg***, who laid the foundations of chronobiology as a scientific discipline in 1948 (Halberg, 1969). He proved that all biological values recur in cycles (ca. in 12-hour (ultradian), 24-hour (circadian), 7-day (circaseptan), or even longer cycles). These rhythms can be controlled by phase changes of the rhythms of exogenous environment and they emerged in the process of evolution. Their genetic determination was gradually confirmed at the molecular level, too (Pennisi, 1997). *Alexei Alexeyevich* ***Ukhtomsky*** (1936) was the first scientist to look into the problem of chronome in physiology when he called attention to the individual understanding of physiological time (chronotype). He adverted to its importance in connection with analysis of time mechanisms and principles of the ontogeny of a human being. Later on, Halberg introduced a new term **"chronome"** (from chronos – time and monos – rule) to name the system controlling the oscillations of biological variables in an organism. The mapping of a chronome, similarly to the mapping of a genome, could not only broaden our horizons but also be useful for practical purposes. It is very common that a change in average value of a biological variable due to disease follows after a change in its cyclic behaviour (Kuhlman et al., 2007; Singh, 2009; Halberg et al., 2006, 2007).

Based on the above mentioned findings that were especially interesting for medical science, "***The Society for Research on Biological Rhythms***" was founded by seven scientists in Roneby, Sweden in 1937. It was later renamed "***International Society for Chronobiology"*** (ISC), during the meeting in 1971 in Little Rock, Arkansas (Pauly and Scheving, 1987). In 1949, the 3rd international conference was held in Hamburg. The 4th one took place in Basel, Switzerland, in 1953 and was attended by many significant and influential chronobiologists of the 20th and 21st centuries (Holmgren et al., 1953; Menzel et al., 1955; Lemmer, 2009).

Jűrgen Aschoff, (1913 – 1998) who is deemed to be one of the founders of modern chronobiology participated in this conference, too. He worked as a director of Max Planck Institute for Behavioral Physiology in Andechs, Germany. The most famous of his experiments are those carried out with volunteers in isolation where they were continuously observed under constant conditions (Figure 1.5). Groups of teachers and students from the University of Munich spent periods of several-week in isolation while some of their physiological variables were measured with typical German precision (especially basal temperature, sleeping cycles, quality and chemistry of urine etc.) (Aschoff, 1990).

Figure 1.5 Interior of the "shelter" in Andechs, where volunteers spent periods of several-week cycles in isolation while rhythmical changes in their behaviour and certain physiological parameters were being observed (by Zeman, 2006).

Franz Halberg (1919 – 2013), referred to as the father of modern chronobiology, nicknamed the "Lord of Time", also attended the conference (Figure 1.6).

Figure 1.6 Franz Halberg

His contribution to chronobiology will be remembered together with his outstanding work throughout his life. He collected a great amount of information on his own, but also with cooperation of the expanding network of his colleagues all over the world. He developed inferential statistical methods to analyse and interpret biological rhythms.

Halberg founded the first chronobiological laboratory at the University of Minnesota, introduced the term circadian into scientific vocabulary in 1959 and was a joint author of the first chronobiological dictionary in 1977. In 1997, he became a co-founder of the worldwide project

BIOCOS focused on research of biological systems (BIO) in their environment (COS – cosmos). This international project gathers reference values all over the world, especially the data on blood pressure and heart rate, expressed in terms of time, sex and age in order to identify deviations in physiological range so that an early prophylactic intervention could both reduce consequences of the disease and serve basic transdisciplinary research (Halberg et al., 1998; Cornélissen et al., 2013a, b, c, d). In 2006, Halberg presented a graphic symbol that is now globally used as a "logo" for chronobiology as transdisciplinary science in scientific literature (Figure 1.7).

Figure 1.7 Logo of chronobiology as an independent and transdisciplinary discipline (by Halberg, 2011)

Other outstanding scientists who enriched the field of chronobiology and attended the conferences as well were primarily physicians such as ***Arthur Theodor Jores.*** He carried out very important research and observations on the rhythmicity of kidney function, pain sensation and other phenomena of medical chronobiology. ***Werner Menzel*** (1908 – 1998) did a lot of significant research in the field of clinical chronobiology. ***Günther Hildebrandt*** (1924 – 1999) from the University of Giessene was also one of the participants and his principal concern was to introduce chronobiology into medicine. He studied numerous fields of chronobiology including balneology, pain perception, lungs and heart functions.

The following conference in 1955 was attended by the botanist ***Erwin Bűnnin***g from the University of Tűbingen who is also considered to be one of the founding fathers of chronobiology and, along with Jürgen Aschoff; he is associated with the theory of internal clock (Bünning, 1935, 1936, 1963; Aschoff, 1990).

The question of endogeneity (i.e. rhythms endogenously generated in organism) seems to be a matter of course today but heated debates with arguments for and against had lasted for over 200 years and did not end until the half of the 20th century. In ***1960***, the first symposium of chronobiology took place in Cold Spring Harbor, Florida, where the foundations of this new field were laid. Scientific studies presented served as a model for identification and solving of the most pressing problems of chronobiology at the time (Aschoff, 1960; Pittendringh, 1960) Even today, the results of this conference provide inspiration for various scientific discoveries in various spheres of life from understanding of regulatory mechanisms of clock genes (Roenneberg and Merow, 2005; Dardente and Cermakian, 2007; Menaker, 2007; Brunner et al., 2008; Hastings et al., 2008; Illnerová and Sumová, 2008; Roenneberg et al., 2008; Takahashi et al., 2008) to the application of chronobiology into practice. Nowadays, similar conferences and symposiums are held regularly. They concentrate on different topics arising from the wide-ranging research carried out in the field of chronobiology in order to exchange experts' findings and experience.

Nevertheless, the human – environment relationship still represents a substantial problem. Just like any other living organism, a human being is a part of biosphere functionality and quality of which depends on ties to the external environment. Dependence of living organisms on external conditions is manifested by their adaptability. Inadequate adaptation is incongruous with lasting existence and vice versa, the adequate adaptation is necessary for the evolution of species. For this reason (to study mechanism of cosmic impact on biosystems) the international project BIOCOS (BIOsphere and the COSmos) was launched 30 June 1997 in Moscow, with the participation of researchers from USA, Europe, Russia, China, Japan and India. Prominent chronobiologists from Slovakia and The Czech Republic were also engaged in the project.

In this regard, it is important to mention the Russian scientist of world importance *Alexander Leonidovich* ***Chizhevsky***, the founder of heliobiology, who, from 1930s to 1950s, was probably one of the first researchers to discover certain solar activity repeating periodically in biosphere. Using a large amount of factual material, Chizhevsky (1976, 1979) he proved that human biological rhythms including human social rhythms depend on periodic solar activity. He also derived the principles related to e.g. epidemics of various diseases (Jagodinskij, 1987).

Chronobiology as a scientific discipline has gradually expanded to the point that now it constitutes a transdisciplinary field of study encompassing other domains that have become subjects of other independent studies (Rapoport et al, 2012):

Chronophysiology deals with time manifestations of physiological processes and evaluates circular interactions of nervous, endocrine, metabolic and other characteristics of an organism, that are subject to changes over time, as well as their interactions with environment (Scheving, Halberg and Pauly, 1974).

Chronopathology is a study of time variability of various biological characteristics that either determine diseases or are their consequences (psychoses, cancer, endocrinopathies, etc.) (Scheving, Halberg and Pauly, 1974; Švorc et al., 2008).

Chronopharmacology studies:
a) dependence of drug effects on time,
b) impact of the drug on time structure of the organism or its parts.

It covers:

- *Chronotoxicology* is a study of injurious and undesirable effects of chemical and physical agents including: toxins, pollution products and drug overdose in dependence on time and their impact on the time characteristics of the organism (Lemmer and Portaluppi, 1997; Reinberg, Lewy and Smolensky, 2001).

- *Chronotherapy* tries to prevent or treat diseases related to time characteristics (e.g.: corticosteroid therapy at doses simulating adrenocortical cycle required in case of Addison*'s* disease) (Haus et al., 1973; Ahlers, 1984, Mehling a Fluhr, 2006; Švorc et al., 2008).

Chronohygiene concentrates on the issue of human physical and psychological performance. Its main area of interest includes changes resulting from various factors from transmeridian flights to the impacts of shift work. We may cautiously talk about domains such as e.g. c*hronogenetics,* analyzing time continuity in this field of study or *chronogerontology* that analyzes timing within the process of aging (Zaguskin, 2010).

Chronopsychology focuses on rhythmicity mechanisms and functions within the scope of psychological variables such as memory, perception and emotional processes (Skočovský, 2004).

Blooming power of chronobiology also affected the "Sports Science" (Atkinson, Drust, Edwards, Postolache, Reilly, Šapošnikova, Waterhous), and within this field the so-called ***sports chronobiology*** has been formed. This discipline studies time frames for an effective development of movement predispositions and skills and their respective biochemical, physiological and psychological functions. Its main objective is to observe periodisation of sport training and of training process (microcycles, mesocycles, annual and multiannual cycles), focusing on adaptation mechanisms, timing in sports performance, physical fitness and also on elimination of the impact of desynchronisation factors (e.g. transmeridian flights, training at different altitude etc.) (Komarov and Rapoport, 2000; Postolache, 2005; Šapošnikova and Tajmazov, 2005; Michael, 2011) In Slovakia, the application of biorhythms into sports was studied by Valšík, Marcinková, Bartošík, by Štulrajter in the past and by Lipková, Sedliak, Jančoková, Pivovarniček, Kalinková, and others nowadays.

Academician *Ladislav* ***Dérer*** is one of the pioneering and internationally highly respected scientists in the field of human biological rhythms, especially from the point of view of medicine. The contribution of his work published in 2010 was appreciated by Prof. Halberg, who emphasized three points of Dérer's heritage: discovery of circaseptan rhythm alternations in the number of leucocytes in the blood of patients with chronic leukaemia, application of inferential statistics and the search for cosmic factors affecting diseases. His clinical intuitions and bold extrapolations were elaborated by his follower and successor Prof. *Miroslav* ***Mikulecký*** (a chronobiologist, or rather a chronocosmobiologist). The scope of his work covers biological rhythms and their relations to astronomical and geophysical cycles. *Michal* ***Zeman*** achieved results of international importance in the fields of chronobiology, endocrinology and developmental biology (Zeman et al., 2013). Some representative metabolic parameters were analysed by *Ivan* **Ahlers** (1984). Prof. *Helena Illnerová* is also an internationally recognized authority. Thanks to her contribution, The Czech Chronobiological School became very well known in scientific circles all around the world. She was the first in the world to make some groundbreaking discoveries. Her major subject of study is the time-keeping programme of mammals, including humans. The programme involves management and molecular mechanisms of daily and seasonal rhythms and their synchronisation with an external day.

Problems related to rhythmical changes in blood pressure and other biological parameters are the subject of study of the medical team from the Clinic of Physical Training Medicine and Rehabilitation at St. Anne´s University Hospital in Brno headed by Prof. *Jarmila Siegelová*, Prof. *Zdeňek Placheta* and Prof. *Peter Dobšák* (their research is related to the findings of the BIOCOS project). Other significant works from the field of chronobiology were written by a physiologist and prof. *Bohumil Fišer* from Brno (Homolka et al. 2010).

Historical timeline of the science chronobiology and also theoretical basis of chronobiological methodology, in present days, create indispensable aspect of revival and knowledge of latent natural biological rhythms which are one of the primary elements of retrospective view on philosophical regard of "cyclicality of time". The formation and development information of mentioned science are shared by scientists who report them through adequate statistical analysis of hypothesis timelines but also the way to the exact new chronobiology.

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2 BIOLOGICAL RHYTHMS IN NUROMUSCULAR PERFORMANCE

Milan Sedliak

Daily variation in many biochemical, metabolic and behavioural processes is a fundamental component of human physiology. The presence of daily variation is therefore no surprise when physical performance is considered. A term *diurnal*, used within this text, refers to daily rhythms in physical performance and means "day-related", in contrast to a term *nocturnal* which means "night-related". Up to date, a vast majority of scientists have examined rhythmicity of physical performance only during the light phase of 24 hours.

Physiological factors related to physical performance, such as metabolic variables (oxygen consumption, carbon dioxide output) and cardiorespiratory response (minute ventilation, heart rate, cardiac output, blood pressure etc.) have been shown to vary throughout the day at rest and/or during exercise. Also numerous sports tasks, e.g. standing long jump, tennis service, and swim time-trials exhibit diurnal variation (Atkinson and Speir, 1998; Kline et al. 2007; Reilly and Down, 1992; Winget et al., 1985).

It needs to be emphasized that it would be incorrect to speak of a single diurnal performance rhythm. For instance, Reilly et al. (2007) published an article consisting of two separate studies, during which different physical performance variables and football-specific skills were evaluated. The results of alertness and dribbling time tests were highest and those of fatigue lowest at 20:00 and all-specific skills of juggling performance peaked at 16:00. Also choice reaction time, flexibility, and right-hand grip strength were best between 16:00 and 20:00. Some more complex skills requiring a combination of coordination, postural control and/or strong psychological component tend to peak earlier in the day, e.g., the accuracy of first tennis serves (Atkinson and Speirs, 1998). However, the speed of first serves was highest at 18:00, compared to 14:00 and 09:00 h (Atkinson and Speirs, 1998). Also gross motor skills including anaerobic power output and self-chosen work-rate peak later in the early evening (Drust et al., 2005).

2.1 Diurnal variation in muscle strength and power

When focusing more specifically on maximum muscle strength and power, similar diurnal patter has been repeatedly reported in a temperate environment (around 17 – 23 °C) by numerous research groups. Morning nadirs (time of trough, or daily minimum) and afternoon maximum values is a common finding in both dynamic and isometric conditions with voluntary or electrically evoked contractions (Coldwells et al., 1994; Gauthier et al., 1996; Deschenes et al., 1998; Callard et al., 2000; Castaingts et al., 2004; Giacomoni et al., 2005; Guette et al., 2005a; Nicolas et al., 2005; Sedliak et al. 2008; Mora-Rodrıguez et al., 2012).

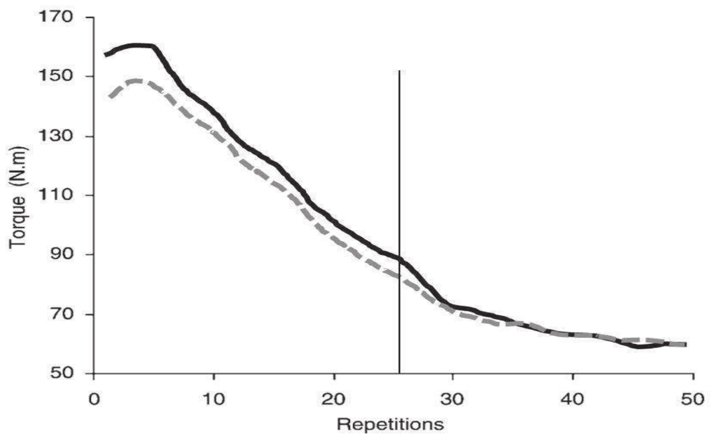

Figure 2.1 Relationship between mean torque values during isokinetic knee extension at the angular velocity of 2.09 rad. sec^{-1} and repetitions at 06:00 h (dashed grey line) and 18:00 (black line). The vertical line is a borderline to mark statistically significant differences (on the left) observed between 06:00 and 18:00. *Adopted from Nicolas et al. 2005.*

Under dynamic isokinetic conditions, diurnal variation is significant in both slow and fast speed of knee extensors and flexors movement, regardless of its expression as either peak torque or maximum work (Araujo et al., 2011). Interestingly, the skeletal muscle seems to be more fatigable in the evening compared to the morning (Figure 2.1, Nicolas et al., 2005).

Peak-to-trough variation of maximum strength and power has been reported to range from 5 % up to 21 % (Coldwells et al. 1994; Guette et al., 2005a). Even if considering only the lower end of 5 to 10%, it is considerably large not only for sports performance but also for any human activity requiring maximum/near to maximum strength and power. For instance, the risk of falls in elderly population could hypothetically be higher in the morning hours than later throughout the day. To prevent falls after, e.g., tripping, rapid force generation is required to perform some quick balance-correcting movements, especially in the lower extremities.

If an older individual has already reached his/her maximum power to prevent falling during the day, another power decrease of about 10% in the morning could mean an insufficient power level leading to a fall in case of loosing balance.

It needs to be pointed out that the above stated facts come from the studies performed on men. Based on very limited data, minimum-to-maximum difference of muscle strength seems to be smaller in women. In the very first study with female subjects, Phillips (1994) attempted to compare diurnal variations in maximal knee extension strength between men and women. A significant time-of-day effect for muscle strength was demonstrated only among men. In another study, Giacomoni et al. (2005) found less pronounced daily variations in a group of females compared to that of males. However, they admitted that their result has to be interpreted with caution as the female sample was very heterogeneous in regard to habitual physical activity. Another study from the same research group found 2,6% higher muscle strength at 18:00 compared to 06:00 h, but only under an electrical stimulation. The phase of menstrual cycle did not affect daily variation in their female sample. However, the phase of menstrual cycle seemed to have greater effect on female muscle strength than did the time-of-day effect (Bambaeichi et al., 2004). Clearly, very little is known about the rhythm characteristics of maximal muscle strength of females and further studies are required.

Putting the above facts together, it could be concluded that the phase (clock hours) of daily performance peak may depend to some extent on the task and variable involved. However, no single physiological variable related to a sports performance or task has been reported to peak in the morning soon after waking up (around 06:00 - 09:00 h). On the contrary, this is the time of day when physical performance is at its lowest point, at least when measured during daytime only. It needs to be mentioned that night-time performance values have not been widely studied. So the real performance nadir may be theoretically located during the night. A term "morning performance deficit" could be used to refer to this phenomenon.

2.2 Is the diurnal variation in muscle strength and power real?

Although diurnal variation in muscle strength and power is commonly reported, the exact mechanisms responsible for such an oscillation are not well understood. Actually, there has been scientific controversy as to the origin of diurnal variation in muscle strength (and other performance variables). In a thought-provoking review article from 1999, Youngstedt and O'Connor (1999) asked a question: is there a circadian rhythm of athletic performance? They proposed that diurnal variation in muscle strength and physical performance, in general, could be caused or affected by across-a-day differences in the following confounding factors: nutritional status, joint stiffness, sleep inertia, the time of usual activity, previous rest, environmental and body temperature, motivation and expectancy. These authors also called for more methodologically sound experiments to clearly distinguish between possible endogenous and exogenous factors.

Since then, several scientific manuscripts have been published to address possible confounding factors suggested by Youngstedt and O'Connor in 1999.

For instance, skeletal muscle stiffness is indeed higher and muscle temperature is lower in morning hours compared to the latter time of day (Onambele-Pearson and Pearson, 2007; Edwards et al., 2013). A proper passive and/or active warm up prior to morning testing could therefore reverse this morning feature and decrease/increase the morning muscle stiffness/temperature, respectively, to the afternoon levels. Subsequently, also morning strength would be improved to the afternoon level. Several authors have tested this hypothesis. Souissi and co-workers (2010) found that a 15 minute long active warm up improved morning performance compared to a 5 minute active warm up. However, even after the 15 minute warm up, both peak and mean mechanical power during the Wingate test were still significantly lower compared to the afternoon. Edwards and colleagues (2013) used even more sophisticated research design. They manipulated both core and muscle temperature by passive (whole body heating in a chamber at 35°C) and active warm up procedures. For the first time, they also controlled the efficacy of the active and passive warm up procedures by measuring intramuscular temperature. Edwards et al. concluded that raising morning rectal temperature to evening values by two different types of “warm-up” did not increase muscle strength (grip strength, maximum isometric and isokinetic knee extension) to values found in the evening. Racinais et al. (2005) published contradictory results. Strength varied with time of day when tested at 20.5°C. On the other hand, after one hour spent passively in a room heated to 29.5°C, the power increased resulting in diminishing the morning performance deficit. Taken together, the findings on the influence of morning warm-up on diurnal variation are conflicting, no doubt due to the differences in the experimental design e.g., the duration and intensity of the warm-up protocol, the site of temperature measurements, and the type of performance variable measured (Edwards et al., 2013).

Another possible confounding factor listed by Youngstedt and O'Connor was motivation. Giacomoni and colleagues (2005) induced superimposed electrical twitches to the muscle through the skin during voluntary isometric contractions. The superimposed electrical twitches technique allows assessing how much extra force can be generated by adding electrical impulses. Theoretically, if force is not further increased by electrical stimulation, voluntary activation and hence motivation, is maximal. Giacomoni and colleagues found that diurnal variation was significant only under electrical stimulation and suggest that motivation could have a masking effect on diurnal rhythm in muscle performance. On the other hand it also means that when the masking effect is removed, significant diurnal variation in muscle strength is present.

Based on the literature available up to date, we can be confident to state that diurnal variation in muscle strength and power is not merely a result of one or more confounding factors. However, various masking effects and confounding factors are likely to negatively affect the precise measuring of the diurnal variation extent.

We found, in a series of experiments, that the diurnal patterns of muscle strength and power were affected by confounding factors such as anticipatory stress and learning and/or improved inter-/intra-muscular coordination. This was the case despite a thorough familiarization procedure prior to the experiments. For instance, we tested power output during loaded squat jumps in untrained individuals and also in individuals with a 10-week training history of squat jumping (Sedliak et al., 2008). A loaded squat jump is a skill demanding multi-joint movement requiring rapid recruitment of many muscle groups in a proper time order. Indeed, untrained individuals showed lower diurnal minimum-to-maximum differences (~ 4%) compared to the trained ones (8%) suggesting a masking effect of skill level. The role of improved technique with repeated testing was again confirmed with untrained subjects in our later study (Sedliak et al., 2011). The time of the first session in that study was counter-balanced and randomized. Explosive leg press with a load of 50% of one repetition maximum (1-RM) was chosen as a test. Leg press exercise could be considered less skill-wise demanding compared to loaded squat jumps. Because it is performed in a sitting position with the torso supported by a back rest, the postural balance control requirements during the movement are reduced. As expected, a significant 8% mean difference was found between morning performance and the individual highest value in mean power output. However, the highest power output was typically exerted either during the third session or the last fourth test session (14 subjects out of 17 subjects) and the lowest in the morning (8 cases) or during the first session (in 10 subjects, including 3 subjects in the group starting the first session at 08:00 h). It is probable that learning, improved inter/intra-muscular coordination, training status, and skill level could be important confounding factors in explosive dynamic movements during the repeated testing. If technically demanding multi-joint dynamic actions need to be tested in untrained individuals or individuals unaccustomed to the specific test, a short-term task-specific conditioning training may be required in order to fully adapt to the testing demands.

Psychological factors are also capable of masking the diurnal variation in strength and power. For example, isometric strength levels during the first morning test session are higher compared to the morning test on the following day (Sedliak et al., 2008). Also morning serum cortisol concentrations were higher on the first test day compared to the consecutive morning (Sedliak et al., 2007). Anticipation of physical exercise was shown to increase stress levels and stress-related steroid hormone cortisol an hour prior to unfamiliar exercise but these responses disappeared already after the first test session (Mason et al., 1973). Anticipatory stress induces most likely elevated catecholamine concentrations which, in turn, can improve strength production (French et al., 2007). Increased circulatory catecholamine levels in the morning hours, induced via psychological stress or other factors may somewhat decrease the morning performance deficit. This hypothesis was partly confirmed by a Spanish study using high doses of caffeine (Mora-Rodriguez et al., 2012). Caffeine ingested in the morning hours induced significant increase in catecholamine levels and improved muscle strength to the afternoon levels. However, the "morning" tests were actually performed between 10:00 – 11:30 h in that study. It remains questionable whether caffeine would be similarly effective also in earlier morning hours (07:00 – 09:00 h).

Even if the existing scientific literature was convincible that the morning performance deficit in muscle strength and power is not an artefact, another question would arise. Is there an endogenous component in diurnal variation of neuromuscular performance? This question can not be answered based on the above-mentioned studies due to their testing design. Most of them were conducted under a protocol called "cyclic Latin square" (Folkard and Monk, 1980). In the cyclic Latin square protocol subjects perform the first session at different time of day in a counter-balanced order. The consecutive tests are separated by at least eight hours to avoid a cumulative fatigue onset due to the repeated testing. Subjects are not usually required to stay in a laboratory between the tests. Thus the data representing one diurnal cycle are collected across several days and might be actually a mixture of both diurnal and inter-day variability (Gleeson and Mercer, 1992). Other research groups used multiple testing within 24 hours (Callard et al., 2000; Gauthier et al., 1996, 1997). The between-test intervals are shorter in these protocols, e.g., Gauthier et al. (1997) measured six times per diurnal part of one day with 3-hour rest intervals. Our group used 4-hour rest intervals and the testing was expanded over two consecutive days, excluding the night time (Sedliak et al., 2008). It must be mentioned that no significant effect of cumulative fatigue was observed even with between-test intervals of 3 to 4 hours. There are, however, some methodological limitations with all the above laboratory protocols. Except for very few studies using also night time testing hours (e.g., Giacomoni et al., 2005; Araujo et al., 2011), the data available on muscle strength and power are limited to normal waking hours in humans. More importantly, in all the above-mentioned experiments, the subjects were not separated from the civil day time clues, like sunlight, usual times of food intake, social interactions etc. The presence of these environmental and social zeitgebers and/or factors able to mask circadian rhythm parameters make the separation of endogenous and exogenous rhythm components impossible. As a result, the endogenous component of the rhythm cannot be definitely proven.

In chronobiology, special laboratory-based protocols are used to asses whether daily (diurnal) variation in a selected variable has an endogenous, genetically driven component. Such protocols attempt to standardize or reduce the exogenous components of the rhythm, like energy intake, activity, posture, sleep, ambient temperature or light (Kline et al., 2007). These environmental and behavioral factors may "mask" the measurement of endogenous circadian rhythms. Several chronobiological protocols have been used with human subjects – free running protocol (Kleitman 1963), constant routine protocol (Czeisler et al., 1992; Duffy and Dijk, 2002) forced desynchronization protocol (Duffy et al., 1998; Dijk et al., 1992) or ultra short sleep/wake schedule (Buysse et al., 2005). A great review on the pros and cons of these chronobiological protocols when used in the area of sports and exercise chronobiology has been published by Reilly and Waterhouse in 2009. Briefly, the constant routine protocol requires the subjects to remain awake and sedentary for at least 24h in a constant environment, engage in similar activities throughout (reading or listening to music), and take identical meals regularly. It is clear that having subjects in recumbent posture dramatically restricts the variety of the performance tests. In addition, during each constant routine cycle, only a single measurement can be made, after which some time for recovery sleep and re-adjustment to a normal lifestyle is required. With the required minimum of 8 data collection points, the experiments would spread beyond 3 weeks in total per one individual (Reilly and Waterhouse, 2009). Also the forced desynchronization protocol spreads well beyond several consecutive days of stay in a laboratory per subject; even if a selected parameter can be sampled frequently, e.g., blood parameters. Testing physical performance parameters is more time-demanding. For some tests involving anaerobic or aerobic endurance, a minimum 8-hour rest period between each of the test exertions is needed to prevent cumulative fatigue effects (Drust et al., 2005). Shorter rest intervals could be administered for maximum strength and power. Actually, the only study supporting the notion of a strong endogenous influence in maximum muscle strength was done using a 28-h forced desynchronization protocol by Sargent and co-workers (2010). Eleven young male participants were kept in a laboratory for 12 days under a 9,3 h sleep and 18,7 h wake period. Static postural balance and maximum grip strength of the dominant hand were obtained every 2,5 h during wake. The circadian rhythm of muscle hand grip strength but not of static postural balance was present, with the highest values around the biological evening and the lowest around the core body temperature minimum (Sargent et al., 2010). Similar protocol could be used in future to examine circadian rhythm of other muscle groups in protocols involving not only static, but also high-resistance dynamic and explosive type of contractions during complex movements, e.g., loaded squat.

The ultra short sleep/wake schedule is another “unmasking” laboratory based protocol allowing the control for e.g., confounding effects of sleep and nutrition, thus separating the endogenous and exogenous components of biological rhythm (Buysse et al., 2005). From the practical point of view, the ultra short sleep/wake schedule is perhaps the most suitable in the area of sports and exercise chronobiology. It allows for multiple performance assessments over a short period of time with a relatively little sleep loss. The first, and by the year 2013 the only study within sports and exercise chronobiology done by employing the ultra-short sleep/wake schedule was published by Kline and colleagues in 2007 on swimming performance. Their schedule consisted of repeated 120 minute periods of out-of-bed wakefulness in dim light followed by 60 minute periods of attempted sleep in darkness, repeated throughout the 50-55 hour experiment. At minute 90 of each 120-min wake period, the participants ate a standardized meal. Each swimmer performed six maximal-effort 200-m swim trials, separated by 9 hours. The results of Kline and co-workers clearly showed that the fasted times could be achieved between 11:00 and 23:00 h, while the two time points with the slowest swim times were 05:00 and 08:00 h in the morning.

To conclude, very limited data obtained in humans either with forced desynchronization or ultra short sleep/wake schedule protocols suggest that the worst periods of day to perform well are indeed the end of the night and early morning hours. However, the clear direct evidence that there is a large endogenous component to the daily variation in muscle force production, e.g., from the central and/or peripheral clocks, is presently unsubstantiated. A challenge for future studies in the area of sports and exercise chronobiology is to verify an endogenous circadian component in muscle strength, power, and other types of exercise under appropriate chronobiological techniques.

2.3 Body temperature and exercise rhythms

Kline et al. (2007) examined circadian rhythm in swim performance not only relative to environmental clock times, but also to body temperature circadian rhythm. They found that the swim performance was worst from 1 hour before to 1 hour after the minimum of body temperature and best from 9 hours after to 5 hours before the minimum of body temperature.

Body (core) temperature has a well-established circadian rhythm. Together with the melatonin rhythm, circadian changes in core temperature are often used as a marker for the body clock. In subjects living a conventional life style, circadian changes in core temperature show maximum values with a plateau at about 14:00 to 20:00 h, and a minimum at about 05:00 h (Waterhouse et al., 2005). It is obvious that the circadian rhythm of core temperature coincides well with diurnal variation in muscle strength and power. Thus, there are several possibilities regarding the relationship between these two parameters. Firstly, there is no relationship and the similarity between these diurnal patterns is a mere coincidence. Secondly, the parallel variations in temperature and torque are independent and may stem from the drive of a common oscillator as proposed by Reinberg et al. already in 1988. Finally, the causal relationship is present where the diurnal variation in muscle strength and power is driven/moderated by the circadian rhythm in core body temperature. As to the mechanisms, the increase in force-generating capacity of the muscle and improved peripheral neural function due to higher evening core temperature and subsequently also local muscle temperature has been proposed (Melhim, 1993; Coldwells et al., 1994; Martin et al., 1999; Giacomoni et al. 2005). Reduced twitch time course or increase in the speed of contraction was suggested as a possible mechanism. Until recently, however, no study actually measured temperature inside the tested muscles. Two subsequent articles published in 2013 by a research group from Liverpool show that the local muscle temperature in vastus lateralis muscle indeed varies with the time of day, although with a smaller amplitude than does the core temperature (0,3 °C and 0,6 °C; respectively, Edwards et al., 2013).

More interestingly, they also examined the effect of manipulating the core and intramuscular temperature on diurnal variation in various indices of muscle strength and power. They used two different experimental approaches. In the first experiment, passive or active increasing of the morning core and intramuscular temperature to the afternoon levels could not diminish the morning performance deficit in grip strength, isokinetic knee flexion and extension force both at slow and fast speed, respectively (Edwards et al., 2013). In the second experiment, the researchers decreased subjects' afternoon rectal temperature to the morning values by cold water immersion. The post-cooling afternoon intramuscular temperature was found to be actually lower than the actual morning intramuscular temperature. As a result of artificially decreased core and rectal temperature in the afternoon, significantly reduced force or power towards morning values was observed (Robinson et al., 2013). These contradictory findings highlight the methodological issues related to different physiological mechanisms involved in cooling versus warming the core and muscle and its effects on performance, as previously suggested by Racinais and Oksa in their review (2010). As concluded by Robinson and colleagues (2013), the morning performance deficit in muscle force and power, when diurnal variations in core and muscle temperatures are evident, cannot be attributed wholly to the body temperature circadian variation.

2.4 Local and/or peripheral origin of circadian rhythm in muscle strength and power

Robinson and colleagues (2013) also concluded, in accord with the views of Guette et al. (2005b) and Martin et al. (1999), that morning-to-evening differences in muscle force and power involve both body temperature-dependent and temperature–independent local/peripheral mechanisms. An important question arises: what are these local/peripheral mechanisms? Theoretically, local mechanisms are located within the muscle cells. Diurnal differences in the ratio of cross bridges in the weakly to the strongly bound state, in intracellular calcium and inorganic phosphate concentration were proposed among the possible intracellular mechanisms (Martin et al., 1999; Onambele-

Pearson and Pearson, 2007). Also regulation of some clock and clock-related genes in skeletal muscle may vary with the time of day (Zambon et al., 2003). Peripheral mechanisms include changes within the central and peripheral nervous system involving, for instance, CNS activity, nerve conductivity and/or reflex function.

Another question is what it the relative contribution of the local versus peripheral mechanisms to the diurnal variation in muscle strength and power. There are various methodological approaches enabling to address this issue. For instance, muscle tone was measured in one of our studies by a computer-controlled tonometer device (Sedliak et al., 2011). Muscle tone has been proposed to indirectly estimate a) the state (and changes) of the viscoelastic and mechanical properties of the joint–tendon–muscle complex (Watkins, 1999) and, in case of some pathological conditions, it also reflects the state (and changes) of the central nervous system-related activity, such as activity of alpha motoneurons and/or activity of muscle spindles or gamma motoneurons. We, however, failed to observe any diurnal changes in muscle tone. Hence, muscle tone could be disregarded as a possible (co)-factor contributing to diurnal variation in muscle strength and power.

Another experimental approach frequently used to study the mechanisms of neuromuscular performace is surface electromyography (EMG). Surface EMG measures the electrical activity present on the skin surface, where it is spread from skeletal muscle cell membranes upon their depolarization causing subsequently a contraction of the depolarized muscle cells. The depolarization can be induced voluntarily via motor neuron firing and/or with various types of artificial external stimulation. Commonly used external stimulus types are transcutaneous electrical stimulation of muscle and peripheral motor nerve, and electromagnetic stimulation of the motor cortex of the brain via a transcranial magnetic stimulation (TMS) method in the recent years. The basic approach is to evaluate how much EMG signal is present during voluntary contractions. The first chronobiological study using EMG technique during voluntary isometric contractions of elbow extensors was published by Gauthier et al. in 1996. They found that the EMG signal was the biggest at 09:00 h in antiphase to the diurnal rhythms of the torque peaking in the afternoon. Gauthier and co-workers (1996) also used so-called neuromuscular efficiency measure, which is the ratio of the torque produced to EMG signal. More torque produced with less EMG activity (less neural input) means higher neuromuscular efficiency. The torque/EMG ratio was significantly lower at 09:00 than at 18:00 h meaning that neuromuscular efficiency is higher in the afternoon according to the study of Gauthier et al. (1996). They concluded that diurnal variation in torque is due to both the contractile state of the muscle and central nervous system command. Since then, numerous chronobiological studies have been published using various techniques and analyses of EMG and muscle groups. The summary is presented in Table 2.1.

Overview of the scientific studies on diurnal variation in neuromuscular performance using surface EMG. Abbreviations: CNS – Central nervous system, H reflex - Hoffmann reflex, IT – Interpolated twitch, MEP - Motor-evoked potentials, MVC – Maximal voluntary contraction, RMS = Root mean square, TC – Tetanic contraction

Table 2.1, part 1

Authors & year of publication	Sample size & test design	Test & muscle(s) tested	Muscle strength	EMG and muscle activation	Neuromuscular efficiency	Antagonist co-activation	Suggested mechanism(s) for diurnal variation
Gauthier,A. Davenne,D. Martin,A. Cometti,G. Van Hoecke,J.**1996**	7 males, 6 females 06:00, 09:00,12:00,15:00, 18:00, 21:00, 24:00 across the same day	elbow flexion, isometric **MVC at 90º** and at 25, 50, 75% of MVC **elbow flexors,** nondominant arm	Peak torque **highest at 18.00,** lowest **at 09:00**,	maximum RMS of biceps brachii. **higher at 09:00** than **18:00**	maximum at **18:00**, minimum at 09:00 RMS/torque ratio	—	both **neural** and **contractile state of muscle**
Martin,A. Carpentier,A. Guissard,N. van Hoecke,J. Duchateau,J. **1999**	12 males, 1 female 07:00 and 18:00, counterbalanced, within 24 h	thumb adduction, isometric **MVC** and at 25, 50, 75% of MVC, **TC, IT**, adductor policis, left arm	Peak torque **higher at 18.00** than **at 07:00** (8.9%)	absolute RMS - **no difference**, muscle activation - **no difference** (07:00-97,1%, 18:00-98,5%), tetanus torque **higher at 18:00**	**no difference** - RMS/force	—	**contractile state of muscle**
Castaingts,V. Martin,A. Van Hoecke,J. Perot,C. **2004**	11 males, 06:00 and 18:00 within the same day	plantar flexion, drop jumps, isometric **MVC at 90º**, 25% of MVC, **T reflex, IT, jumping height,** soleus and gastrocnemius muscles	Peak torque **higher at 18:00** than **at 06:00** (8,6%), Drop jump height **higher at 18:00** (10.9 %)	mean amplitude during MVC - **no difference**	el.stimulation and drop jump – higher at 18:00, reflex stim.MVC and 25% MVC25 - unchanged	—	for efficiency: both **peripheral** and **central mechanisms** – test depended!
Nicolas,A. Gauthier,A. Bessot,N. Moussay,S. Davenne,D. **2005**	12 males, 06:00 and 18:00, separated by 36h	isokinetic knee extension, 50 **MVC** repetitions, vastus medialis, lateralis, rectus femoris and biceps femoris, dominant leg	Peak torque **higher at 18:00** than **at 06:00** (7.7%)	RMS of agonist muscles - **no difference**	fatigue protocol: decrease **higher at 18:00** but during first 20 reps only	biceps femoris % RMS - **no difference**	for fatigue: **peripheral mechanisms** - higher contractile capacity but lower fatigue resistance at 18:00
Guette,M. Gondin,J. Martin,A. **2005**	10 males, 06:00, 10:00, 14:00, 18:00, 22:00, minimum 8h separation	unilat. knee extension, isometric **MVC at 90º, IT**, vastus medialis, lateralis, rectus femoris and semitendinosus, dominant leg	Peak torque **highest at 18:00, lowest at 06:00** (6.6%)	M-wave, muscle activation, RMS/M-wave ratio - **no difference**, rate of torque development - **lower at 06:00** than at 14:00, 18:00 and 22:00	—	semitendinosus % RMS - **no difference (9.3-11.6%)**	modification **at the muscular level**
Guette,M. Gondin,J. Martin,A. **2005**	12 males, 06:00-08:00, 17:00-19:00 within the same day	unilat. plantar flexion, isometric **MVC at 90º**, H reflex, M-wave, **twitch torque,** soleus muscle, dominant leg	Peak torque and **higher in the morning** than afternoon (4.7%),	Normalised EMG (RMS/M-wave) and H-wave twitch torque **higher in the morning** than afternoon	—	—	spinal reflex excitability not involved in reduction of force
Guette,M. Gondin,J. Martin,A. Perot,C. Van Hoecke,J. **2006**	11 males, 06:00-08:00, 17:00-19:00 within the same day or two consecutive days	unilat. plantar flexion, isometric **MVC at 90º, IT, TC,** soleus, gastrocnemius med. and lat., tibialis anterior, dominant leg	Peak torque and **higher in the morning** than afternoon (7%),	**Higher morning** normalised **soleus** EMG (21,6%) and muscle activation (6,8%), single twitch and tetanus torque - **unchanged**	—	tibialis anterior % RMS - **no difference** (17%)	**impairment of the central command**

Table 2.1, part 2

Authors & year of publication	Sample size & test design	Test & muscle(s) tested	Muscle strength	EMG and muscle activation	Neuromuscular efficiency	Antagonist co-activation	Suggested mechanism(s) for diurnal variation
Giacomoni,M. Billaut,F. Falgairette,G **2006**	12 males, 08:00-10:00, 17:00-19:00, at least 36 hours recovery	unilat. knee extension, isometric **MVC at 90°**, vastus lateralis, dominant leg	**no difference** in peak torque MVC	**no difference** in RMS of vastus lateralis	**no difference** in torque/RMS ratio	—	not reported
Giacomoni,M. Edwards,B. Bambaeichi,E. **2005**	12 males, 8 females, 02:00, 06:00, 10:00,14:00, 18:00, 22:00 randomly over 3-4 days	unilat. knee extension and flexion, **isometric MVC at 90°, IT,** isokinetic **MVC**	**no significant** peaks at 14:00 or 18:00 for or isometric and isokinetic peak torques during flexions and extensions	**highest** superimposed twitch torque **at 18:00**, **lowest at 06:00** only **in males**	—	—	not reported, suggested masking effect of motivation
Racinais,S. Blonc,S. Jonville,S. Hue,O. **2005**	11 males, 07:00-09:00, 17:00-19:00, two times both in random order in normal and warm conditions	knee extension, isometric **MVC** and at 25, 50, 75% of MVC, vastus lateralis	Peak torque **higher in the afternoon (+8.4%)** but not in hot and humid environment	**no difference** in RMS of vastus lateralis	—	—	**contractile state of muscle,** partly due to low morning muscle (body) temperature
Onambele-Pearson,N.L. Pearson,S.J. **2007**	12 males, M=7, N=5; 07:45, 17:45, counterbalanced, within 24 hours	unilat. knee extension, isometric **MVC** between **90 and 30°, IT,** biceps femoris	Peak torque **higher in the afternoon** at knee angles from **75 to 90°**	**no difference** in muscle activation (91% and 88% for morning and evening, respectively)	—	biceps femoris % RMS - **no difference** (4.5% and 4.2%)	**contractile state of muscle,** unknown mechanism proposed to counteract 21% evening decrease in patellar tendon stiffness
Sedliak M., Finni, T., Cheng, S., Haikarainen T., Häkkinen K. **2008**	32 young untrained males, 07:00, 12:00,17:00, 20:30, repeatedly over 2 consecutive days	knee extension, isometric **MVC** and at 40 % of MVC, vastus lateralis, medialis, rectus femoris, biceps femoris	Peak torque **lower at 07:00 (-6 to -8 %)** compared to other test times on day 2 only	**no difference** in RMS of all quadriceps femoris muscles during MVC or 40 % of MVC	**higher at 20:30** compared to **07:00** during **40 % of MVC,** first day only, **no difference** during MVC	biceps femoris RMS - **no difference** during or 40 % of MVC	**contractile properties of muscle**
Tamm, A.S., Lagerquist, O., Ley, A.L., Collins D.F. **2009**	Morning chronotype (3 females, 6 males), evening chronotype (1 female, 8 males), 09:00, 13:00,17:00, 21:00 within the same day	plantar flexion, isometric **MVC, IT, MEP, H reflex, M-wave,** soleus, lateral gastrocnemius, medial gastrocnemius, and tibialis anterior	peak torque in morning chronotype **lower at 09:00** compared to **17:00** (+8 %) and **21:00** (+13 %), **no difference** in evening chronotype	normalized **EMG lower at 09:00** compared to 17:00 and 21:00 **(evening type only)**, **no difference** in muscle activation, **cortical excitability highest at 09:00 and 21:00 in morning and evening group, respectively**	**no differences**	Tibialis anterior average **EMG higher at 09:00** compared to **17:00 and 21:00 in morning** chronotype	**central - increased CNS drive** to the muscle due to concomitant increases in spinal and cortical excitability - **chronotype dependent**
Sedliak M., Haverinen, Häkkinen K. **2011**	17 young untrained males, 08:00, 12:00,16:00, 20:00, repeatedly over 2 consecutive days	bilateral leg extension at 107° as isometric **MVC** and in dynamic explosive mode, **mean power output**, vastus lateralis, vastus medialis, biceps femoris	**peak force** and **mean power output at 08:00 significantly lower** compared with the individual highest peak force	RMS of vastus lateralis and vastus lateralis + medialis **lower at 07:00** compared to **20:30, significant correlation between RMS** of v. lateralis **and peak force**	—	biceps femoris RMS - **no difference** (from 20 % to 23 % of RMS during knee flexion MVC)	both **peripheral** and **central mechanisms**

Intriguingly, various studies have yielded conflicting results. Briefly, Castaingts et al. (2004) reported, similarly to Gauthier et al. (1996), that both central (neural input to the muscles) and peripheral (contractile state of the muscle) mechanisms may alter across a day. On the contrary, Martin et al. (1999), Nicolas et al. (2005) and Guette et al. (2005b) suggested that agonist (but not antagonist) muscle tissue and its contractile properties are the source of diurnal changes in peak torque. A similar conclusion was drawn by Giacomoni et al. (2005), reporting a significant diurnal variation only when electrical twitches were superimposed during MVC, but in men only. They proposed that a motivational component could have a masking effect on the diurnal variation in voluntary maximum strength of the knee extensors. Contradictory results came also from our laboratory. In the first study, measuring isometric peak torque during knee extension over two consecutive days, the EMG signal did not vary with the time of day (Sedliak et al., 2008). In the second study using a counter-balanced clock time of the first session, an EMG signal was smaller at 08:00 compared to 20:00 h and co-varied similarly with the maximum isometric force during leg extension on a leg-press device. Moreover, the daily changes in EMG signal from the vastus lateralis muscle were significantly correlated with muscle force produced during the same test action. We concluded that diurnal changes in neural drive, motor unit and/or muscle membrane properties cannot be fully disregarded as possible additional sources of variation in muscle strength and power. These conflicting results from our laboratory and also in literature could be, in part, accounted for by one or more of: differences in the test design and/or the test mode, muscle groups tested (upper versus lower extremities), training background and test-specific skill level of the subject. Another important issue is the methodological differences in the surface bipolar EMG data recording and analysis procedures, especially when EMG is measured during voluntary contractions only. In addition, despite thorough control of the measurement procedures, EMG is always subject to various sources of error (Keenan et al., 2006). Therefore, it is advantageous to combine voluntary EMG recordings with other laboratory techniques.

Alexander Tamm and co-workers published in 2009 perhaps the most comprehensive experimental work in this field up-to-date combining voluntary EMG with electrical stimulation and also transcranial magnetic stimulation. Contrary to the majority of studies, they selected subjects belonging either to the extreme morning or evening chronotypes. They interpreted their results as follows: in the morning chronotypes, cortical excitability was highest at 09:00 h, spinal excitability was highest at 21:00 h, and there were no significant differences in isometric EMG and torque produced by calf muscles over the day. In contrast, evening chronotypes showed parallel increases in cortical and spinal excitability over the day, and these were associated with increased EMG and torque. Tamm et al. (2009) proposed that the simultaneous increases in cortical and spinal excitability increased central nervous system drive to the muscles of evening people, thus increasing torque production over the day. Combining these results with the rest of scientific literature available, it seems apparent that inputs form the central nervous system are, at least partly, an important source of diurnal variation in muscle strength and power. Further studies are warranted to clearly confirm or deny the importance of the local intracellular factors.

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3 TIME-OF-DAY-SPECIFIC TRAINING ADAPTATIONS

Milan Sedliak

Speculation that adaptations to exercise training might be specific to the time of day of training was first mentioned in a book "Body time; physiological rhythms and social stress" (Luce, 1971). The theoretical basis for this assumption was based on a circadian variation in human physiology functions related to performance.

Several questions emerge regarding the possibility of training adaptation to specific time of day: for instance, could morning performance deficit be diminished by regular morning training? Could a regular exercise at certain clock time lead to differentiated training adaptations compared to other times e.g., morning versus evening training schedule? Could a repeated or chronic exercise induce a phase shift/modulation of a circadian clock? The next chapter tries to shed some light on these questions.

Firstly it must be pointed out that the scientific data related directly to time-of-day-specific training adaptations are very limited.

The first direct evidence that time of day might significantly influence training adaptations in humans or as the authors entitled it "circadian specificity in training" was given by Hill et al. (1989). They used combined cycling or running exercise either as interval or continuous training sessions at about 90 to 100 % of VO_2 max. These authors reported that after a 6-week interval training period the subjects who trained in the morning between 06:00 and 08:30 h had a relatively higher ventilatory threshold in the morning, while the subjects who trained in the afternoon between 15:30 and 18:00 h had relatively higher values at that time of the day. Later Torii et al. (1992) demonstrated that aerobic training had a significantly higher effect in the afternoon (15:00 h) compared to the morning (09:00 h) and evening (20:00 h) training sessions. However, it was probably due to a methodological bias rather than a real adaptation effect, as all subjects were tested only in the afternoon between 14:00 and 16:00 h. Hence, the afternoon training group had an advantage of being tested at the training specific clock-time as compared to the morning and evening training groups. Indeed, a later study confirmed that greater improvements (in time to exhaustion and oxygen deficit after interval training) can be expected to occur at the time of day at which training is regularly performed, but the magnitude of adaptations is similar. High intensity interval training mode was used by Hill et al. (1998). Over a 5-week period repeated bouts of cycling lasting from 1 to 3 minutes were performed either in the morning or in the afternoon four times a week. They concluded that greater improvements can be expected to occur at the time of day at which high-intensity training is regularly performed.

3.1 Time-of-day-specific adaptation to resistance training – maximum strength and power

A similar pattern of time-of-day-specific training adaptation as reported by Hill et al. (1998) was found in the first resistance training study carried out by Nizar Souissi et al. (2002). In the experiment of Souissi and colleagues, two groups of young adult males performed an identical 6-week progressive high-load type of training either only in the morning (07:00–08:00 h) or only in the evening (17:00–18:00 h). 14 physical education male students trained twice a week using a leg extension device. Time-of-day-specific adaptation was present despite the fact that the training volume was rather low. The morning performance deficit diminished in the morning training group but remained in the afternoon training group. In other words, after 6 weeks of resistance training the men, who trained in the morning, but not in the afternoon, could perform equally well both in the morning and afternoon hours. This was true for both isokinetic peak torque during knee extension (Figure 3.1) and, interestingly, also for peak anaerobic power during the Wingate test. Importantly, no significant difference between the two groups was observed in the magnitude of peak torque and peak anaerobic power improvement, as well as in one repetition maximum (1-RM) knee extension (maximum load supported).

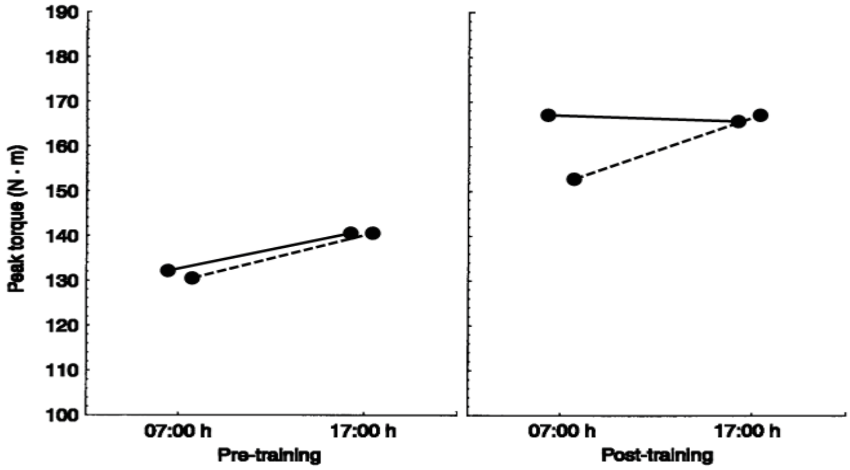

Figure 3.1 Isokinetic peak torque for knee extension of the groups at the two times of day before and after training (mean ± SD). black line - morning training group, dashed line - evening training group. *Adopted from Souissi et al. 2002.*

A Tunisian-French group lead by Nizar Souissi published in 2012 a series of manuscripts extending the first resistance training study to a broader spectrum of performance variables and also population types. Besides maximum strength test and Wingate test, unloaded squat and countermovement jumps were tested before and after a time-of-day-specific resistance training in young male adults and also in 10- to 11-year-old boys (Chtourou et al., 2012a; Chtourou et al. 2012b; Souissi et al., 2012). One of these studies implemented a tapering period during the final two weeks of a 14-week resistance training (Chtourou et al., 2012b). Tapering studies are of high practical relevance as they are frequently used in competitive sports. The taper is a training phase of progressive reduction in the training load for a variable period of time before a major competition to allow for physiological and psychological recovery from accumulated training stress. Taken together, all three studies from this research group found that adaptation to strength training is greater at the time of day at which training was scheduled than at other times. The 2 weeks of tapering resulted in further time-of-day–specific adaptations and increases in short-term maximal performances (Chtourou et al., 2012b). However, neither of these studies directly addressed possible mechanisms behind the reported time-of–day-specific adaptations.

Another training experiment came from our lab (Sedliak et al., 2008). We used a slightly different research design. Resistance untrained subjects were at first pre-conditioned for ten weeks by training exclusively between 17:00 and 19:00 h. Subsequently they continued with a 10-week time-of-day-specific training period. Subjects were randomly assigned either to the morning or afternoon training group with training times being 07:00 to 09:00 h and 17:00 to 19:00 h, respectively. We increased the training frequency from 2 sessions per week during the preparatory training to 5 sessions within 2 weeks during the first half of the time-of-day-specific training period up to 3 sessions per week during its second half. The training was a combination of high resistance/high speed and hypertrophy protocols. The training volume was considerably higher compared to the study of Souissi et al. (2002) due to the use of multiple exercises for extensors muscles - half squats, loaded squat jumps, leg presses, and knee extensions within a single session. Various indices of maximum strength and power were tested before and after the 10-week time-of-day-specific training period: 1-RM maximum half squat, loaded squat jumps with 60% of 1-RM and maximum isometric knee extension and flexion tests. Surface EMG measurements during isometric test were also taken throughout the day.

Our results were similar to the findings of Souissi et al. (2002). The morning performance deficit in maximum isometric strength (approximately 9 %) of the afternoon training group persisted also after the time-of-day-specific training. In the morning group, however, the morning performance deficit decreased from pre-training value of 10% to 2,7 % after the training. In other words, the morning group improved by 13 % when measured at the training-specific time (07:00 h), but only 4,6 % when tested at 17:00 h. However, the EMG activity (calculated as root mean square) of the trained muscles could not explain the trend of the morning group to increase their performance more at the time of day of training (07:00 h) than at another time (17:00 h). The time-of-day-specific training period resulted in a significant EMG increase of both training groups, which is a typical finding with this type of resistance training (e.g., Häkkinen et al. 1995). Training groups showed no significant diurnal variation in EMG neither before nor after the training. Further studies using and combining more advanced laboratory techniques are needed to address possible time-of-day-specific training adaptations within the central and peripheral nervous system.

Similar time-of-day-specific training adaptation as seen in MVC was observed in power output during loaded squat jumps with 60 % of 1-RM. The afternoon group performed the jumps relatively better in the afternoon while the morning group could exert higher power outputs at 07:00 h. It needs to be mentioned that in the morning training group this feature was present already at Pre. A possible reason was lower than normal 17:00 h values rather than high 07:00 h performance. As stated in the previous chapter, the loaded squat jump results may be somewhat affected by lower skill levels when tested in previously untrained subjects and in subjects with short training history.

Putting the above results together, one finding seems to be repeating across the studies. Strength gains during the training lasting 6 weeks and longer seem to be rather similar regardless of time of day of training. That is the case for both designs when strength tests are performed at training specific times (Souissi et al., 2002; Sedliak et al. 2008) or training non-specific times (Sedliak et al., 2008) Moreover, the findings are reproducible with various types of dynamic (1RM half-squat, isokinetic knee extension) and isometric maximum strength tests.

However, our latest study suggests that maximum strength gains may be impaired when resistance training is performed in the morning during the initial 3 weeks of an 11-week training program (Sedliak et al., 2012). In this study, we measured maximum strength not only before and after the training period but also every 3 weeks throughout the 11-week of time-of-day-specific training in untrained young men. As seen in Figure 3.2, subjects training in the afternoon showed a typical adaptation curve with more pronounced strength gains during the first 3

– 4 weeks of training compared with the following training weeks. The pronounced strength gains are believed to occur mainly due to changes of neural factors, as proposed already in late seventies and early eighties by Moritani and DeVries (1979) and Paavo Komi (1986). In contrast, there was almost no increase in maximum isometric and isokinetic strength among the men training in the morning during the first three weeks of training. The morning training group compensated for the performance deficit from the 4th to 9th week of training. In the last 3 weeks of training, there was no significant difference in maximum strength gains between the morning and afternoon training groups.

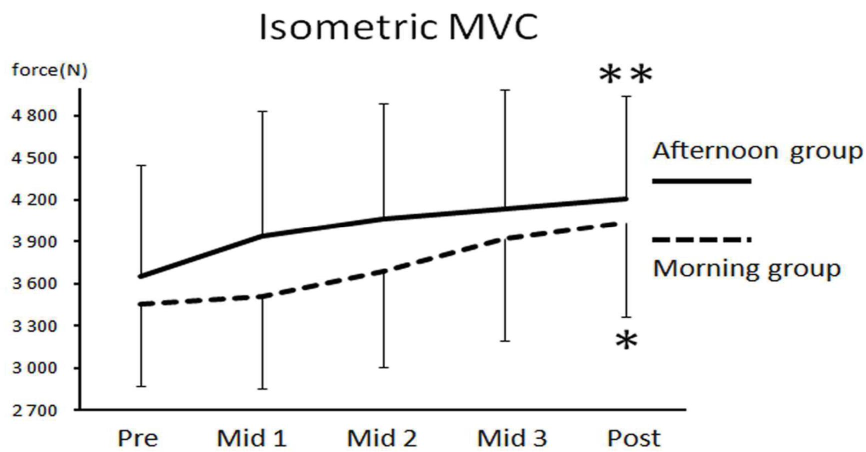

Figure 3.2 Changes in maximum voluntary isometric strength measured before (Pre), at week 3, 6, and 9 (Mid 1, Mid 2, Mid 3, respectively) and after (Post) 11 weeks of time-of-day-specific resistance training in the morning and afternoon training groups (mean ± SD). * ** - significantly higher compared to Pre at $p<0.05$ and 0.01, respectively.

Interestingly, results of a study done by C. Martyn Beaven and colleagues (2010) showed a similar adaptation feature for explosive power but not for maximum strength. Resistance-trained semi-professional rugby players trained for four weeks in the morning or in the afternoon. The two 4-week training periods comprising of maximum and explosive strength squat exercises took place during the pre-season training block and were separated by a full rugby season and an off-season. They concluded that the increase of 1-RM box squat strength after the 4-week resistance training was similar regardless of the time of day performed. In contrast to maximal strength, greater improvement of peak power at a load equivalent to 50 % of 1-RM during a countermovement jump-squat was observed when training was performed in the afternoon. It is possible that any impairment of maximum strength gain during the initial phase of morning training is less pronounced or absent in trained athletes compared to untrained individuals. However, short-term increases in explosive strength seem to be problematic also among athletes when training is performed in the morning hours.

Time-of-day-dependent differences in explosive power after 4-week speed-power-oriented training program were also claimed in a short report by Oschütz (1993). Three groups of young, sport studies students trained at different times – at 08:00 h, 14:00 h, and 18:00 h. The students who trained at 18:00 h experienced superior training gains in leg extension power and standing broad jump. It must be noted that a low sample size per group (n=4) was used in the pilot study of Oschütz and no statistical analysis of the data was provided.

The reasons of hindered early-training stage adaptation in the morning can only be speculated at this moment. However, it is tempting to give a practical implication that the same relative load may lead to different (being more demanding) physiological responses if a high intensity workout is required in the morning before 09:00 h in people unaccustomed to the morning exercise. It could possibly increase the risk of overreaching if the training clock times for performing high load/high volume resistance training are frequently changed between morning and afternoon hours. On the other hand, regular morning resistance training lasting more than 6 weeks is tolerated well by majority of healthy young people. However, no data of various patient groups and evening chronotypes are available up to date.

So far the only training study reporting no effect of time of day was published by Blonc et al. (2010). Five weeks of both morning and afternoon sprinting and jumping training resulted in similar 5-6 % increases in unloaded squat and countermovement jumping height and peak power during cycling sprints but failed to show any time-of-day effect on either performance or training benefit. However, experimental work of this research group was performed in warm (~ 28-29°C) environment of French West Indies compared to moderate (~ 20-21°C) environment in the rest of the studies. Indeed, previous studies conducted in the warm environment show stability in performance throughout the day. Blonc et al. (2010) speculated that relatively stable light and temperature conditions over the day and entire year may lead to specific physiological adaptations to exercise via influencing the circadian regulation of some neurohormonal metabolisms. To understand the true importance of the environmental conditions for testing and living they also highlighted a need of a comparative study with the same subjects in both tropical and moderate conditions.

3.2 Time-of-day-specific adaptation to resistance training – skeletal muscle hypertrophy

Besides neural adaptations, repeated resistance training leads to morphological changes in skeletal muscle tissue. A typical example of morphological changes is skeletal muscle hypertrophy, or, in other words, increases of muscle mass. Different types of resistance training induce muscle hypertrophy to a different extent. Discussing this topic in details is beyond the scope of this book. Briefly, the so-called hypertrophic type of training using 60-80 % of 1RM, 6-12 repetitions per set, 3-5 seconds repetition duration, and 2-4 sets per session is considered the most potent stimulus for muscle hypertrophy (Kraemer and Häkkinen, 2008). Among the main physiological features in hypertrophic type of training resulting in a stimulation of skeletal muscle protein synthesis are longer time under contraction and increased muscle acidosis.

In general, muscle hypertrophy/atrophy at the cellular level is a net result of an increase in protein synthesis minus protein degradation. Already a single bout of resistance exercise is a potent stimulus for increasing the post exercise rate of protein synthesis per se, both in the acute recovery phase and lasting up to 48 h (MacDougall et al., 1995; Phillips et al., 1997). More specifically, during an acute bout of resistance exercise, protein degradation overrides protein synthesis (Rennie and Tipton, 2000). Immediately after the exercise termination protein synthesis and degradations are increased in order to facilitate cell remodelling and reparation processes, which can last up to 48 hours post exercise (Phillips et al., 1997). In case of amino acids and other nutrients availability in the cells during the recovery periods the net result is positive protein balance and subsequent muscle hypertrophy (Rennie and Tipton, 2000; Wolfe, 2002).

It must be realised that at the cellular level, protein synthesis/degradation of various cell fractions is affected (i.e. myofibrillar, mitochondrial and sarcoplasmic). The time course of changes in protein synthesis seems to vary for different cell fractions (Burd et al., 2012). They showed that there was no detectable increase in rates of myofibrillar protein synthesis after 6 hours of recovery but a significant increase at 24–30 hour recovery period after the termination of an acute bout of low-load, high-volume resistance exercise (30 % of 1-RM). In contrast, sarcoplasmic protein fractional synthetic rates were increased at 6 hours but not at 24–30 hours post exercise. To add to the complexity of matter, mitochondrial protein fractional synthetic rates were significantly above the baseline values at both 6 and 24–30 hours post exercise, with the peaks reached during the later sampling point (Burd et al., 2012). However, if for example a loading protocol of shorter duration but higher percentage of 1-RM (thus less dependent on mitochondrial oxidative functions) would be implemented, mitochondrial protein turnover could hypothetically affected to a lesser extent. Indeed, at this point it is not exactly known what the relative contribution of different cell fractions to the overall hypertrophy of different skeletal muscle fibre types after various exercise loading types of varying duration is.

The situation is somewhat clearer at the macroscopic level of skeletal muscle hypertrophy. In their classic study MacDougall et al. (1984) indicated that the proportion of muscle comprised of connective and other noncontractile tissue was the same (approximately 13 %) for bodybuilders with apparent muscle hypertrophy, and for untrained individuals. An increase in anatomical cross-sectional area (aCSA) of the exercised muscles/muscle groups can be seen over a relatively short period of time (8-12 weeks). A typical range of knee extensors muscle hypertrophy reported during a 10-week period in previously untrained subjects is on average 8,5 %, ranging between 1,1 % and 17,3 % (Wernbom et al., 2007). Similarly to the strength gains, the increase in aCSA progressively declines over time (e.g., a year) as an individual is approaching his/her genetic potential (Alway et al., 1992). Biological factors such as muscle fibre type distribution, endocrinological profile, macronutrient intake, age and gender have been recognized for its importance in adaption to resistance training in general (Crewther et al., 2006; Folland and Williams, 2007; Hulmi et al. 2007; Kraemer and Ratamess, 2005).

Surprisingly, despite a quite long history of research on time-of-day-specific adaptations to exercise (resistance training), no attention was paid to skeletal muscle hypertrophy. The very first study on this topic was published by our research group (Sedliak et al., 2009). In that experiment, both strength and hypertrophic adaptations to morning (07:00 to 09:00 h) versus afternoon (17:00 to 19:00 h) resistance training were studied. Thus, the training design was a combination of 10-week high resistance/high speed and hypertrophy protocols, identical to the training program used before (Sedliak et al., 2008) and described above. The actual hypertrophic type of training (60-80 % of 1-RM, 6-12 repetitions per set, 3-5 seconds repetition duration, 2-4 sets) was performed every second session, i.e. once or twice a week. All training sessions were planned as whole-body periodized programs with the main focus on the knee extensors muscles being exercised always at the beginning of a session. Magnetic resonance imaging was used to visualised and calculate cross-sectional areas (CSA) and quadriceps femoris muscle volume. When compared with the control group, the quadriceps femoris muscle volume increased significantly after the time-of-day-specific training period in both training groups. The average increase in volume was 2,7 % and 3,5 % in the morning and afternoon groups, respectively. It was concluded that strength training in the morning and afternoon hours was similarly effective when aiming for muscle hypertrophy over a shorter period of time e.g., 2-3 months.

Interestingly, there was a tendency for difference in the relative quadriceps femoris volume increase, although statistically insignificant and minor (0,8 %) in magnitude, between the training groups in favour of the afternoon group. This tendency was more pronounced (1 – 1,5 %) when considering the mid-section of the quadriceps femoris cross-sections. In the world of competitive sports like bodybuilding similar differences in muscle mass gains could be of practical relevance. It is however questionable to what extent were the time-of-day-specific differences in hypertrophic adaptations real effects of time of day. For instance, the training outcome at the group level could have been affected by the between-group variability in factors that were not / could not have been controlled for during randomizations of subjects into the training groups. It might be that subjects with testosterone levels closer to the upper physiological limits could have an advantage over those closer to the lower limit. Evidence implies that an increase in muscle strength and size may be positively related to resting total serum testosterone concentrations (Bhasin et al., 2001; Kvorning et al., 2006). Furthermore, the inter-individual difference in responsiveness to training due to fibre type distribution (Campos et al. 2002; Thorstensson et al. 1976) and/or greater pre-training muscle satellite cell presence (Petrella et al., 2008) might be among potential confounding factors of the study.

As mentioned above, the pilot study of Sedliak et al. (2009) aimed to address both muscle strength and hypertrophy adaptations. Therefore a combination of high resistance/high speed and hypertrophy trainings was applied. Literature as well as practical experience proves that various types of resistance loading stimulate muscle growth to a different extent. For instance, a high-load neural protocol of relatively short time under contraction does not fully activate signalling pathways leading to hypertrophy (Hulmi et al., 2012). In addition, the group of previously untrained young men underwent a preparatory training period before entering the actual time-of-day-specific training. The preparatory training consisted of a 10-week period and all subjects trained exclusively between 17:00 to 19:00 h. These two factors were most likely responsible for the fact that the average gains in muscle mass were half of the size typically seen in a similar population of subjects.

We therefore decided to take a step back and to examine gains in muscle mass in a group of resistance training novices with a training design typically used to stimulate muscle hypertrophy (Sedliak et al., 2011). For each knee extensor and flexor exercise, longer time under contraction was used, compared to our previous experiment. Each repetition consisted of 2-second and 3-second concentric and eccentric contractions, respectively. Importantly, muscle biopsies were taken before and after the training period so the hypertrophy adaptations could be studied also at the cellular level. Young adult men trained for 11 weeks either between 07:30 - 08:30 h or 16:00 - 17:00 h. Similarly to our earlier study (Sedliak et al., 2009), both training groups showed apparent level of muscle hypertrophy. The average cross-sectional area of skeletal muscle cells increased in participants training in the afternoon hours by 23 %. The average increase in participants randomized to the morning training group was 17,6 %. This between-group difference was not statistically significant. However, there was the significant difference in inter-individual variation at the level of hypertrophic adaptation between the groups. In other words, there was a significantly higher number of men who did not exhibit any measurable increases in muscle cell cross-sectional area after 11 weeks of morning training period compared to those training in the afternoon hours (Figure 3.3). The main question is whether these various responses to time-of-day-specific resistance training were real effects of time of day or caused by various confounding factors. It is of course impossible to make a concluding statement based on the above findings although many possible confounding factors were controlled. For instance, the training volume of both training groups was identical in relative measures. Beside thorough sleep and dietary habits instructions, a post-training recovery drink containing whey protein and maltodextrin was provided after every session to all participants for a better control of nutrient intake and timing. In addition, data on signalling pathways involved in skeletal muscle hypertrophy also support the possibility of hypertrophic adaptations being time-of-day-dependent.

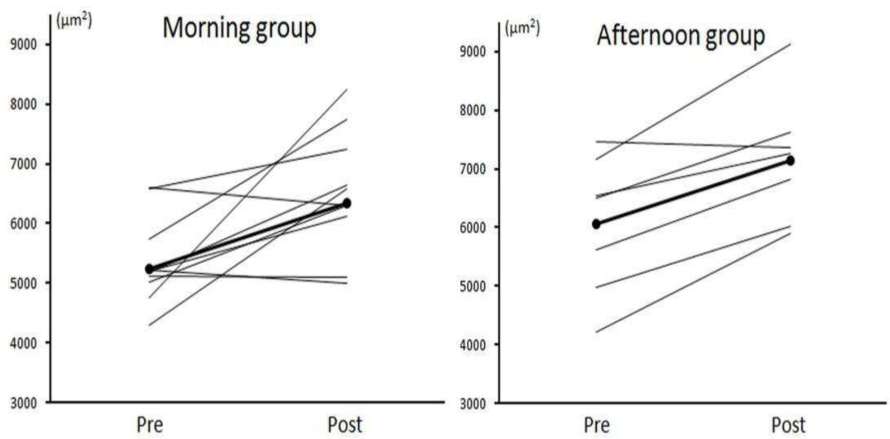

Figure 3.3 Absolute changes in average muscle cell cross-sectional areas of vastus lateralis taken before (Pre) and after (Post) 11 weeks of time-of-day-specific resistance training in the morning and afternoon training groups (left and right panel, respectively). A thick line represents means of the groups, thin lines represent individual values.

Briefly, as stated earlier in this chapter, the increased rate of protein synthesis compared to protein degradation at the cellular level over time is required for inducing hypertrophic training adaptations. There are several possible ways of protein synthesis enhancement. One of the well studied cellular mechanisms is the activation of specific signalling pathways via phosphorylation.

Phosphorylation of specific proteins in protein kinase B/muscle target of rapamycin/p70 ribosomal S6 kinase signalling pathway (Akt/mTOR/p70S6K) and to some extent also in mitogen-activated protein kinases (MAPK) signalling pathway has been shown to positively regulate muscle growth (Wolfe, 2002; Terzis et al., 2008; Shi et al., 2009). Further, resistance exercise primarily aimed at increasing muscle hypertrophy is a potent stimulus to the increase of mTOR and

MAPK signalling (Wolfe, 2002; Terzis et al., 2008; Hulmi et al., 2009, 2010). At least signalling through rapamycin sensitive mTOR complex 1 (mTORC1) is needed to induce protein synthesis after resistance exercise (Drummond et al., 2009). Phosphorylation of selected proteins after an acute bout of heavy resistance loading performed either in the morning or afternoon hours was studied by our group (Sedliak et al., 2013). The main finding was that phosphorylated eukaryotic elongation factor 2 (eEF2) and p38 mitogen-activated kinase (p38 MAPK) showed significantly larger between-subject variability in the exercise response in the morning group compared to a more consistent exercise response in the afternoon group (Sedliak et al., 2013). It is questionable to what extend there is causality between high morning between-subject variability in the acute responses (cell signalling) and in long-term adaptations (cell hypertrophy). However, another data from our lab show that time-of-day-specific long-term adaptations exist also in signalling pathways. For instance, p70 ribosomal S6 kinase (p70S6K) exhibited reduction in its phosphorylated portion after 11 weeks of afternoon resistance training. Similarly decreased p70S6K phosphorylation, and thus activity within the Akt/mTOR/p70S6K signalling pathway has been reported in resistance-trained but not endurance-trained men after resistance exercise (Coffey et al., 2006). In contrast, in men training between 07:30 – 08:30 h for 11 weeks elevated levels of phosphorylated p70S6K persisted in a similar way as in untrained controls (Figure 3.4). The same feature of significantly blunted post-loading signalling in the afternoon but not morning training group after time-of-day-specific training was observed also in phosphorylated eEF2. These preliminary cell signalling data suggest that despite similar outcome in cell hypertrophy measures, the hypertrophy mechanisms may differ between morning and afternoon hours. Specifically for activation of cell signalling pathways leading to protein synthesis, afternoon training leads to typical post-training decrease in the activation while morning training results in similar activation as seen in pre-training state or in controls. It could be speculated that unchanged activation of cell signalling pathways during a period of morning resistance training may compensate for some other contributing factors (e.g., hormonal, metabolic, myogenic) that are less/more activated in the morning compared to the afternoon hours.

Indeed, experiments on animal models showed, for instance, that there was a circadian variation in the mRNA expression of the myogenic regulatory factors MyoD, myogenin, MuRF1, Akt1, and ribosomal protein S6 and also in phosphorylated levels of Akt and ribosomal protein S6 in rodent skeletal muscle (Andrews et al., 2010; Shavlakadze et al., 2013) Clearly, further studies with more complex research design are needed within this field of research.

Figure 3.4 Relative changes in phosphorylated p70 ribosomal S6 kinase after an acute bout of heavy resistance exercise in the morning and afternoon training groups before (left panel) and after (right panel) 11 weeks of time-of-day-specific resistance training and in controls (mean ± SD). *, ** - statistically significant within-group change from pre-loading state at $p<0.05$ and $p<0.01$, respectively. $p<0.05$ – significantly lower relative change in the afternoon training group compared to the morning training group. *Adapted from Sedliak et al., 2012.*

Circulating hormones and growth factors like testosterone, growth hormone, cortisol, Insulin-like growth factor 1 (IGF-I) have also been recognised for their important role in muscle mass accretion, in general. For instance, testosterone is an anabolic hormone promoting, among others, protein synthesis in muscle tissue (Ferrando et al., 1998), the result being increased muscle mass and strength (Kraemer et al., 1990). Testosterone was shown to increase muscle protein synthesis and attenuate muscle protein degradation, increase muscle sensitivity to IGF-I via up-regulation of the IGF-I receptors (Thompson et al., 1989), and increase satellite cell proliferation resulting in muscle fibre hypertrophy (Doumit et al., 1996, Sinha-Hikim et al., 2003). The correlation was reported between changes in isometric strength and testosterone suggesting that testosterone may be an important signalling factor for strength development (Ahtiainen et al., 2003). In contrast, cortisol is typically considered a catabolic hormone counteracting the effects of testosterone, although its role in the process of adaptation to strength training may be more complex (e.g., increasing availability of free amino acids post exercise for subsequent adaptive protein synthesis, Viru and Viru, 2001). Interestingly, a positive correlation between acute elevations in cortisol after acute loading and increases in type II CSA were found (West and Phillpis, 2012). Cortisol is clearly more than a catabolic agent, it serves, among other functions, also as a signalling molecule for synchronizing various secondary oscillators with the SCN (Balsalobre et al., 2000).

While the importance of resting hormonal concentrations on resistance training adaptations is widely accepted, a scientific controversy has recently been going on regarding the role of acute elevations of hormones and growth factors after a bout of exercise. Several studies suggest that muscle hypertrophy can be achieved without acutely elevated hormone levels, provided that the protein availability is sufficient (Wilkinson et al., 2006; West et al., 2009, 2010). Discussing the role of hormonal system in details is beyond the scope of this book and the readers are advised to see relevant reviews (e.g., Kraemer and Ratamess, 2005; Spiering et al., 2008; Hayes et al., 2010).

A review article specifically related to interaction of time-of-day-specific resistance training and hormonal system was published in 2010 by Hayes, Bickerstaff and Baker. Although a comprehensive review of literature was given, the authors were not able to clearly conclude that diurnal differences in resting and/or acute changes in circulating hormones play a significant role in adaptation to time-of-day-specific resistance training. At this point, results from acute studies are conflicting while number of long-term training experiments is limited and findings are inconclusive (e.g., McMurray et al., 1995; Kraemer et al., 2001; Nindl et al., 2001). For instance, our research group found that diurnal variation of resting testosterone was not affected by time-of-day–specific resistance training (Sedliak et al., 2007). Interestingly, early morning (07:00 h) resistance training caused reduction in slightly elevated pre-training morning cortisol values. However, this finding was attributed to psychological adaptations, i.e., lower anticipation stress and accommodation to early waking, rather than chronic changes in diurnal variation of cortisol, as anticipation of stressful events causes an increase in cortisol (Mason et al., 1973; Michaud et al., 2009). In addition, it could be hypothesized that the 10-week preparatory training period and the subsequent time-of-day-specific training period would not be sufficient to induce a significant phase shift on testosterone and cortisol rhythms, mainly due to a rather low training frequency (Sedliak et al., 2007). Subsequent sessions were always separated by two or three days to allow an adequate recovery in order to avoid overreaching, overtraining, and/or injury. Rest days may have provided sufficient time to reset any possible phase-shifting effects of the morning or afternoon exercise, since the subjects were instantly exposed to other strong environmental and social synchronizers - zeitgebers (sun light-dark cycle, work schedule, social contacts etc) of circadian rhythms. Again, there is a need for more thorough experiments examining not only circulating hormonal levels but also their specific effects in the tissue if interest, e.g., receptor content and its changes in skeletal muscle.

3.3 Resistance exercise as zeitgeber

Another important questions rise within time-of-day-specific training adaptations to resistance training. Does resistance exercise possess properties of a zeitgeber? Can acute and/or repeated exercise modify circadian period?

Light is a powerful stimulus able to advance or delay human circadian system. Besides light, several nonphotic stimuli, mostly food intake and social contacts, but also chemical compounds like melatonin, stimulants or hypnotics and, importantly, exercise, have been proposed

(Mistlberger and Skene, 2005). Animal studies demonstrated that exercise is a sufficient environmental cue to affect clock gene expression in both central clock and peripheral tissue (muscle) (Maywood et al., 1999; Wolff and Esser, 2012).

However, it is difficult to address zeitgeber properties of exercise and also its effect on circadian period in humans. For instance, methodological issues with prior studies such as light exposure during exercise, the length of study, and the method of measuring period confounded those evaluations of the effect of exercise on human circadian period. As a result, the findings and their interpretations are rather contradictory. Cain et al. (2007) found no effect of chronic exercise on endogenous circadian period as measured by either core body temperature or melatonin. They used a 20-h forced desynchrony protocol, in which subjects were exposed to exercise across circadian phases under dim light conditions over 24 beat cycles. The exercise consisted of three 45-min sessions per wake period on a cycling ergometer. The first bout began 0,75 h after wake time, the second bout began 4,5 h after wake time and the third bout began 8,25 h after wake time. Target exercise intensity was ~65 % of maximal heart rate. Cain et al. (2007) also admitted the possibility that exercise of higher intensity than cycling at ~65 % of maximal heart rate could modify the endogenous circadian period. For instance, Beersma and Hiddinga (1998) reported the trend toward shortening of circadian period (tau = 23,98) with high-intensity cycling exercise. However, it must be realised, that the exercise stimulus in the above experiments was administered daily. Daily administration of some types of training, e.g., heavy resistance training targeting for muscle hypertrophy, is not advisable due to high risks of overreaching, overtraining, and/or injury.

Whether exercise can modify the circadian period or not, it seems clear that performing an exercise induce phase shifts in humans (Van Reeth et al., 1994; Buxton et al., 1997). Subjects who completed three 45-minute bouts of cycling exercise over seven consecutive nights showed a significantly greater shift in the dim light melatonin onset, dim light melatonin offset and midpoint of the melatonin profile compared with non-exercising controls (Barger et al., 2004). Most studies of exercise and shifting of circadian rhythms have relied on endurance exercise. Less is known on the possible effects of resistance exercise. In the only study on humans, an acute bout of resistance exercise was shown to induce changes in molecular clock gene expression in skeletal muscles (Zambon et al., 2003).

Phase shifting properties of exercise could be of a high practical relevance in case of weakened or disturbed input from a photic zeitgeber e.g., after transmeridian flights or in people living at higher latitudes. As concluded by Schroder and Esser in their review (2013), although studies on animals suggest that an optimal exercising time of day to enhance the robust nature of circadian rhythms at the molecular level may exist, there is still much to be determined in humans. Further studies implementing also various types of resistance exercise are needed.

3.4 Final conclusions and practical implications

Based on the present and the previous chapter, the following recommendations could be given to sport and research professionals and all involved in resistance training:

In a person unaccustomed to the morning exercise, voluntary strength (maximum, explosive) and short-term performance is on average 5-10 % lower in the morning compared to the rest of the day. Ideally, maximum strength, power and brief anaerobic performance tests should not be performed before 09:00 h.

Morning resistance training performed regularly for at least 5 weeks can improve morning short-term neuromuscular performance to the daily maximum level. Magnitude of strength and power gains is similar regardless of time of day of training.

Strength and power athletes required to compete in the morning may be advised to train **regularly** in the morning hours prior to competition for at least 5 weeks. In general, athletes required to compete at a certain time of day (i.e., when the time of competition is known) may be advised to coincide their training hours with the time of day at which one's critical performance is planned.

Avoiding morning maximum strength and power training if training period is **shorter than 3 weeks** may be advised.

Muscle hypertrophy is similar regardless of time of day of training over a shorter period (2 – 3 months). No data over shorter and longer period of time-of-day-specific training are currently available.

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4 RAMADAN AND SPORTS PERFORMANCE

Handhom Alabed and Jim Waterhouse

PART I
RAMADAN AND ATLHLETIC PERFORMANCE

Ramadan, the ninth month of the Islamic year, requires Muslims to fast between the hours of sunrise and sunset, taking in food and fluids outside the hours of daylight. Those who choose to prepare for daytime fasting will have to rise earlier than normal; in addition, as individuals recuperate in the evening, often with friends, bedtime might be delayed. That is, the hours of sleep might be curtailed in Ramadan. This combination of factors has widespread negative effects upon general daytime activities and performance. For example, Ramadan has been associated with increases in the frequency of road traffic accidents and individuals' irritability.

The first issue of concern to the athlete is the changes that occur during the four weeks of daytime fasting in Ramadan.

4.1 Changes Observed during the Four Weeks of Ramadan

4.1.1 Energy balance

Energy balance is determined by energy expenditure and energy intake. The expenditure of energy is affected by the level of activity and energy intake is determined by the quantity and quality of food available and the opportunity to ingest it.

There is also a need to maintain hydration status. Muslims become dehydrated during the daylight hours during Ramadan but it is unclear if they are chronically hypohydrated throughout the Holy month. Some forms of endurance exercise may be affected when the loss of body water exceeds 2 % of body mass, even though all-out anaerobic

performance might be maintained for a few seconds with body mass losses of up to 5 %. Athletes may lose sweat at a rate of 2 $l.h^{-1}$ during strenuous exercise, especially in the heat, and this cannot be replaced during the daytime in Ramadan.
Imbalances in energy stores do not occur as quickly and they are less of a threat to health. Nevertheless, weight changes might influence performance and, when the diet is deficient, a shortage of macro-nutrients could adversely affect physical activity. Even so, there is no evidence of adverse health effects due to negative water and energy balances.

Reduced body mass is commonly present in Ramadan but changes in energy balance are not consistent between studies. For example, some studies have reported no change in body mass or the subcutaneous and visceral distributions of fat or waist, hip and thigh circumferences, implying a balance between energy intake and expenditure. Other studies also found no overall effect on energy intake or body mass, even though hunger was increased during the daily fast and the higher levels of hunger, at least in women, were attributed to their having to prepare the food that was to be eaten after sunset. Yet other studies have reported that the energy intake of subjects actually increased during Ramadan; this increase was due to the meal eaten after sunset, which was often in the form of fat and protein rather than carbohydrate and contributed 65 % to the total daily diet.

However, most studies indicate that both energy intake and expenditure decline during Ramadan, the fall in energy expenditure being due to a lower activity profile in the daytime. This fall might also be accompanied by adoption of a less healthy diet; it has been noted that calcium was missing from the food eaten after sunset, and in has been reported that Muslims increased the consumption of animal proteins in their diet at the expense of fresh vegetables.

Altered eating habits will change gastrointestinal function and might lead to an increase in gastrointestinal complaints. For example, gastric acidity has been found to be increased during Ramadan, even though this need not be accompanied by symptoms of indigestion.

4.1.2 Medical considerations

Compliance with drug therapies falls during Ramadan and provides a source of concern in the case of those being treated for hypertension. There is also evidence that younger subjects who are susceptible to diabetes experience particular problems when observing the fasting regimen. By contrast, patients with cardiovascular disorders do not seem to be at greater risk. There are potential consequences with regard to gastric acidity associated with the hours of fasting in individuals who have previously had duodenal ulcers; patients healed of this condition are considered to have an increased risk of relapse due to continuously low gastric pH and high plasma gastrin concentrations during the hours of fasting.

The fasting regimen imposed by Ramadan can have beneficial effects on some haematological and biochemical profiles. For example, an increase in plasma high-density lipoprotein cholesterol has been consistently observed, this increase persisting for 20 days after the fast. Beneficial effects of the Ramadan fast have also been reported for apolipoprotein metabolism and plasma levels of leptin and neuropeptide Y. However, it is possible that, in night-workers, there is a link between the amount of glucose eaten at night and a changed cholesterol profile that would be a risk factor for cardiovascular morbidity.

Females might be affected differently from males since a prolonged negative calorie balance might lead to anovulatory menstrual cycles. The menstrual health status of women fasting during Ramadan requires further investigation.

4.1.3 Implications for sport and athletics

With regard to those undertaking training sessions in sports and athletics, physical performance is compromised in Ramadan, although the deterioration is not uniform over all aspects of performance. For example, there are reports of changes in soccer players' abilities as follows: a deterioration in VO_2max - but not sprinting ability or agility;

decreased aerobic capacity, endurance and jumping ability - but no change to sprinting or agility; decreased ability to perform exercise at 75% VO_2max; no clear changes in speed, power, agility, endurance and dribbling skills; a biologically insignificant decrease in maximal heart rate - but no change in perceived exertion; and a general decrease in fitness and tests of skill (speed, agility, dribbling and endurance). Moreover, subjective assessments have indicated that sports performance deteriorates and that the exertion required to undertake a training session is increased, although such negative effects do not persist for long after the end of the Holy month.

Even though some aspects of sports and athletic performance might deteriorate in Ramadan, it is not clear to what extent physiological variables associated with physical activity also deteriorate. For example, there are the following reports: no deterioration in sedentary subjects exercising at about 70% VO_2max under thermoneutral conditions; substantial decreases in maximal voluntary contractions and endurance of elbow flexors; and no significant changes in vital capacity, FEV_1, peak expiratory flow and maximum voluntary ventilation in healthy subjects.

That is, some aspects of sports performance are compromised but other aspects of it (sprinting and agility, for example) seem comparatively immune to this deterioration. However, the individuals taking part in many of these studies were highly motivated and aware that their performance was being measured; these circumstances might well have increased their efforts to oppose any deterioration. The issue of motivation is important, and will be returned to later on more than one occasion.

4.2 Reasons for Changes in Athletic Performance during the Four Weeks of Ramadan

Any decrements in performance in athletic performance during Ramadan might derive from disturbances of the sleep-wake cycle, changed food and fluid intakes, or an interaction between these factors.

The evidence for the role played by each of these factors will now be outlined.

4.2.1 Sleep loss

Sleep patterns are changed in Ramadan. In one study, bedtime was delayed by more than 1 h which, coupled with a constant wake-up time, led to reduced sleep at night. Daytime fatigue is also increased, as is the frequency of napping. Further, sleep architecture has been found to change, there being increases in sleep latency, non-REM sleep and Stage 2 sleep, but a decrease in slow-wave sleep. Such changes might derive in part from the raised rectal temperatures that have been observed to exist during the night in Ramadan.

Sleep loss produces little direct effect upon muscle activity, but it has an indirect effect upon physical performance via changes in mental performance, coordination and motivation. That is, sleep loss results in falls in performance at tasks requiring sensorimotor coordination or cognitive processing. This decrement is proportional to the amount of sleep lost and the size of the neural component of the task. Motivation is lost also, and this negatively affects performance at repetitive tasks or training sessions, where the aim is not immediately realised. These issues will be addressed further when mental peformance is considered.

4.2.2 Fasting

Alertness and mood will be negatively affected by fasting. One study concluded that subjective alertness decreased during daytime fasting but recovered in the evening after the fast had been broken. These changes were partly attributed to reduced energy intake, mood improving after food and fluid had been taken in. It is generally accepted that eating, particularly carbohydrates, maintains glucose levels in the blood and so promotes alertness and improves mood; therefore, food and fluid restriction might contribute to deteriorations in mood and mental performance and to increased irritability, all of which have been observed during the month of Ramadan.

4.2.3 General conclusions

The general conclusion from these results is that there is evidence for dehydration and a change in metabolism during Ramadan, with fats becoming more of a source of energy than is normally the case when not fasting. Changes to sleep architecture and metabolism are unlikely to be influenced as much as are mood and performance by the subjects' awareness that they are being tested; that it, "increased effort" is unlikely to have played a significant role in these changes. The changes in sleep habits and food and fluid intakes cause at least some aspects of performance to deteriorate during the course of the four weeks of Ramadan. However, many of the changes are not progressive during the Holy month because each evening provides opportunity to recuperate from the period of fasting and to prepare for the next day of fasting.

4.3 Changes during the Course of the Daytime Fast in Ramadan

Far fewer studies have investigated changes in performance *during the course of a day of fasting* - that is, the development of any deterioration as the length of time spent fasting increases. Such changes require consideration of performance levels found in individuals living normally (in the absence of daytime fasting); this issue is fundamental because there are many types of "performance" and these show different profiles during the course of a day.

4.3.1 Normal rhythmic changes seen during the course of a day

Performance varies during the course of the 24 h, partly due to the "body clock". Therefore, a brief account of this and some of its properties now follows.

4.3.1.1 The body clock and zeitgebers

The body's physiology and biochemistry are not constant but vary during the course of the 24 h. These daily changes result from a complex interaction between the environment and an internal structure, the "body clock", the site of which is the paired suprachiasmatic nuclei (SCN) at the base of the hypothalamus. These clusters of cells receive a direct input from the eyes via the retinohypothalamic tract and also a humoral input from the pineal gland. The pineal gland secretes the hormone melatonin into the blood and cerebrospinal fluid during the hours of darkness, and there are melatonin receptors on the SCN.

Rhythmic neural and humoral inputs to the SCN, particularly the 24-h light-dark cycle, enable the phase of the body clock to be synchronised to that of the environment. The rhythms that adjust the body clock are known as zeitgebers (from the German for "time-givers"). The mechanism by which such phase adjustment is achieved is complex but, in essence: bright light in the morning (from about 04:00 h, a time approximately equal to that of the temperature minimum, until 10:00h) advances the clock and bright light in the evening (from about 22:00-04:00 h), delays it. Melatonin secretion also affects the phase of the body clock but in the opposite direction to light; in the morning, melatonin delays the body clock, and in the evening advances it. Since bright light suppresses melatonin secretion, morning light advances the body clock not only directly but also indirectly by suppressing melatonin secretion and so opposing the delay that melatonin would have exerted at this time of day.

Light and melatonin are the main zeitgebers in humans, but there is also evidence that exercise and mealtimes can act as weak zeitgebers. Exercise produces a small delay to the body clock when undertaken in the evening and night, and a small advance when taken around noon and in the early afternoon. Mealtimes might also act as a zeitgeber, particularly by reinforcing an individual's sleep-wake cycle, and the rhythms of social and mental activity might play similar roles. In practice, the main zeitgebers (the light-dark cycle and rhythm of melatonin secretion) as well as the subsidiary ones (rhythms of physical, social and mental activities, sleep and mealtimes) together produce a synchronised "package" which adjusts an individual's physiology and biochemistry to accord with daytime activity and nocturnal recuperation.

Rhythmic outputs from the SCN are transmitted to hypothalamic nuclei that control body temperature, food intake and hormone secretion, to the raphe nucleus (which is involved in sleep regulation) and to the sympathetic nervous system; as a result, the rhythmic output from the SCN-melatonin system pervades the whole body.

4.3.1.2 Endogenous and exogenous components of a measured rhythm

Measured daily rhythms are not produced by the body clock or the environment and individual's sleep-wake cycle alone; instead, they are produced by the combined effects of endogenous (due to the body clock) and exogenous (due to the environment and lifestyle) components. The nature of the exogenous influence depends upon the variable under consideration. For example: core temperature is raised by activity and lowered by the change of posture associated with sleep; mental performance is promoted by comfortable and quiet surroundings, and inhibited by noise and light that is too dim or bright. These two components are illustrated for the rhythm of core temperature in Figure 4.1. In this Figure, the temperature rhythm of 8 males is shown when living normally (sleeping from midnight-08:00 h) and then when undergoing a "constant routine". In this routine, subjects are required to stay awake and sedentary (or even lying down) for a period of at least 24 h in an environment that is constant with regard to temperature and lighting. The normal daily intake of food is divided into 24 equal "snacks". The rhythm remaining in these circumstances cannot be attributed to food intake, the environment or the sleep-wake cycle; therefore, it is termed the endogenous component of the rhythm and attributed to the internal body clock. The *difference* between the two curves (those obtained during the constant routine and in the same subjects when living normally) is due to rhythmic changes in the environment, the individual's sleep-wake cycle and the rhythmic intake of food; it is termed the exogenous component of the measured rhythm.

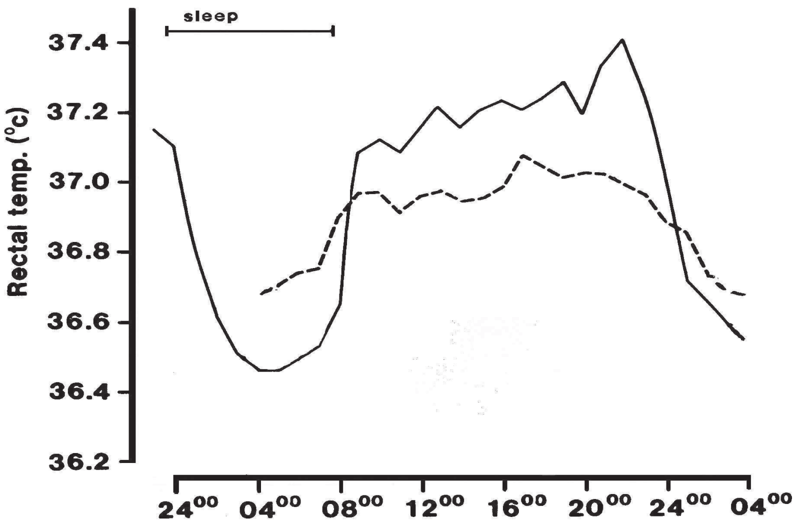

Figure 4.1 Mean daily changes in rectal temperature measured hourly in 8 subjects: living normally and sleeping from 24:00-08:00 h (solid line); and then woken at 04:00 h and spending the next 24 h on a "constant routine" (dashed line). *Based on Minors, D. and Waterhouse, J. (1981): Circadian Rhythms and the Human. John Wright, Bristol.*

This concept of endogenous and exogenous components applies to all rhythms, but their relative size depends upon the variable under consideration: for core temperature, the two components are of about equal size (see Figure 4.1); for melatonin and cortisol rhythms, the endogenous component is larger; and for rhythms of heart rate, blood pressure and urine production, the exogenous component is larger. For mental performance, the position is slightly more complex (see below).

4.3.2 Rhythmic changes in performance measures

Before considering the effects of Ramadan upon the changes during a daytime fast, rhythms of performance that exist under normal circumstances (when subjects eat and drink during the daytime and have normal amounts of sleep at night) need to be considered.

4.3.2.1 Physical performance

Many aspects of human performance, including athletic performance, vary throughout the 24 h. Many of these rhythms, particularly those which require muscle strength, are parallel to the circadian variation in body temperature (peak in the late afternoon), and a causal link has been proposed. Other performance rhythms (actions requiring high levels of sensorimotor coordination - aiming tasks and movements requiring fine balance, for example - or actions requiring large amounts of cognition – decision-taking, for example) tend to peak earlier in the daytime, around noon or the early afternoon. This earlier phase probably reflects effects due to neural influences, including cognition (see below).

The effect of this balance between the strength and sensorimotor control elements of a task upon the measured rhythm is illustrated by the timings of the rhythms of the first and second serves in tennis and badminton. In both games, the first serve stresses muscle strength and is observed to peak at about the same time as the peak in body temperature; by contrast, performance at the second serve, which stresses placement, neuromuscular coordination and tactics (cognition) rather than strength, peaks earlier in the day, around noon.

4.3.2.2 Mental performance at "simple" and "complex" tasks

The above issues are important also when the timing of rhythms for different types of mental performance is considered. For simple mental performance tasks (ones involving little cognitive processing - simple reaction time, for example), the rhythm is timed similarly to that of core temperature. A partial explanation of this is that neural activity, including the rate of neural conduction, increases with temperature. By contrast, for subjective assessments of mood and more complex mental tasks (those requiring substantial cognitive or neuromuscular coordination - mental calculations, decision-taking and tracking objects on a computer display screen, for example), the time of peak of the rhythm is earlier, around noon or the early afternoon. These differences in timing arise because of the amounts "mental fatigue" - a deterioration that is progressive with increasing time awake – that are associated with different tasks. This deterioration is superimposed upon the component of the rhythm that is parallel to that of core temperature. That is, the rhythm of performance at a mental task, like the temperature rhythm, consists of exogenous (environmental lighting, temperature and noise in the case of mental performance) and endogenous components but, unlike the temperature rhythm, the endogenous component is due not only to the body clock but also to time awake, which increases mental fatigue. The greater the amount of cognition required by a particular mental task, the more important is this deterioration due to time awake.

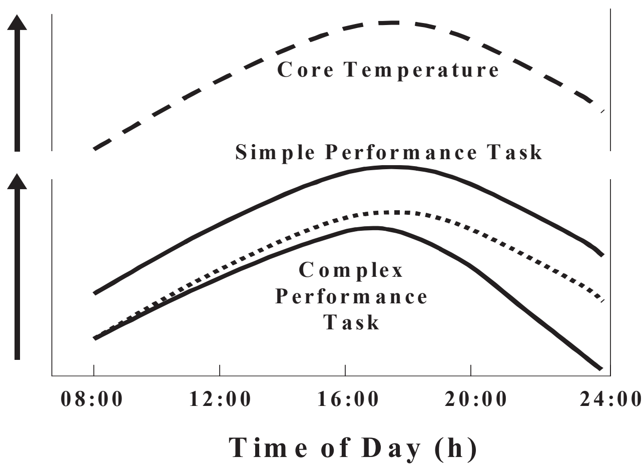

Figure 4.2 Diagrammatic illustration of the daytime rhythms of, top, core temperature (dashed line) and, bottom, simple and complex performance tasks (full lines). Whereas the rhythm of the simple performance task is parallel to that of core temperature, that of the complex performance task falls away more quickly, due to the increased effects of time awake, and so shows a peak earlier in the daytime. The dotted line (parallel to the rhythm of core temperature) shows the hypothetical time-course a complex performance test would show in the absence of these effects of mental fatigue. Higher core temperature and better mental performance are upwards. *Based on: Valdez, P., Reilly, T. and Waterhouse, J. (2008). Rhythms of mental performance. Mind, Brain and Education, 2: 7–16.*

Such an interaction between time awake and the component of mental performance parallel to the daily rhythm of core temperature applies to mental processes in general, and has been used to model alertness, for example. With this model: during the morning, an individual's mental ability increases with the rise in core temperature, any effects of time awake being small. In the afternoon, the high core temperature offsets the increasing effects of time awake, the result of which is that there tends to be a performance plateau; in the evening, performance falls due to the declining core temperature at this time coupled with the increasing effects of time awake.

This model explains why simple mental performance tasks which are little affected by fatigue will be more closely in phase with the rhythm of core temperature (peaking in the late afternoon) and why more complex tasks, which are more susceptible to the effects of fatigue, will decline sooner in the daytime and show daily rhythms that are phased earlier.

Thus, the more a task is affected by this deterioration due to time awake, the earlier will the timing of the peak of the rhythm become, as is illustrated in Figure 4.2. How time awake produces mental fatigue and sleep dissipates it (below) remain to be determined in detail.

Deterioration in cognitive performance is reversed by sleep. The timing of sleep is due to an interaction between increasing sleep pressure and 24-h rhythmic influences, and has been described by the "sleep homeostat" model. This model proposes that being awake leads to an increase in "sleep pressure", which is monitored by the sleep homeostat, and that, as sleep pressure increases, so does the tendency for an individual to feel tired and fall asleep. However, the times of falling asleep and waking up are determined not only by this sleep pressure but also by a "sleep threshold" and "waking threhold", both of which vary rhythmically and in parallel to the rhythm of core temperature. In the evening, sleep occurs because of the combined effects of increasing sleep pressure and a declining core temperature (sleep threshold). During sleep, particularly slow-wave sleep, sleep pressure declines. Waking up in the morning is due to a combination of decreased sleep pressure and a rising core temperature (waking threshold).
Another important factor affecting mental performance is sleep loss, as little as 2 h of which can cause a decrement. The sleep loss need not be

associated with a single night but could, instead, be cumulative - say, 0,5 h per night for 4 successive nights. The most obvious effect of sleep loss is daytime subjective fatigue, but objective tests of performance also show deterioration. Small sleeps (naps) in the daytime can alleviate the effects of sleep loss, the total amount of sleep obtained per 24 h rather than its distribution throughout the day seeming to be the important issue. However, there are two caveats to this last statement: (1) Immediately after any sleep or nap, there is a temporary period of decreased mental ability until the subject has woken up fully; this decrement is attributed to "sleep inertia"; (2) Naps substantially shorter than 1 h provide insufficient time for slow wave sleep (Stages 3 and 4) - the type of sleep that seems to have most recuperative value - to be reached. However, there is some recent evidence that *the act of falling asleep itself* is able to produce an improvement in performance after having woken up.

4.4 Altered Daily Rhythms in Ramadan

Accepting that a measured rhythm has endogenous and exogenous components, that the exogenous component reflects an individual's environment and lifestyle, and that the body clock can be adjusted by zeitgebers, it would be predicted that many daily rhythms are altered during Ramadan.

4.4.1 Hormones and the sleep-wake cycle

The rhythms of cortisol and testosterone normally display peaks in the morning, around the time of waking, but, during Ramadan, it has been reported that there is a shift in the time of secretion onset with both hormones, as well as an altered profile of cortisol secretion - with reduced secretion in the morning and increased secretion in the evening. An enhanced peak in prolactin secretion and a diminished and delayed peak in melatonin secretion have also been described. Eating only in the the early and late parts of the day also leads to a delay in the time of peak serum leptin, the delay being about 5 h by the 23rd day of Ramadan.

Delayed bedtimes and waking times in fasting subjects have been reported during Ramadan, a disturbance of the normal sleep-wake cycle that is exacerbated by the observation that Muslims often combat the rise in daytime fatigue by having a daytime nap more frequently during Ramadan. In Ramadan also, reduced sleep latency during daytime naps has been observed in Muslim subjects, indicative of fatigue.

4.4.2 Gastrointestinal activity and the metabolism of absorbed foodstuffs

The alterations of the pattern of food intake will have a large effect upon many aspects of gastrointestinal activity. In addition, the large meal in the evening is likely to hinder sleep onset and upset the normal balance between daytime metabolism of glucose and nocturnal metabolism of fat from adipose tissue.

Even though mealtimes have only a weak role as a possible zeitgeber (above), the type of food eaten might exert an effect. There is evidence that serotonin modulates sleep and metabolism. Dietary tryptophan is the biochemical precursor of serotonin and plasma tryptophan rises after ingesting carbohydrate; therefore, it has been argued that a high-carbohydrate meal would induce drowsiness and promote sleep. Serotonin may have a role also in regulating the secretion of pancreatic insulin; inhibition of serotonin decreases insulin secretion, and sleep is reduced when subjects are deprived of food. These findings imply that fasting during Ramadan would render a nap more difficult to take in the daytime (with lower insulin levels) even though this would be offset by increased fatigue due to the decreased amount of nocturnal sleep.

The normal pattern of eating in adults is reflected in similar rhythms of gut motility, the secretion of digestive juices, the absorption of digested food, and blood concentrations of glucose, amino acids and lipids. However, there is also evidence that weak, clock-mediated rhythms are present: the gastrointestinal and metabolic effects produced by identical meals display some daily variation; metabolic responses to a glucose load are less rapid in the evening than in the morning; and gastric emptying and blood flow are greater in the daytime - leading to a faster absorption of foodstuffs from the gastrointestinal tract even though, by contrast, the absorption of some drugs from the gastrointestinal tract is greater in the hours after waking due to an empty stomach. Also, several hormones (insulin, ghrelin, leptin, growth hormone, glucagon and cortisol, for example) are involved in the metabolism of absorbed foodstuffs and the secretory profiles of these change during Ramadan, although it is not clear if the changes are fully in accord with altered mealtimes.

4.4.3 Possible causes of the altered rhythms

In summary, many rhythms are observed to change during Ramadan, but these changes cannot be interpreted as being due to a change of only the endogenous or exogenous component of the daily rhythm; they are likely, instead, to be some mixture of these two components. For example: (1) Changes in the secretion of hormones associated with food intake and metabolism will reflect altered mealtimes and nocturnal sleep, and taking daytime naps – but it is unclear if such changes to the exogenous components of these rhythms offers a full explanation of the observed differences, or if changes to the body clock (the endogenous component) also exist; (2) Mental performance will be compromised due to partial sleep loss and to rising earlier (increased time awake), but a changed body clock might also play a role - any of these changes could cause deterioration in daytime activities and decreased desires to be physically or mentally active; and (3) The rhythms of body temperature, cortisol and melatonin during Ramadan show reduced amplitudes and phase shifts, from which it is concluded that major chronobiological and behavioural changes occur during fasting. This conclusion is undoubtedly true, but the role played by the body clock in these changes cannot be deduced from such observations.

Thus, it is also possible that, as well as changes in the exogenous components of rhythms, the phase of the body clock will have changed insofar as the zeitgebers have changed. Rising earlier in the morning will expose the individual to artificial light earlier in the daytime and

this will tend to advance the body clock. By contrast, extended light exposure in the evening will tend to delay the body clock, and so it is not possible to predict the direction or size of the shift of the body clock produced by the changes in light exposure. Since activity is a weak zeitgeber, increased physical activity in the morning and evening might also change the timing of the body clock. To the extent that mealtimes act as a zeitgeber too, these also will alter the body clock in Ramadan.
Special chronobiological protocols are required to establish the relative roles played by the endogenous and exogenous components of each rhythm. These protocols have been described in detail but have not been applied at all fully in a sporting context, and certainly not to athletes fasting in Ramadan. The position remains unclear, therefore.

4.4.4 Implications for the athlete during Ramadan

Combined effects of a changed sleep-wake cycle, increased fatigue and altered patterns of food and fluid intake are likely to affect many daily rhythms during Ramadan, including those associated with mental performance, important amongst which will be changes in motivation. That is, the athlete will be required to continue the arduous and repetitive task of training in spite of changed metabolic status, decreased physical and cognitive abilities, and reduced motivation. Implications of these changes for training schedules are considered in Part III.

PART II
A LABORATORY-BASED STUDY OF CHANGES DURING A SINGLE DAY OF FASTING

4.5 Changing Effects during the Course of a Daytime Fast

The changes found in Ramadan will not be expected to be the same at all times of the daytime fast, due not only to the presence of rhythmic changes during the course of the day but also to the length of time that individuals have been fasting. Previous work by our group (Waterhouse et al., 2008a; 2008b, 2009) has investigated in detail the changes that take place during the course of the daytime in Ramadan. Our aim was to obtain answers to the following questions:

Question 1. How much do the changed times of sleep affect sleepiness in the daytime, and what factors influence whether or not a nap is taken at a particular time?

Question 2. To what extent are changed patterns of eating and drinking before sunrise and after sunset during Ramadan associated with hunger and thirst at these times, or do other factors become more important?

Question 3. Do individuals' desires to perform physical and mental tasks change during the daytime in Ramadan, and are less physical, mental and social activities actually performed?

Question 4. Is there evidence that dehydration develops during the daytime fast?

Question 5. Do objective measures of performance show deterioration during the course of the daytime in Ramadan?

Our main findings have been: (1) Less physical, mental and social activities are performed in the daytime, but there are also significant *increases* after sunset; (2) Daytime fasting is compensated by increased fluid and food intakes in the hours before sunrise and, particularly, after sunset; (3) Sleep at night is altered in Ramadan; daytime sleepiness increases, and more naps are taken in the daytime - the reason cited for this often being to catch up on lost sleep; (4) Urine osmolality (a measure of body dehydration) increases throughout the hours of fasting but not on control, non-fasting days; and (5) Several objective measures of physical and mental performance show progressive daytime deterioration during fasting.

All these results can easily be incorporated into the above account of the negative effects produced by the demands of Ramadan.

However, investigation of these changes in Ramadan are time-consuming and arduous, can only be performed once per year, and recruitment of non-Muslim subjects is obviously difficult. A simpler alternative is desirable, therefore. A pilot study (Alabed, 2010) indicated that many of the effects seen in these larger, more complex studies could be replicated in a simpler study in which there was only a single day of fasting (equivalent to the hours between sunrise and sunset). This alternative protocol was obviously far less demanding on the subjects and the experimenters, and the increased ease of recruitment of subjects associated with these changes meant that non-Muslims also would volunteer. We present here new results from a larger study that investigated this protocol further – by comparing a number of subjective and objective variables in non-Muslim subjects during a single control day and a single day of fasting.

4.6 Methods

4.6.1 Subjects and protocol

Eighteen male undergraduates from Tripoli University (age range: 18–21 years) were recruited by word of mouth for the study. The experiments were completed in July, 2012 and had previously been approved by the University Ethics Committee. Subjects initially underwent a familiarisation session when the various tests were described and subjects were required to practise them. The main experiment (begun at least one week after the familiarisation session) was in two parts: a non-fasting (control) day and a fasting (intervention) day. The order in which the two experimental days took place was randomly selected by the experimenters, but the subjects knew of this order at least a week in advance – so that they had an opportunity to eat/drink prior to sunrise (07:00 h) on the testing day and to go to bed/rise earlier if they wished to do so.

On the control (non-fasting) day, subjects were free to choose when to sleep, and what and when to eat and drink; on the fasting day, subjects were free to choose when to sleep and what to eat and drink before 07:00h and after 18:00 h. Food and fluid intake were prohibited between 07:00 h and 18:00 h but subjects were free to nap if they chose to do so.

4.6.2 Measurements made

On each experimental day, subjects attended the laboratory at 09:00, 12:00, 15:00 and 18:00 h in order to perform a series of tests and give a urine sample; they also answered the questionnaire again at home, when choosing to retire to bed at the end of the day. The tests and samples were given in the following order: questionnaire, urine sample, hand grip strength (dominant hand), vertical jumps, accuracy at throwing darts and the Stroop test.

Subjects were required to give information about their daily activities and feelings over the course of the day. They answered the questionnaire: (1) at 09:00 h, which reflected activities after waking; (2) at 12:00 h, which reflected morning activities; (3) at 15:00 h, which reflected activities in the early afternoon; (4) at 18:00 h, which reflected late afternoon activities towards the end of the period of fasting; and (5) on retiring to bed (designated 24:00 h in Figure 4.4), which reflected evening activities after breaking the fast. The methods of scoring the questionnaire were identical to those that had been used previously (Waterhouse et al., 2009).

The urine samples were analysed for osmolality (Osmocheck Pocket Pal OSMO, Vitech Scientific Ltd, Japan); this provided a measure of dehydration of the body.

Hand grip strength of the dominant hand was investigated using a dynamometer (Handgrip Dynamometer TRK5106. Jump MD, TAREK Scientific Instrument Score, Japan). The subject recorded grip strength on 3 occasions separated by 10-sec intervals, the maximum of the three values being recorded. This is a test of muscle strength using a comparatively small group of muscles.

Jump height is a further example of a test of physical strength but, unlike grip strength, involves the integrated actions of several groups of muscles. Subjects performed 3 maximal vertical jumps using the "stand-and-reach" method (Reilly et al., 1997). Keeping the feet flat on the ground, subjects stood side-on to a wall and reached up with the right arm; the wall was marked by the tip of the fingertips, onto which chalk powder had been placed. The subjects then jumped vertically as high as possible using both arms and legs to assist in projecting the body upwards. The wall was touched at the highest point of the jump. The difference in distance between the standing height and the jump height was the height jumped. The best of three attempts was recorded.

Throwing darts has been used as a model for investigating rhythmic and time-awake factors that influence this test of sensorimotor coordination (Edwards et al., 2007; Edwards and Waterhouse, 2009). Details of the method and scoring system used are given in these papers. In brief, the total score (higher means better performance), the number of misses (higher means worse performance), and the mean score per hit (ignoring the misses) were used as measures of throwing accuracy.

The Colour-Word Stroop Test (CWST) assesses working memory and attention, and so would be expected to show a rhythm peaking around noon (Folkard, 1990; Waterhouse et al., 2001) as well as deterioration due to restrictions of food and fluid intakes. The test consisted of the subject viewing 20 separate cards. Each had a colour - "red", "orange", "green" or "brown" - typed on it in one of these four colours. However, in many cases, the word was typed in a colour that was different from the meaning of the word – the word "orange" might be typed in green, for example. The participant was required to state the colour in which the word was typed, not the name of the colour that was typed. (In the

example given, the correct answer would be "green" rather than "orange"). Incorrect answers had to be corrected by the subject. The total time taken to answer all 20 questions correctly was recorded on a stopwatch.
After the tests had been completed, subjects were free to leave the laboratory and continue their activities until the next testing session.

Subjects varied in their experience of having throwing darts before the experiment, but none of them had any previous experience with regard to answering the questionnaires or performing the other tests. Also, none of them was aware of possible effects of fasting.

4.6.3 Statistical analysis

The data were analysed by the Statistical Package of Social Sciences, version 17 (SPSS Inc, Chicago, IL) for Windows. For most data, two-way ANOVA with repeated measures was used; the main factors were Condition (2 levels, Controls vs. Fasting) and Time of Day (4 or 5 levels, pre-09:00, 12:00, 15:00, 18:00 h for all variables and also on retiring, 24:00 h, for the results from the questionnaires). When fractions of possible occasions were compared, the data were arcsine-transformed before ANOVA. Greenhouse-Geiser corrections were used and significant differences within the main factors were assessed using Bonferroni corrections. To compare nominal data (if subjects chose to eat or drink before sunrise, for example), McNemar and Cochran tests were used. Correlations between variables were assessed using the method of Bland and Altman (1995), a method which corrects for multiple pairs of values being obtained from each subject.

Exact P values are reported; significance was set as $P<0.05$, though occasions where $0.05<P<0.10$ have been reported as "marginally significant".

4.7 Results

4.7.1 Questionnaires

4.7.1.1 Drinking

There was a significant increase in the number of subjects drinking in the early morning before the day of fasting (13 out of 18, compared with only 6/18 on the control day, P=0.016). The most frequent reason cited for drinking was "Thirsty". "Preparation for fasting" was cited only on the fasting day, even though this difference was not significant (P=0.25) due to the small sample size. All subjects drank after 18:00 h on both days. Again, "Thirsty" was cited most frequently on both days and "Recover from fasting" was cited more frequently on fasting days (P=0.002) (Figure 4.3).

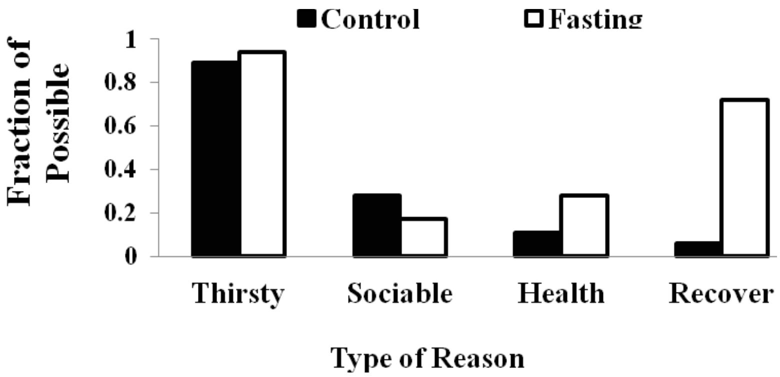

Figure 4.3 Reasons for drinking after sunset; fraction of possible occasions shown

4.7.1.2 Eating

There was a non-significant increase in the number of subjects eating before the day of fasting (12/18 compared with 7/18 on the Control day). "Hungry" was cited most frequently as the reason for eating on both days; "Prepare for fasting" was cited only on fasting days. After 18:00 h, "Hungry" was cited most frequently on both days and

"Recover" was cited significantly more frequently on fasting days (P=0.002).

4.7.1.3 Physical, mental and social activities

The amounts of these three type of activity actually performed all showed a significant difference with Time of day (P<0.0005). Activities were low early in the morning and showed higher values in the later morning and afternoon. Values in the evening, after the end of the fast, tended to be highest. However, there were no significant differences between control and fasting days and no significant interactions. By contrast, the amounts of physical and mental activity that subjects wished to perform not only showed significant effects of Time of day (P=0.004 or less) - values being highest around noon and the early afternoon and then declining after this time - but also showed a significant difference between control and fasting days (P=0.031 or less) - lower values being associated with the fasting days. There were no significant interactions. Figure 4.4 illustrates the representative results for the amount of mental performance wished for.

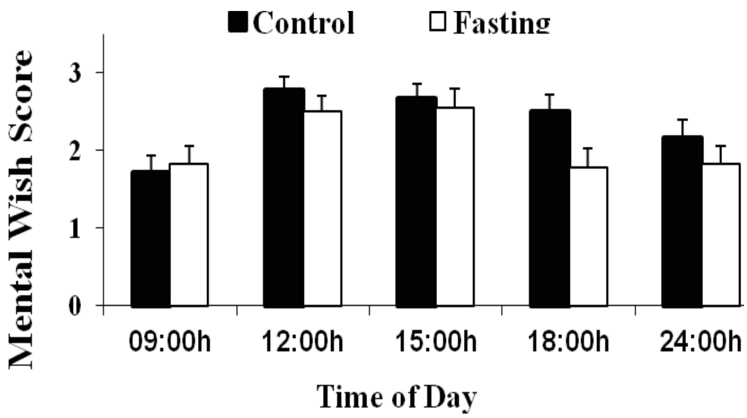

Figure 4.4 Effect of time of day upon the desire to perform mental activity on control and fasting days. Mean +SE

4.7.1.4 Fatigue

Fatigue showed a profile that was the inverse of that shown in Figure 4.4 There was a significant difference between the times of day ($F_{2.8,}$

$_{47.6}$=4.8, P=0.006) with fatigue falling during the morning and then rising throughout the afternoon and evening, to show a maximum in the evening. Even though fatigue tended to be higher on the day of fasting, this difference was not significant. There was no significant interaction between Time of day x Condition.

4.7.2 Urine osmolality

Figure 4.5 shows mean urine osmolalities during the course of the control and fasting days. There were significant effects of Condition ($F_{1, 17}$=30.7, P<0.0005), Time of day ($F_{2.3, 39.8}$=5.6, P=0.005) and an interaction between Time of day x Condition ($F_{2.5, 41.7}$=15.4, P<0.0005). The results show that the urine was fairly concentrated after waking from the night's sleep on both control and fasting days; urine osmolality then fell during the daytime on the control days, when daytime fluid intake was allowed, but tended to increase further during the daytime on the fasting day.

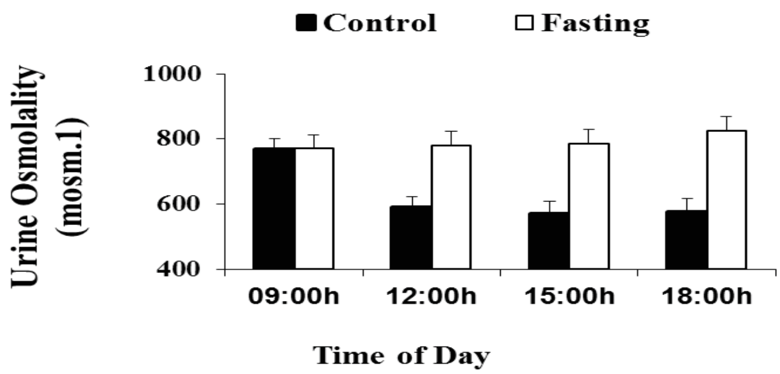

Figure 4.5 Mean +SE of Urine Osmolality under control and fasting conditions

4.7.3 Performance measures

For hand grip strength, there were no statistically significant effects due to Time of day, Condition or the interaction between these two factors.

For jump height, there was no significant effect of Condition ($F_{1, 17}$=1.4, P=0.26) but a significant effect of Time of day ($F_{2.5, 43.2}$=11.2, P<0.0005), performance improving throughout the daytime and evening. There was also a significant interaction between the two factors ($F_{2.4, 40.1}$=4.9, P=0.009), the improvement during the daytime being less marked on the fasting day, particularly in the late afternoon (Figure 4.6).

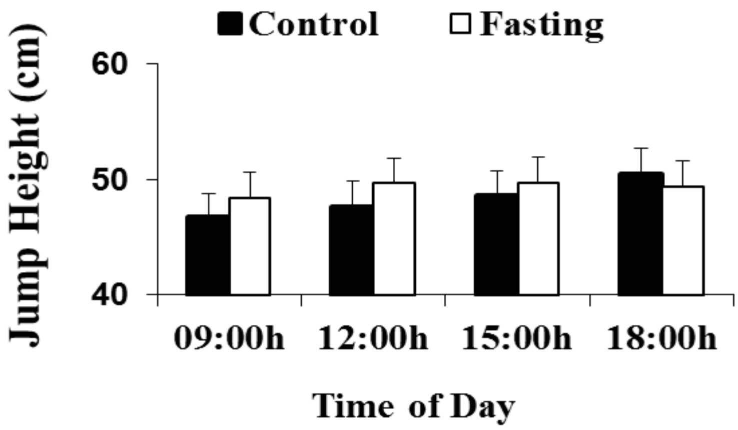

Figure 4.6 Maximum height jumped. Mean + SE

When throwing darts was considered, the number of misses (zero scores) and score/hit showed no significant effects of Condition, Time of day or interaction between these two factors. The total score for darts also showed no significant effect of Condition or Time of day, but an interaction that was marginally significant ($F_{2.6, 44.8}$=2.3, P=0.096), because the total score fell towards the end of the day during fasting only (Figure 4.7).

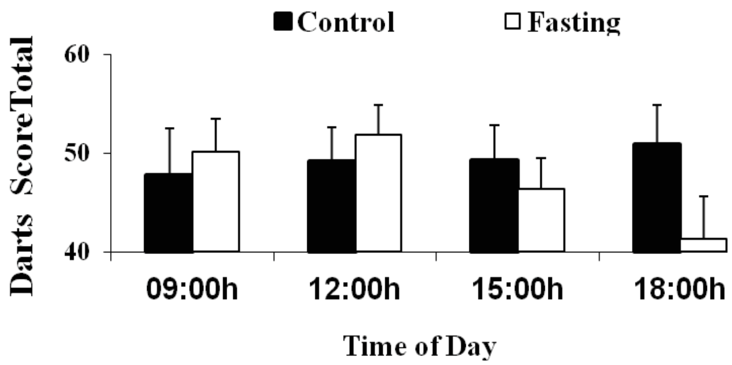

Figure 4.7 Total score for darts 4-17. Mean + SE

The Stroop test showed no significant effect of Condition ($F_{1,\ 17}$=2.5, P=0.13) but there was a highly significant effect of Time of day ($F_{2.0,\ 33.7}$=10.8, P<0.0005), performance improving (time taken decreasing) as the day progressed (Figure 4.8). There was no significant interaction between Time of day x Condition (P=0.62).

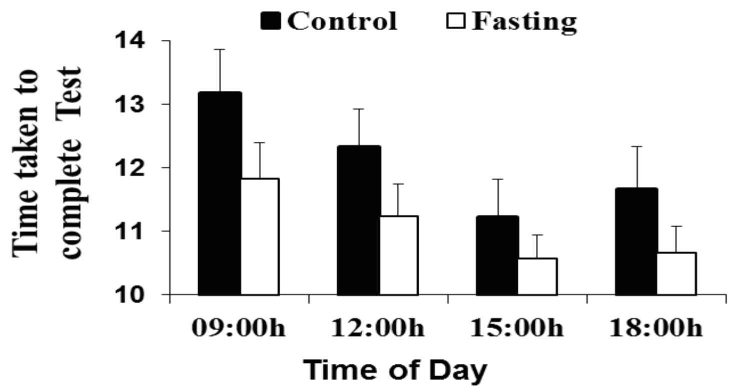

Figure 4.8 Time taken to complete test. Mean + SE

4.7.4 Correlations between the variables

The three scores for physical, mental and social activities that had been performed were summed (Score P), as were the two scores for the wished-for amounts of physical and mental activity (Score W). Values from all four times of day (09:00, 12:00, 15:00 and 18:00 h) and both control and fasting days were combined (a total of 8 pairs of values for each individual. The significant correlations were:

Score P vs. Fatigue =-0.16; Score P vs. Score W =+0.39; Score P vs. Time taken for Stroop test =-0.20.

Fatigue vs. Score W =-0.62

Score W vs. Urine =-0.18

Darts total score vs. Darts number of zeros =-0.74

Time taken for Stroop test vs. Grip strength =-0.24; Time taken for Stroop test vs. Jump height =-0.32

There were no significant correlations between performance at darts and the other variables.

4.8 Discussion

There was clear evidence for changes during fasting to: drinking and eating habits, amounts of wished-for physical and mental activity, and the hydration status of the body. There was also limited evidence to support the view that subjects made preparations before the time of fasting and replenished food and fluid after the fast. By contrast, the changes observed in grip strength, performance at the Stroop and jump tests and the ability to throw darts accurately were less clear.

The preparations for fasting and recovery from it afterwards agree with previous work upon subjects during Ramadan (Waterhouse et al., 2008a, 2008b, 2009). That is, as argued previously (Waterhouse et al., 2008b), the link between fluid and food intakes and the amount of drink or food ingested can break down in some circumstances – for example, when the meal serves a social function, intake might be greater than required metabolically (de Castro, 1987; Waterhouse et al., 2005). Whilst it can be argued that the observed preparations for a fast are intuitively likely, it must also be remembered that the fast lasted for one day only (unlike the situation in Ramadan) and the subjects had no prior knowledge of the demands of Ramadan, none of them being Muslim.

The subjects tended to show decreases in physical, mental and social activities during fasting and increased amounts of these in the evening after the end of the fast. Similar, and stastistically significant, profiles were seen for the amounts of physical and mental activity that subjects wished to undertake. These results support those found by us previously (Waterhouse et al., 2008a, 2008b, 2009) and indicate that subjects "spare" themselves when fasting. They also support the view that fasting has negative effects upon performance in general (see, for example, Kadri et al., 2000; Karaagaoglu and Yucecan, 2000; Leiper et al., 2003; Roky et al., 2000, 2004). Related to these changes in activity, and accepting that there are direct effects of activity upon core temperature, it is interesting to note that Roky et al. (2000) reported a daytime decrease in oral temperature between 09:00-20:00 h, and an increase between 23:00-24:00 h. In the current study, the amounts of activity actually performed and wished for tended to increase in the evening and exceeded those on control days, but these increases were not as marked as found previously (Waterhouse et al., 2008a, 2008b, 2009). The comparative lack of increase in activity after the end of the fast in the present study is likely to reflect the lack of a social role played by food intake in the present study (de Castro, 1987, 1997, 2000) - a role that would be expected to be more marked in a Muslim community during Ramadan than in non-Muslim students performing a single day of fasting and being able to go home after the laboratory tests at 18:00 h.

Urine osmolality was quite high on waking on both days, indicating the development of mild dehydration during sleep. The subsequent fall during the daytime on control days was due to the intake of fluids; by contrast, osmolality (and dehydration) continued to rise on the fasting day. Such results have been found previously in Ramadan (Reilly and Waterhouse, 2007; Waterhouse et al., 2009; Alabed, 2010). The observation that, at 09:00 h on the fasting day, urine osmolality was not lower than on the control day indicates that fluid intake before the start of the fasting period had not corrected overnight dehydration. That is, even though subjects were more likely to drink before the start of the fasting period, the amount they drank was insufficient to remove the mild dehydration that had arisen overnight.

With grip strength, no rhythm was demonstrated as well as no significant difference between the fasting and control days. It must be concluded either that this aspect of physical performance does not change with the amount of fasting undertaken in this study or that, as performed by these subjects, the test was not sufficiently sensitive. By contrast, jump height rose significantly as the day progressed and the two days differed, the rise during the course of the fasting day being less marked. This difference was most marked at 18:00 h when the dehydration due to fluid restriction was most marked. This result is in contrast to that of Judelson et al. (2007), who found no significant differences in jumping ability with dehydration levels leading to 2.5% and 5% body mass reductions, but the difference might reflect the fact that Judelson et al. had also required subjects to perform an exercise-induced heat stress trial the previous day.
With regard to physical performance in general, it has often been considered that muscle power is comparatively immune to the negative effects of sleep loss and fasting (Reilly et al., 1997). By contrast, motivation to perform activities and sensorimotor control (of fine movements in particular) are both affected negatively by sleep loss and fasting (Reilly and Waterhouse, 2009), and these factors might have contributed to the decline in physical performance observed later in the daytime on the fasting days in the current study.

The Stroop test showed a clear circadian rhythm, with performance improving (time taken to finish the test decreasing) until about 15:00 h. These results accord with those from other tests of mental performance which tend to peak slightly earlier than core temperature (Folkard, 1990). Even though performance was lower on the fasting day, the difference was not statistically significant and, again, possibility indicates that the test was not sufficiently sensitive for this type of study. Such a reservation applies also the the task of throwing darts, where no statistically significant rhythms were found. This finding contrasts with previous work (Edwards et al., 2007), where rhythms peaking in the afternoon were found. Also, there were no statistically significant effects of fasting upon performance at darts in the present study. Nevertheless, there was a marginally significant interaction between Time of day x Condition, and inspection of Figure 7 suggests that this is due to a deterioration from 15:00 h onwards during the fasting day. The subjects' inexperience in throwing darts might have decreased the sensitivity of this test, and more practice during familiarisation sessions might have improved its value. However, assessments of performance at darts were consistent insofar as a poorer performance, as assessed from the total score, was associated with an increased number of zeros scored.

Whilst causal links cannot be deduced from correlations, the following scenarios can be imagined: (1) If individuals are tired (Fatigue), they tend to perform less physical, mental and social activities (Score P) and wish to do less (Score W); and (2) If subjects are dehydrated (Urine osmolality), then one of the general effects of this is to feel less inclined to perform physical or mental tasks (Score W). There might also be correlations between different performance tasks that are similarly affected by fasting and time awake. For example: (1) The less activities that have been undertaken (Score P), the poorer will performance be at some tests (more time taken to perform the Stroop test); and (2) Poorer performance at one task (time taken to perform the Stroop test) is likely to be associated with poorer performance at other tasks (Grip strength and Jump height). It is clear that much further work is required to assess these suggestions with regard to causal links.

4.8.1 General conclusions and implications for studies of Ramadan

The present results support the concept that daytime fasting and some degree of sleep loss are associated with general declines in performance and the sense of well-being, a conclusion that has been drawn from our previous studies (Waterhouse et al., 2008a, 2008b, 2009; Alabed, 2010) and reviews of the field (Reilly and Waterhouse, 2007; Wilson et al., 2009; Maughan et al., 2010; Waterhouse, 2010; Shephard, 2012). The detailed cause of such deterioration cannot be deduced from the present study but it is important to note that the deterioration is worse as the time spent fasting increases. What the present results also show is that many of the results previously observed in field studies of Ramadan - when recruitment was almost inevitably restricted to Muslims, the experiment could be performed only during Ramadan itself, and the experiment necessarily took 4 weeks to complete - can be duplicated by this much shorter protocol. However, the physical and psychometric tests employed in the present study did not show deterioration as clearly as had performance at a set bout of exercise, a test that had been used in a previous field study (Waterhouse et al., 2009). Whether this difference reflects the insensitivity of the tests to effects of fasting, the different type of subject, the difference between one day and 4 weeks of fasting, or some combination of these factors, is unclear.

Nevertheless, an important implication of the present investigation of some of the effects of fasting is that, as with studies upon Ramadan, individuals who have tasks to carry out will be less well able to perform them and less motivated to do so, particularly as the time spent fasting increases during the course of the daytime.

PART III
IMPLICATIONS FOR TRAINING IN RAMADAN

It has already been mentioned that food and fluid restriction, combined with some degree of sleep loss, contribute to deteriorations in mood and mental performance, and that at least some of these changes will be important for those who undertake tasks that are repetitive or where the ultimate aim is not immediate but sometime in the future. Athletic training is a good example of this. That is, training will seem to be more arduous in the month of Ramadan and is also likely to be performed less well.

4.9 Time of Training

4.9.1 During normal circumstances

The time(s) at which individuals train often depend upon their lifestyle and other commitments. Consequently, training often takes place in the early morning (before work), at lunchtime, or in the evening (after work). The value of training for the development of muscle power or endurance depends upon the amount of work performed - rather than the individual's perception of effort involved, for example. The amount of work performed is generally greatest around the time of peak of core temperature (in the late afternoon) because, at this time, the rhythm of physical performance is at its maximum and the rating of perceived exertion for any given amount of work is least. Both of these reasons will contribute to the fact that training earlier or later in the day might be less effective. An additional factor that is important when the time of training is considered is that training that requires concentration and the development of cognitive and mental performance skills (archery, for example) is best performed in the late morning, effects of time awake not having become marked by this time.

Apart from training at a time when physical performance is not at its peak, there are other reasons why early or late in the daytime is non-ideal. Early in the morning, soon after waking, the intervertebral discs of the spinal cord are slightly swollen due to having absorbed fluid during the sleep period when the spine was unloaded. Such swelling might increase the risk of damage (a "slipped disc") until this excess fluid has been expelled from the discs. This loss of excess fluid is normally brought about by gravity acting upon the body mass and has occurred about 1-2 h after becoming upright. In addition, the cardiovascular response to a set amount of exercise is greater in the morning than later in the day, the blood pressure rising more at this time. Whilst the possible damage this might cause has not been assessed epidemiologically, it coincides with the time of the highest frequency of cardiovascular morbidity from ischaemia and haemorrhage, and so caution is advised. To the extent that such rhythms in morbidity have an exogenous component, training immediately after a siesta or nap would also be counter-indicated. Training sessions are not advised in the evening, since they are likely to impede sleep onset due to the raised core temperature that they produce.

4.9.2 During Ramadan

For individuals training during Ramadan, there will be several problems - due to fasting (negative effects of lack of food and fluid intakes), increased fatigue (curtailed nocturnal sleep) and increased time awake (rising earlier to prepare for fasting). These factors that will make a set amount of training more difficult, will lead to individuals performing their schedules less conscientiously, and/or will lead to the work-load during training being decreased. Moreover, any undesirable after-effects of training might last for some hours in Ramadan. For example, training in the morning, 2-3 h after the pre-sunrise meal, will lead to the normal losses of fluid and energy - but with no opportunity for their rapid restoration, following the end of the exercise, as generally occurs. It is also the case that the effects of fasting will be most marked in the late afternoon (just before the end of the fast at sunset), at a time that is asssociated with "best performance" on non-Ramadan days. Nevertheless, even if exercise intensity and the general standard of training are lower than normal, continuing training will be better than foregoing training altogether.

Can the standard and value of training be maintained in such circumstances? One possibility is to consider if the time of training can be changed so that the sessions are still as effective as normal.
There is some suggestion that it is possible to habituate to training at a particular time of day. Thus it has been found that competitive performance in cycle time-trials was improved by training for some days before the trials at the same time as when the trials were to take place. To what extent this concept might be applied to Ramadan is unknown; for example, might training be as effective as normal if it were delayed until after sunset? The first intake of food after sunset is typically dates taken with water, and this will replenish some of the

fluid and calorie deficits accumulated during fasting. After the absorption of this meal, but before the main evening meal, there might be the possibility of exercise training. There might also be the additional benefit of exercising after darkness has fallen when, in hot climates, the high environmental temperatures can be avoided.

However, evening training might have other effects upon the body. It is possible that training at this time will delay the body clock due to the zeitgeber effect of exercise at this time. If this were the case, then training would be taking place closer to the times of peak of performance and this would increase the work that could be done, the motivation to perform maximally, and the value of the training – all of which are advantageous. On the other hand, delaying the body clock in this way would have the negative consequences that the propensities both to get to sleep and to wake up in the morning before sunrise would also be delayed. Some studies indicate that retiring and rising times can be substantially delayed in Ramadan, with individuals rising quite late in the morning and their training (in the evening after sunset) appearing to be maintained qualitatively and quantitatively. Whether the phase of the body clock changes in such circumstances is not known.

The concept of changing the times of training during Ramadan on the basis of a chronobiological rationale is comparatively new, and far more work on its efficacy and other consequences for the individual is required before it can be recommended. It must also be remembered that, even though adopting such training regimens might be acceptable in Muslim countries, these practices are likely to be impossible in other countries – in Europe and the USA, for example - where training takes place in the daytime to fit in with the lifestyles of the (non-Muslim) majority of the population.

4.10 General Conclusions

A. It is clear that daytime fasting in Ramadan has many effects on an individual's physiology, psychology and biochemistry, and that these affect daily performance, athletic training and sports skills. The evidence indicates that most changes during the Holy month are not progressive, individuals recuperating from each day's fast during the evening.

B. However, mental and physical performance does deteriorate during the course of the daytime fast by an amount proportional to the length of time the individual has been fasting. This deterioration has important implications for training, particularly the motivation to do so regularly, effectively and conscientiously.

C. Many of the changes observed relate to alterations of the daily rhythms of many variables, but the relative importance of the endogenous (clock-driven) and exogenous (environmentally- and lifestyle-driven) components of these rhythms has not been determined.

D. Investigations of Ramadan are necessarily time-consuming, but new results from a laboratory-based experiment indicate that a single day of fasting can replicate many of the changes seen during the daytime in Ramadan itself. This simpler protocol can be of value not only in studying the effects of Ramadan but also, because the protocol is less arduous for the subject, in more easily recruiting subjects (including non-Muslims) for experiments.

E. Accepting that training in Ramadan poses several problems for the Muslim athlete, the possibility of changing the time of training until the evening and after the fast is an attractive one, but this requires further scientific study to establish whether training at an altered time is equally effective and if any adverse changes to an individual's physiology, biochemistry and psychology are also produced.

PART IV
FURTHER READING AND REFERENCES

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5 DESYNCHRONISATION OF CIRCADIAN RHYTHMS IN ATHLETES: JET LAG SYNDROME

Pavel Homolka et al.

Biorhythms related to astronomical phenomena determine periodic quantitative and qualitative changes as well as the behaviour of living organisms. Each person has their own internal rhythmic cues called *endogenous oscillators* ("internal clock"). Circadian rhythm is one of the fundamental long-term biorhythms. It lasts approximately 24 hours and it is mainly synchronised by external rhythmic cues, especially the light-dark cycle and social factors (time familiarity, behaviour of the surroundings). Sudden changes of *external rhythmic cues* (e.g. a change in the light-dark cycle resulting from trans-meridian air travel or from night-shift work) lead to rhythmic desynchronisation. Adaptation to the changes varies interindividually, as does resynchronisation, which lasts several days and manifests itself first as restoration of the sleep-wake rhythm and later as re-establishment of the rhythm of all the other functions. (Placheta et al., 1999).

5.1 Travel Fatigue

Elite and high-performance athletes spend dozens of hours on international flights and cross multiple time zones in a short time on a regular basis. They travel to participate in club or international competitions and tournaments. In other instances the athletes pursue high-altitude training or better weather conditions for their training. During the sport season, top hockey, football and tennis players travel across every continent and their bodies have to adjust to different time-zones and climates very often. After their return home they have to re-adjust to their home environment. This is accompanied by travel- and delay-related stress, stress caused by unpleasant in-flight experiences, negative emotions, unplanned stops, etc. The passengers usually travel in a sitting position. After several hours, this cramped posture can result in swelling of the lower extremities and muscle spasms in predisposed people. Temporary fatigue during a flight is referred to as "travel fatigue" and it occurs not only on trans-meridian travel, but also during northbound and southbound flights. Temporary symptoms of "travel fatigue" can occur during any longer journey, and they usually disappear quickly. The causes of travel fatigue are listed in Table 5.1.

Table 5.1 Symptoms and causes of travel fatigue *(Waterhouse et al., 2002)*

Symptoms
Fatigue
Disorientation
Headaches
Causes
Disruption of the routine
Hassles associated with travel (checking in/baggage claim/customs clearance)
Dehydration due to dry cabin air

Advice
Before you go:
Plan the journey well in advance
Try to arrange for any stop-over to be comfortable
Check about documentation, inoculations, visas
Make arrangements at your destination
On the plane:
Take some roughage (for example, apples) to eat
Drink plenty of water or fruit juice (rather than tea/coffee/alcohol
On reaching your destination: Relax with a non-alcoholic drink Take a shower
Take a **brief** nap, if you wish

5.2 Jet Lag Syndrome

The sleep-wake rhythm of every person is regulated by their internal **biological clock**. It is located in two small bilateral groups of nerves within the hypothalamus (***suprachiasmatic nucleus*** or ***nucleus supraschiasmaticus – SCN***) and is responsible for generating internal circadian rhythms and synchronising them with a day-night alternation cycle. The term '*jet lag syndrome'* refers to the problems directly related to rapid trans-meridian travel. This process is also known as **circadian dysrhythmia** and is caused by the desynchronisation of body biorhythms because of the time difference in the final destination (Table 5.2). The symptoms can occur after crossing as few as two time zones. The greater the time difference, the more intense the symptoms of jet lag can be. The biological clock will eventually adapt to the new environment and the symptoms of jet lag will subsequently disappear (Lemmer, Kern, Nold & Lohrer, 2002). Desynchronisation of the circadian rhythms can also have a negative effect on the performance of athletes and their support staff. In 2007, the European College of Sport Science (Reilly, 2007) published a practice-oriented paper on this phenomenon. It explains the biological nature of jet lag and contains recommendations on how to prevent its symptoms and overcome it in the shortest time possible. Certain studies have shown that muscle strength decreases and reaction time is prolonged for five days when athletes cross five time zones westwards (Reilly, Atkinson, 2001).

The intensity and duration of jet lag symptoms depend on several factors:
1) the number of time zones crossed,
2) eastward-westward flight direction,
3) ability to sleep during a flight,
4) differences in tolerance to individual symptoms.

The symptoms are generally more intense when flying eastwards. In terms of number of days necessary for sufficient acclimatisation in the new environment, there is a formula of **1 day/1 time zone**, regardless of the flight direction (Waterhouse, Reilly & Edwards, 2004).

In general, there are obvious individual differences in preferred biological clock timing. Some people are colloquially referred to as ***early birds (larks)*** while the others are called ***night birds (owls).*** Experts make a distinction between different circadian types, or chronotypes. These are divided according to their preference for either morning or night hours, which may have a great influence on the speed of the biological clock's resynchronisation with new external time conditions. In theory, morning types may synchronise their biorhythm faster when flying eastwards, and night types when flying westwards (Waterhouse et al., 2004). When crossing more than 12 time zones, it is recommended to divide the journey into two days and have an overnight stop. This is, however, usually not done due to logistic and financial reasons. When planning a flight it is better to choose one with a late afternoon or evening arrival time. This enables the traveller to get a full night's sleep in the new time zone. On the other hand, higher temperature in the new destination or hypoxia can slow down the acclimatisation process.

Table 5.2 Jet lag symptoms

Fatigue and daytime sleepiness at the final destination
Sleep disorders in the new environment: middle-of-the-night insomnia, difficulty falling asleep in the evening, frequent night-time awakening, light sleep
Reduced mental and physical performance, poor concentration and decreased motivation
Headaches
Increased mental instability and irritability
Loss of appetite and indigestion (diarrhoea or constipation)
Alterations in the menstrual cycle in women

5.3 General Recommendations for Coping with Jet Lag Symptoms

The following recommendations are based on the chronobiological and physiological principles of biological clock behaviour. Their role is to help travelling athletes minimise jet lag symptoms and resynchronise their biological clock in the shortest time possible.

- The journey should be planned so that the athlete arrives at the destination where the competition takes place several days in advance. In terms of the number of days necessary for sufficient acclimatisation to the new environment, there is a formula of **1 day/1**

time zone, regardless of the flight direction. The time necessary for adaptation varies. In general, young people cope with jet lag symptoms better and faster than older people. Some studies have shown the necessity of a longer time for biorhythm resynchronisation. Lemmer (2002) observed blood pressure and heart rate changes in a group of athletes while crossing eight time zones eastwards and six time zones westwards. He evaluated their 24-hour blood pressure and heart rate profile chronobiologically using cosinor analysis. He found that even 11 days after the arrival at the final destination, neither optimal blood pressure nor the heart rate had been resynchronised. This may have a negative effect on an athlete's performance. To minimise jet lag symptoms, one can undergo pre-flight preparation one to two days before the flight. This consists of gradual adaptation to a sleep pattern typical for the final destination. When travelling eastwards it is recommended to go to sleep one hour earlier than usual, and when travelling westwards, one hour later. Sleep shifting exceeding two hours seems to be counter-productive, and it can have a negative effect on the training process and sport performance.

- When boarding the plane, it is necessary to set one’s watch to the destination time. It is advisable to start living in accordance with the destination time already while on board (Waterhouse et al., 2004).
- Sleeping during the flight is recommended only it is night time in the final destination. It is optimal to arrive at the destination in the late afternoon or in the evening.Westward flight causes so-called *phase delay* of the biological clock, and this requires you to stay awake for an unusually long time and to be active during the flight. Concerning a quick resynchronisation, sleeping is actually counter-productive. Cabin lighting and social activities can help travellers to stay awake. On the first night at the destination, it is acceptable to go to sleep one to two hours earlier than usual if you are very tired.
- Eastbound flight causes *phase advance* of biological clock. Flights from Europe to Asia and Australia are usually scheduled at night. In this case it is also recommended to sleep only when it is night time at the final destination.
- During the first days after the arrival, athletes should avoid training

in the morning hours. It is advisable to train in the late afternoon and in the evening. After arrival at the final destination, it is absolutely necessary to continue to eat and keep the sleep-wake schedule in harmony with the local time, regardless of one's individual inclinations.

- Morning exposure to sun or light of higher intensity (more than 2000 lux) can help bring the biological clock back to normal.
- Dry aircraft cabin air might cause dehydration and it is therefore recommended to maintain sufficient fluid intake, preferably by drinking mineral water and fruit juices. Drinks containing caffeine and alcoholic beverages are not recommended.
- To prevent swelling, muscle spasms and vein thrombosis, it is necessary to ensure blood circulation in the legs. At least two hours after take-off, isometric exercises of thigh and calf muscles, stretching, frequent walks down the aisles and wearing mild compression stockings promoting venous return are recommended.
- Medication treatment: In cases of difficulty falling asleep, it is possible to take benzodiazepines. Melatonin is an acceptable chronobiotic which supports sleep induction. However, the purity of melatonin bought somewhere other than a pharmacy is questionable, and it might cause undesired side effects. It is recommended to take a dose of 0.3-5.0 mg 30-60 minutes before sleep on the day of the flight and for the first few days after arrival.
- Dietary adjustments: it has not yet been reliably proven whether they accelerate the resynchronisation of the biological clock with the external environment. Certain studies recommend a higher protein intake in the morning after waking up and higher carbohydrate intake before going to sleep. In general, there is consensus about the right meal timing being more important than the actual nutritive value of the food. (Reilly & Waterhouse, 2005).
- For athletes, the first training in the new destination should be planned as soon after arrival as possible.

5.4 Experience of the Czech Olympic Teams with Trans-meridian Travel

Problems possibly related to the Czech Olympic teams' trans-meridian travel were considered and addressed at:

the 1988 Summer Olympics in Seoul,
the 2000 Summer Olympics in Sydney,
the 2002 Winter Olympics in Salt Lake City,
the 2008 Summer Olympics in Beijing,
the 2010 Winter Olympics in Vancouver.
The Czech athletes, their management team and their healthcare management team had to address two problems:

- jet lag syndrome
- problems related to the shift in sleep-wake rhythm

In sports, these problems are dealt with by attempting to adapt the athletes to the local conditions optimally and quickly. This process is known as acclimatisation. According to the healthcare personnel and coaches, as well as the athletes themselves, the second problem poses more difficulties. It affects regeneration, training schedules, preparation for the competition as well as the whole acclimatisation process in a more obvious way than jet lag syndrome. Surprisingly, when travelling westwards, the biggest complaints do not concern expected fatigue in the late afternoon when people in Europe are already asleep. On the contrary, it concerns predawn awakening and the inability to catch up on lost sleep. If we consider sleeping to be the most important regeneration method, its duration, its quality and the time taken to "catch up on lost sleep" are the essential factors influencing sports performance. On top of that, the participation of the Czech athletes in the Winter Olympics was made even more difficult because they had to adapt to a higher altitude. Questions were raised about how to use that to their advantage in the training process (or whether to avoid it as it was a negative regeneration factor), presenting practical issues such as where to stay, sleep and regenerate, taking the altitude of the actual competition into consideration. *(Note: This is a real puzzle for top athletes who aim to win medals. To speed up acclimatisation and improve pre-competition preparation, their management teams sometimes even refuse accommodation in the Olympic village with the rest of the athletes, preferring to find accommodation on their own at what seems to them a more suitable altitude. This approach is most common for cross-country skiers, but recently it has also been adopted by biathletes. In the 2002 and 2006 Olympics, the best Czech cross-country female skier, Kateřina Neumannová, chose to sleep at the altitude of the competition – outside the Olympic village.)*

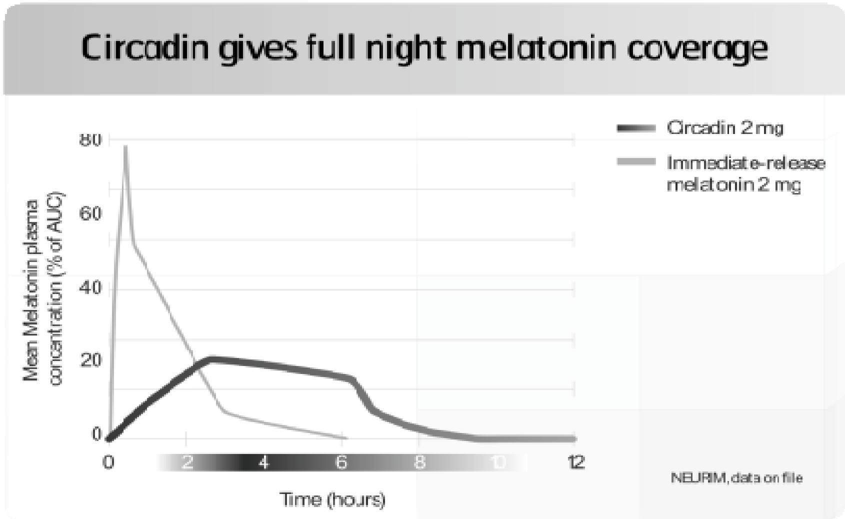
Other negatives are related to the time difference. They are not easy to classify or measure, and what is more, they show large interindividual and even intraindividual heterogeneity. Therefore they were addressed individually from case to case. There is a common stereotype often found in the literature: westward travel is accompanied by fewer difficulties than eastward travel. However, this is only true if the athletes are prepared for the time difference and particularly for the sleeping difficulties. In our experience, westward travel is subjectively considered to be more problematic. When analysing the group diagnoses and complaints of the members of the Czech Olympic team, for example during the 2000 Summer Olympics in Sydney, we find only one (woman) Olympian who complained about acclimatisation difficulties (B12 IM was administered then). The Chinese Olympics in Beijing (+8 hours) caused no major problems for the Czech Olympians (e.g. evening fatigue or having to force oneself to get up in the morning).It is possible to influence sleep cycle problems systematically. Surprisingly, there is practically no problem with the time when one goes to sleep. The majority of the athletes were able to adapt to the bedtime of the new destination almost immediately. However, as mentioned above, the fundamental (solvable) problem is how to eliminate annoying awakening in the middle of the night after travelling westwards. In practice this concerns the west coast of North America, where the time difference reaches nine hours, which was the case for the 2002 Winter Olympics in Salt Lake City and the 2010 Winter Olympics in Vancouver. If medications are not used, it takes five to seven days to stop night-time awakening, which the athletes usually do not appreciate. Before describing the particular methods and means of coping with this phenomenon, it is necessary to mention that cabin crew members often encourage their passengers to adopt a certain sleeping, waking and eating schedule which is difficult to resist.

What were the methods and means used in the case of the Czech Olympians?

5.5 Altering Biorhythms by Using Medications

a) Melatonin

Melatonin is a hormone produced endogenously in the pineal gland. Its dynamics depend on the light-dark cycle. Exogenous administration aims to harmonise sleep cycle and eliminate jet lag symptoms. For example, during the preparation for the 1988 Summer Olympics in Seoul, it was considered merely a potential possibility, but in the course of the last 15 years, starting with the Sydney Olympics, administering melatonin has become common practice. At that time, there was no registered medication containing melatonin in the Czech Republic. An easy solution was the use of Bio-Melatonin, produced by the Danish company PharmaNord and sold in Slovakia. The still-valid recommended dosage is one 3.0 mg dose of Bio-Melatonin taken one hour before bedtime at the final destination, administered at the airport or onboard. It is necessary to continue taking it for approximately 10 days. While preparing for the sleeping difficulties during the Winter Olympics in Vancouver, the scheme was improved upon by combining it with then newly-approved Circadin, a melatonin medication with prolonged release. The head team physician (the author of this article) and a top sleep-medicine specialist, doc. MUDr. Karel Šonka from the Clinic of Neurology at the General University Hospital in Prague, agreed to try this combination during a short inspection trip to Vancouver in the autumn of 2009. This combination (together with the newly chosen hypnotic) worked well. The reason for its use is demonstrated in the diagram below. A single dose administered before going to bed induces sleep and the prolonged release covers most of the time needed to rest.



Source: corporate documents – NEURIM, Israel

Czech representatives from the Lundbeck company provided the entire Czech Olympic team with the medication, which usually costs more than 400 CZK (Czech crowns), for free. Melatonin is currently considered a standard food supplement (or medication) for athletes who travel long distances. Considering the variance in quality among food supplements and medications with the same active ingredient, it is definitely recommended to use medications.

b) Hypnotics

During the 2002 Winter Olympics in Salt Lake City, it was demonstrated that Bio-Melatonin alone is not enough to fight predawn awakening. The physician of the Czech cross-country skiers, MUDr. Martin Koldovský, decided to combine Bio-Melatonin and Zolpidem (Stilnox, Hypnogen, …) – the only hypnotic used at the time – and to increase the Bio-Melatonin dosage to two pills. The problem was solved and hypnotics for the team were then bought in local drugstores. Seven years later, preceding the 2009 Winter Olympics, doc. Šonka and the inspection team departed for Vancouver. They re-evaluated the use of Stilnox, which was considered less effective in comparison with Zopiclone. Finally, they settled on the common medication Zopitin 7.5, produced by the Finnish company Viabalans. Thanks to its shorter half-life, it does not cause any hangover-like symptoms. People get quality sleep and the risk of becoming addicted is low. Doc. Šonka strictly recommended our team to induce sleep by means of hypnotics and melatonin instead of the more difficult natural way – gradual time rhythm synchronisation – before athletic performance. Each team member was thus provided with a one-week supply of medication. When Czech sport journalists learned of the success, they demanded the medications for themselves. Once again it was proven that melatonin alone has little effect on the duration of sleep. Its effect was not sufficient unless combined with hypnotics. In the search for further methods of sleep cycle harmonisation, a new method, also created in Scandinavia, was considered before the Winter Olympics in Vancouver. It is based on the "smart" use of a powerful light source with a 2000 lux intensity – the Bright Light. It affects melatonin production through the retinohypothalamic tract. It is used to substitute sunlight on days with decreased daylight in the areas near a polar circle, but it can also be useful as a treatment and a means of prevention. Here it would be opportune to discuss the possibilities of objectivisation of the time at which the phenomenon described as acclimatisation in the professional literature (adaptation to local conditions including the time difference) takes place. Although this issue has been dealt with in thousands of publications, in the Czech Republic the research related to the Olympics and sports in general is not very extensive. The first study on this topic, a 1989 paper by MUDr. Jaroslav Novák and Ing. Jan Zelený, was followed by a study by MUDr. Jaroslav Větvička et al. in 1990. At that time, the Laboratory for Clinical Biochemistry and Physiology at the National Health Institute for Elite Sport, where they worked, conducted a unique study. They measured blood and urine levels of cortisol and a number of other parameters at the 1987 Pre-Olympic Basketball Tournament in Seoul. Measuring blood cortisol proved to be a fruitful idea. When crossing time zones (+8 hours) it reacted by dropping, and it subsequently increased gradually between days 8 and 12. This was the first time the adjustment of sleeping and training regime and a special dietary preparation (serotonin precursor tryptophan) were recommended for the sportsmen. The study by Botka et al. published in 2009 (Faculty of Physical Culture, Palacký University, Olomouc) is also worth mentioning. He evaluated the acclimatisation process in his subjects by monitoring the autonomous nervous system (ANS) by means of a spectral analysis of heart rate variability (SA HRV). He then adjusted the timing of the training as well as the training load for the two Czech athletes who crossed several time zones eastwards (+6 h.: Summer Olympics in Beijing) and westwards (-7 h.: World Championship in Bogota). Sudden changes in light and dark exposure cause internal clock desynchronisation in the human body, which is also reflected in the disruption of circadian rhythm in both branches of the ANS. According to the study results, by the third day of acclimatisation after their arrival in Beijing, the ANS function of the participant had successfully adapted, enabling the resumption of the usual training regime, which could even be intensified on the fourth day. In the case of a female swimmer who flew westwards, no major deterioration in ANS function was identified. She thus continued with her standard training load, which had to be reduced on the third day after arrival. Despite the small number of athletes tested, it is clear that acclimatisation to new space-time conditions is highly individual and it does not always follow general recommendations. The SA HRV method therefore seems to be a prospective tool for solving the question of acclimatisation in trained individuals who cross several time zones.

Supported by the European Regional Development Fund - Project FNUSA-ICRC (No.CZ.1.05/1.1.00/02.0123) and the Ministry of Health - grant IGA (NT13434-4/2012).

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EPILOGUE

...once, in the infinite infinity of white and black, of victories and failures, we will all come to understanding that this is where we are and that we are not going anywhere. The only thing to change is our calling and the form of our existence in the Universe full of exact secrets of chronobiological phenomena pieces of which, even from this monograph, will find their place among the stars of next chapters in the invisible galactic publications. There will also be an extract from a potential epilogue. Therefore, savour every shade of all of its colours before additional chapter from another book will come out.

...thinking of our unflagging pride that have lasted from the oldest days until now, ceaselessly reminding ourselves of what distinguishes us from other inhabitants of the Blue Planet, how about leaving questions to philosophers and contemplate the core and meaning of chronobiological views of the Universe with the sinusoids that constitute the gate of our incomprehensible existence in time and space.

... If somebody brought life to us and life in its fundamentals and its form mean movement, then knowledge and understanding of health and the ways to strengthen it and the understanding of diseases from different perspectives of their origin is, was and always will be irrefutably and indisputably connected with prevention and sportsmen and their performance. Chronobiological approach is directly related to sports training, too. Recording of individual state of sportsmen at the time or some other time (in case of an individual or a team sport) of the impact of training and competitive stress is of great importance as far as maintaining of their health and performance is concerned. The right timing of a sportsman's (a human being) performance level in its various forms is the result of understanding of the factual core of the importance of chronobiology in sport where even basic elements of performance such as e.g.: flexibility, muscular strength or reaction time demonstrate rhythmic rises and falls following the circadian model in almost every kind of sport.

Chronobiological aspect, is fundamental in chronobiological research which develops in parallel with pedagogy, psychology, genetics, medical science, heliobiology and also with sport because rhythms of external environment are (de)synchronized in relation to biological rhythms of an organism

Theoretical and practical significance of chronobiological and heliogeophysical research in the field of physical education and sport lies in the formation of scientifically proven approaches to individualisation of pedagogical, psychological, medical and healing effect. This, together with others factors, helps sportsmen maintain their health, keep their competition longevity and perform to the best of their ability when needed the most. Therefore, the correct implementation of particular chronobiological principles into a foresight inventory of sports doctors, fitness coaches, trainers and sports psychologists is important and we need to realize the necessity of chronobiology with respect to its indisputability and existence, with or without us.

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Title: **CHRONOBIOLOGY FROM THEORY TO SPORTS PRACTICE**

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Cover:	František Mereš
Impression:	100 pcs.
Pages:	145 pages; 7,3 AH
Size:	A5
Edition:	prvé
Editor:	Towarzystwo Slowaków w Polsce
Print:	Towarzystwo Slowaków w Polsce
Year of Publication:	2013

ISBN 978-80-557-0634-4