DAMAGE IN SPORTS

The battle against acute injuries, overuse injuries and the overtraining syndrome

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DAMAGE IN SPORTS
The battle against acute injuries, overuse injuries and the overtraining syndrome

Schade door sport
De strijd tegen acute blessures, overbelastingsblessures en het overtrainingssyndroom
(met een samenvatting in het Nederlands)

Proefschrift

ter verkrijging van de graad van doctor aan de Universiteit Utrecht op gezag van de rector magnificus, prof.dr. J.C. Stoof, ingevolge het besluit van het college voor promoties in het openbaar te verdedigen op dinsdag 14 december 2010 des middags te 4.15 uur

door

Sándor László Schmikli
geboren op 19 april 1961 te Haarlem

Promotor: Prof. dr. FJ.G. Backx

Co-promotor: Dr. W.R. de Vries

Content

Damage in ancient boxing

Amykos, groggy on account of the blows, is injured around the mouth and spits blood. When Polydeukes realizes that his adversary is at his mercy, he strikes him with a formidable blow above the nose, exposing the bone of the forehead. Amykos collapses, but manages to get up again. Then Polydeukes strikes again and cuts Amykos' temple, then he aims at the mouth and the teeth make a rattling noise. Amykos falls down again, but succeeds in raising the hand as a sign of giving up. He was close to death ... "

Theocritus (315-250 BC)

1

General introduction

In modern sports, severe local injuries of an acute nature such as sprained ankles, bone fractures, or ruptured ligaments, are very common. Local overuse injuries, such as the tennis elbow, shin splints, or Achilles tendinopathy are well-known problems resulting from a lasting inadequate balance between load and recovery. It is not known, why in some athletes an inadequate balance leads to a gradual onset of local injuries, while in others a systemic maladaptation of body and mind (‘overtraining’) develops.
Evidently, acute injuries, local overuse injuries, as well as systemic overuse and overtraining are aspects of damage in sports that should be prevented when possible. As a contribution to a prevention approach, in the first part of this thesis the focus is set on methods that indicate in which of the modern sports activities damage due to acute injuries and/or local overuse injuries demands preventive measures. Data from the 2000-2005 national survey Injuries and Physical Activity Netherlands (IPAN) were analysed to provide quantitative support for prevention programs against sports injuries by the Dutch government and sports organisations. Also, the currently used sports injury registrations systems in the Netherlands were evaluated on their specific tasks to provide high quality information to enhance sports injury prevention.
The second part of this thesis is focussing on methods to prevent systemic maladaptation in athletes, also known as the Overtraining Syndrome (OTS). The emphasis is on the search for parameters that are able to distinguish non-functionally overreached (NFO) athletes from healthy control athletes. The stage of NFO is considered as a specific phase in the overload process that precedes the stage of OTS, characterized by a reduced performance capacity. The parameters used are overload-related changes in the hypothalamic-pituitary-adrenal (HPA)-axis, mood, and neural network communication in different parts of the brain as measured by means of EEG (electroencephalogram) coherence.

HISTORY OF DAMAGE IN SPORTS

The history of sports goes back a very long time. Gymnasts were performing as much as 6000 years ago in China. In ancient Egypt wrestling, javelin throwing and swimming were very popular. In ancient Persia, sports were often related to warfare skills. Men were trained and drilled physically to stand up against enemies during hostile periods.
Between 800 and 750 BC the institutionalisation of sports began in the Greek town called Olympia. Probably starting as a religious venue, in 776 BC male athletes entered a 190 meter sprinting race to entertain the people in the Olympic stadium in Olympia. Longer races were added after that, with the last run covering the largest distance while wearing full armour. The Olympics were organized every four years, and completed with the addition of sports, such as boxing, wrestling, pankration (a mixed discipline of boxing and wrestling), chariot racing (races with horses and carriage), several other running events, as well as pentathlon[25,27].
In these events an athletic injury was very common. For instance, boxers used leather gloves with metal or wooden parts to hurt their opponent. Even death was of no surprise to the spectators. A fight only ended if the opponent was surrendered like Amykos did, or if he

died. Remarkably, by killing the opponent the survivor of the fight lost the match as an honour to the deceased opponent! In pankration, probably just as much violent as boxing, full contact was permitted with two forbidden acts only: biting and gouging.
Logically, many of the injuries in ancient sports were acute and of a local nature. However, already the ancient Greek coaches must have been aware of the fact that damage in sports occurred in more ways than by means of an acute high impact force only. They had the perfect example of the Greek soldier Pheidippides, who ran a distance of about 42 km from Marathon to Athens to announce the Greek victory after having run already 260 kilometers in two days for requesting help when the Persian invaders landed at the beaches of Marathon. His body was completely exhausted and after arriving in Athens to proclaim victory he collapsed and died. A century later, Greek coaches used a method called ‘tetras’ to structure the balance between training load and recovery to prevent overload. Tetras is derived from the Greek word tetra (or tettares), which means ‘four’. On the first day, training load was more like a preparation with short, but high intensity exercises, followed by a second day with high intensity and high volume sessions. Recovery (physical rest) was given on day three, whereas day four was a transition day with medium intensity exercises. In the same period, the famous Greek philosopher Aristotle (384 - 322 BC) was convinced that physical overload should be avoided. He actually claimed that boys would lose their strength if they started training too young. Aristotle described overuse in high workload athletic training as being ‘evil’ and judged that the way the Spartans trained there youngsters would turn them into ‘savages’. Therefore, he proposed that up to 3 years after puberty, young men should refrain from physical exertion (overuse), and in stead, should focus on intellectual development.

CURRENT SPORTS PARTICIPATION

In the previous century, in some countries, such as Germany, the military arguments were still used to train the youth and prepare them for action. Elsewhere, under the influence of social changes in England starting in the 19th century, sports changed. It transformed into a social activity with clubs and sports unions that organized sports activities in which even women were allowed to participate.
In the 20th century, sports developed into a recreational activity for fun and social coherence. The best athletes ended up in competitive professional sports. Nowadays, these new male and female elite athletes are rewarded with high wages, honour and prestige making them very much similar to the heroic ancient Greek and Roman athletes. They clearly serve as a model for everyone whose desire is to excel and to improve, and to rise from the ranks in our current society.
History has shown that poverty and scarcity of food kept life hard. As a result, the majority of the world population was forced into a physically active lifestyle. Our current industrialized civilisation, however, has brought welfare without much of the physically hard labour from the past. This brought us a physically inactive lifestyle accompanied by inactivity-related diseases, such as obesity, cardiovascular diseases, diabetes mellitus or colon cancer [1,36]. This is the main reason why nowadays, physical fitness is one of the hallmarks in modern sports participation.

In the Netherlands, the prevalence of inactivity-related health issues has been the argument most frequently used in persuading people to adopt an active lifestyle. Such arguments caused a growth in sports participation, notably during the last decades from 32% (4.6 million participants: Van Galen and Diederiks, 1990) in 1986/1987 to 67% in 2006-2008 (11 million participants: Consumer Safety Institute, 2010). However, in the period 1986-2008 another important change took place. After a post-war period of about 25 years with mutual effort to rebuild the nation, the people increasingly insisted on determining the course of their lives, stressing individual rights and self-development. Households became smaller. Social life, though more informal, became more restricted and less prominent to the individual. Increasing commercialization of the individual marked the rise of the double income families, with a relative large number of women leading the way in the rise of part-time working.

With leisure time becoming scarce, the traditional sport participation in the Netherlands changed as well. The top 5 of sports activities illustrates a switch to an increased popularity of non-competitive, non-organized sport activities, such as swimming, cycling, recreational running, and fitness (20% in 1986/1987 versus 38% in 2000/2003, see Table 1.1). A report by the Netherlands Institute for Social Research (in Dutch: Sociaal Cultureel Planbureau; SCP) called “Sports in the Netherlands 2008[56] (in Dutch: Rapportage Sport 2008)” confirms this trend. Apparently, these sports fit the individualized world much better than the traditional organized team sports [47,48,49,60].

Table 1.1.Changing popularity of competitive (team) sports and unorganized, individual sports during the 1986-2008 period: data from five national surveys on sports participation and sports injuries in the Netherlands.

	1986/1987		**1992/1993**		**1997/1998**		**2000/2003**		**2006/2008*****	
Top 5 in sports	Swimming	(13%)	Swimming	(13%)	Swimming	(13%)	Fitness	(17%)	Fitness	(28%)
	Soccer*	(11%)	Cycling	(9%)	Soccer	(9%)	Swimming	(14%)	Swimming	(28%)
	Cycling	(7%)	Soccer*	(8%)	Tennis*	(9%)	Soccer	(13%)	Cycling	(13%)
	Tennis*	(7%)	Tennis*	(8%)	Fitness	(9%)	Tennis **	(12%)	Running	(13%)
	Gymnastics	(6%)	Fitness	(6%)	Gymnastics	(6%)	Running	(7%)	Soccer	(13%)
Total N	4.6 mln		6.3 mln		7.3 mln		7.7 mln		11 mln	

**outdoor only; ** indoor and outdoor; ***methodological changes caused a significant increase of the total number of sports participants (N) and percentages compared to previous surveys* [5]

THE DOWNSIDE OF SPORTS: ACUTE AND OVERUSE INJURIES

Unfortunately, in modern western sports participation has not droped the physical suffering that was so common in ancient sports. Competitive athletes or recreational sports participants still get injured. Sometimes, even lives are lost as a result of sudden cardiac or traumatic death[24]. In addition, the increased number of sports participants has made sports injuries a serious health problem, because the social-economic costs associated to sports injuries have increased accordingly.

A relevant aspect of injuries is the time frame of the local damage. It can range from instant moments (defined as acute injuries) to a gradual development over time (defined as overuse injuries). The concept of both types of injuries is illustrated in figure 1.1, in which load (i.e., exercise load) and capacity (i.e., tissue strength in muscles, bones or joints) are presented as a function of time. In the left figure, the onset of an acute injury is shown. On the right, the development of overuse injuries is depicted by an accumulation of micro trauma.
The white lines in both figures encompass the tissue capacity to endure a certain load. The amplitude of the black dotted line represents the impact of the exercise load. On the left side with a time scale of seconds, the white lines are horizontal indicating stable tissue strength. Initially the load does not exceed the level of micro trauma, indicating no damage at that time. However, after about 2 seconds a strong impact exceeds the level of macro trauma, indicating severe tissue damage with pain. For instance, a fierce kick against the tibia that exceeds the capacity of bone structures (upper white line) during a soccer match will result in an acute fracture. In a similar manner, ligaments and muscles may rupture.
The figure on the right side illustrates the complex process of local overuse injuries. Its development may range from several days to weeks or even months. Therefore, as an example the time scale changed from seconds to several days. A second difference with acute injuries refers to the repeated occurrence of micro traumas due to daily bouts of exercises. For example, during the third bout the exercise load exceeds the white line of pain (i.e., the pain threshold). At that time, micro traumas have already occurred twice. With a repetitive pain experience in the fifth and sixth bout, an athlete may or may not report an overuse injury, depending on the duration of the pain and pain perception. A recovery phase starts when an athlete reduces the load level during exercises (training or game). Therefore, recovery is a relative concept, illustrated by the lowest load levels over time. In case of a too short recovery period, as depicted immediately before the seventh bout, peak load (7^{th} session) exceeds the tissue capacity and a serious damage may occur.
Moreover, the decline of white lines over time on the right side of fig. 1.1 indicates a reduction in tissue capacity and pain threshold over time due to the repetition of micro traumas with short recovery periods. Insufficient recovery causes a reduced capacity of the tissues to sustain a certain load. Essentially, this reduced capacity illustrates the accumulation of persistent micro traumas.

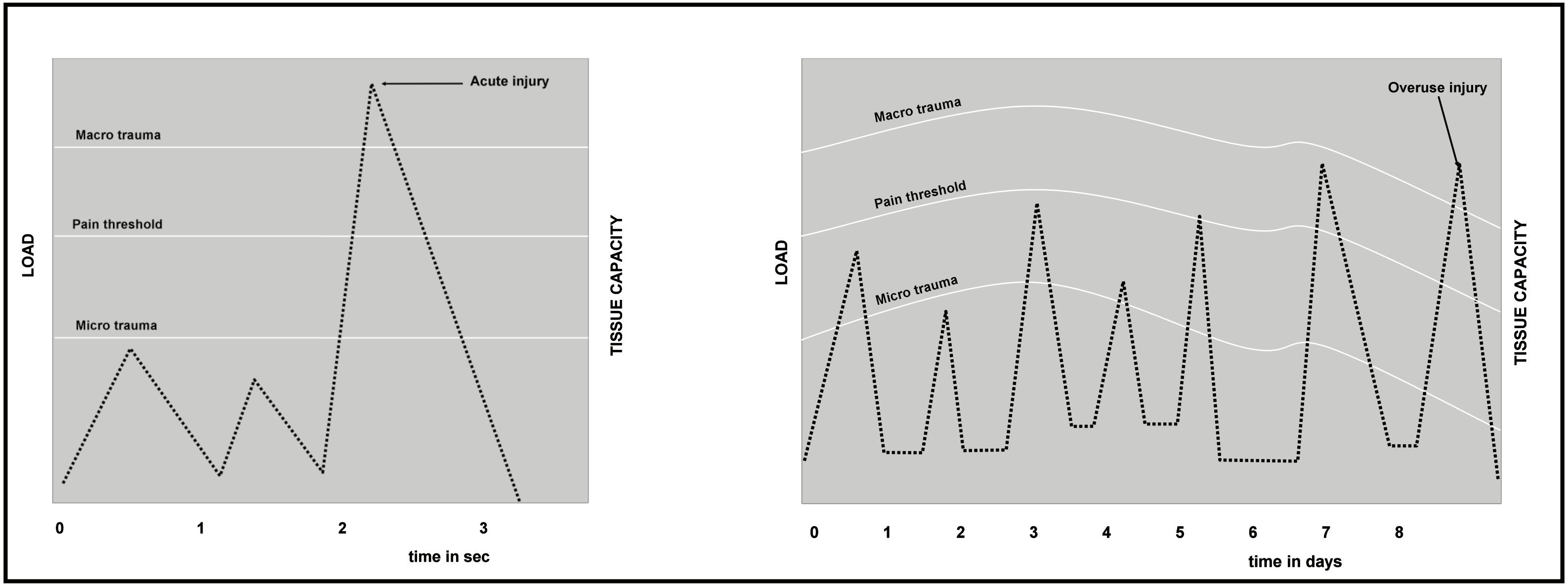

Figure 1.1 Exercise load and tissue capacity as a function of time in acute injuries (left) and overuse injuries (right).

For example, after the fifth bout the lengthened recovery halts the decline of the tissue capacity, as well as the accumulation of micro trauma (AMT, see Chapter 9). AMT is represented by the total area under the load curve during a period of reduced tissue capacity (day 2-8). However, at day 8, a load almost similar to the one during the first bout will now induce pain, which did not happen during the first session. A reduced tissue capacity is typical for the delayed onset of overuse injuries[64].

The right side of figure 1.1 also illustrates why retrospective instruments to register sports injuries have difficulties in estimating the true number of overuse injuries. Generally, a repeated experience of pain is common in sports participation. Using recall periods to register injuries enhances such ‘minor injury-related events’ to be forgotten, even if the pain was initially noticed. Athletes may or may not recognize this pain as part of an ongoing injury mechanism[22]. If the athlete is not capable of interpreting the signals (tiredness and pain during exercise as result of e.g. damaged muscle fibres), he/she may end up with a total rupture of ligaments or muscles. At that moment, the process of overuse will be fully obscured by the major trauma, and as a result, such an injury will be registered presumably as ‘acute injury’ and not as an ‘overuse injury’.

SPORTS INJURY PREVENTION AND REGISTRATION

Government policy

In the Netherlands, the history of sports injury prevention programs goes back to the 1980’s. In 1982, the NISGZ (National Institute for Sports Healthcare) was founded with the explicit task to reduce the negative health effects of sports participation. In 1989, a large scaled prevention campaign called “Mastering sports injuries (in Dutch: Blessures blijf ze de baas)” was organized by NISGZ and the Consumer Safety Institute, but the evaluation of the effects of this campaign was not possible due to a lack of a sufficient and suitable data. Nowadays, specific goals are linked with prevention programs. In 2001, a government policy document called “Sports, Physical Activity and Health (in Dutch: Sport, Bewegen en Gezondheid”[36]) referred to the following goal:

“A reduction of the number and incidence of sports injuries, expressed by a reduction from 13% to 11% in 2005, and to 10% in 2010 (% of athletes/year)”.

In this document, a set of high-risk sports were described that should receive a priority attention in prevention programs. The term ‘high-risk’ was derived from statistics using data from before the year 2000, such as the total number, severity, incidence rates, and medical costs of sports injuries. A significant number of data was derived from a nation wide registration system called “Accidents in the Netherlands (in Dutch: Ongevallen in Nederland/OiN)”, in 2000 renamed as “Injuries and Physical Activity Netherlands (IPAN; in Dutch: Ongevallen en Bewegen in Nederland/OBiN)”. IPAN was designed as a retrospective survey to register sports injuries (medically treated or not), sports participation and physical activity to cover the entire problem of sports injuries. Chapters 2 and 3 of this thesis show how IPAN is set to work in different steps of the prevention sequence model[61]. In Chapter 4, the central topic is set on a historical and functional description of all the registration systems that were used in the period 2000-2005 to obtain statistics on sports injuries in the Netherlands.

Methodological issues

The current methods in registration systems to define the extent of the sports injury problem are subject of international discussion[10,11,13,15,22,35,40,62]. First, there is consensus about the necessity to calculate at least the number of injuries relative to the population at risk (injury rate or incidence). To properly compare the injury risks across various sports or across cohorts in (various) sports, the preferred statistics would be those containing the exposure time as part of the denominator[7,8,61.] This implies that methods without any information about the population at risk or about exposure time would be unsuitable. These methods were described as 'passive methods'[40], which are characterized by the following types of registration:

- medical records, e.g. from an emergency room in a hospital[6,38,50]
- records from insurance companies[43]

Usually, these recordings provide highly selective data with a preference to acute, severe injuries leading to medical care and hospitalisation, and with an enhanced risk of associated costs related to physical disability and work absence.

Second, the use of a prospective instead of a retrospective study design is discussed. Differences between the injury numbers, incidence rates and severity reported in prospective and retrospective studies were mainly explained by recall bias. Recall bias lowers the incidence of sports injuries and increases the proportion of medically treated injuries because minor injuries are more likely forgotten[22,57]. Most authors suggested that future studies on sports injuries should be conducted prospectively and based on cohorts, because retrospective data would be 'of limited value'. A compilation of all recommendations on the registration of sports injuries in general was presented as consensus, although initially specifically developed for soccer[13]. Studies using these recommendations are also often soccer-related[9,23,54].
A prospective method used by physical therapists or physicians to collect injury data regularly (often weekly), may result in timely medical checks of athletes. Although such an approach ensures a valid, reliable and precise registration of all aspects of injuries, it is also a very expensive and hardly manageable in studies with large samples.

The prevention sequence model and IPAN
The prevention sequence model was first introduced by Van Mechelen et al.[61]. This model consists of four steps to be applied in any preventive campaign. Step 1 regards the establishing of the initial extent of the sports injury problem, while in step 4 the effectiveness of preventive measures will be assessed by again establishing the extent of the problem after the introduction of a preventive measure as described in step 3. Step 2 describes the data acquisition on injury mechanisms and risk factors to provide the tools defining the preventive measures in step 3.
Similar to the recommendations by Finch[11], Van Tiggelen et al.[62] modified step 3 of the model in order to improve the effectiveness of the implementation of preventive measures. They described step 1 as:
"data are collected to establish the extent of the injury in the predetermined population".

Especially the last part of this description – **the predetermined population** – implies that like other ‘passive methods’, the IPAN survey can play a significant role in the prevention sequence. At this moment, IPAN has become a continuous survey. Because it collects data on a daily base, its continuous character allows evaluating changes in the extent and severity of the sports injury problem over time. It may even be used to show seasonal effects in sports injuries.
Consequently, the two most important sports injury-related purposes of IPAN are:

1) to provide quantitative and qualitative arguments that enables a focus in sports injury prevention on specific sports or cohorts in sports
2) to evaluate the long-term effect of preventive programs by means of changes in the overall trends of sports injuries

In this thesis, we will not discuss the second purpose of IPAN. In stead, with the use of data from the period 2000-2005, in Chapters 2 and 3 we will present a method that provides arguments to select (cohorts in) sports for injury prevention programs. In Chapter 4 we will discuss the necessity of the use of several ‘passive methods’ of injury registration systems, the possible coherence between these systems, as well as the use of a prospective online registration system that may serve as a valuable instrument in steps 1 and 4 of the prevention sequence model.

In various sports, elite athletes are confronted with an increasing workload. A qualitative study in cycling showed that as an amateur one-third of the participants were confronted with one or more episodes of mental and physical overload. Heavy training sessions often combined with strenuous work or school related stressors, too few phases of tapering, poor communication about training strategies and the shear stress to perform caused the cyclists to experience increasing fatigue without the option to recover, and in the end, lead to a reduced performance. Consequently, they were confronted with a ruined season or with a premature ending of their cycling career[36]

OVERREACHING AND THE OVERTRAINING SYNDROME

The above-mentioned text, originating from the governmental document[36] "Sports, Physical Activity and Health (in Dutch: Sport, Bewegen en Gezondheid)", describes a type of damage in sports that is not yet introduced in the previous paragraphs. The focus is on an insufficient recovery relative to the total load from multiple stressors, leading to a prolonged fatigue and a reduced performance. In the sports medical literature this phenomenon is described as the overtraining process that ultimately leads to a state called the Overtraining Syndrome (OTS).

An overview article[30] described a state of short term overtraining or overreaching as part of a normal athletic training, to be distinguished from a long-term overtraining syndrome (OTS). Meeusen et al.[31], however, introduced a time frame of the overtraining process, in which they suggested to split up the stage of overreaching (OR) into a functional and non-functional stage. Functional overreaching (FO) occurs if an athlete can recover from high intensity/high volume overload training (e.g. during a training camp of a week), because of a sufficient period of rest (usually some days or at most some weeks). In this case, overload causes a temporary disturbance of the cellular homeostasis, also in muscle tissue. Such disturbances mark the start of physiological responses to restore homeostasis, especially during recovery. These responses lead to a desirable training effect with an increased performance capacity: the process of super compensation[63]. Therefore, FO very much resembles the OR interpretation by Lehmann et al.[30].

In the model by Meeusen et al.[31], non-functional overreaching (NFO) is used as a transitional phase between the FO stage and OTS. When an athlete is repeatedly confronted with too much overloading relative to the available time to recover, super compensation will not be achieved and the athlete will become non-functional overreached. Such an athlete suffers from a reduce performance capacity and may start to show various signs and symptoms, varying from psychological to endocrine and immunological deficits. To recover from this state, athletes often need weeks or months by means of an adapted, low-intensity training regime. To some extent, NFO very much resembles the start of a decompensation phase. It is, for instance, characterized by decreased ACTH and cortisol responses[55]. Without an adequate treatment and an adapted training regime, athletes are likely to end up with a full-blown OTS.

Regulatory processes involved in the overtraining process

Several explanations for the overtraining process, the signs and symptoms of the overreached state, and the overtraining syndrome have been discussed in the literature. Apart from an imbalance of the autonomic nervous system [2,14,17,18,19,20,26,28,31], other explanations focussed on:

- neuro-endocrine imbalances associated to the activity of the hypothalamic-pituitary-adrenal (HPA)-axis and the gonadal axis[3,12,29,34,45,65]
- a metabolic imbalance associated to glycogen levels[53]
- a glutamine-glutamate imbalance[16,46,51]
- a neurotransmitter imbalance[4,21,32,33,59]
- immunological imbalances[41,42,44,52]

Unfortunately, according to the most recent reviews, none of the theoretical explanations are able to deliver a diagnostic parameter for the overtraining syndrome[2,17,31,58]. Therefore, nowadays OTS is diagnosed using a per exclusionem protocol, which excludes alternative explanations for the prolonged reduction in performance capacity. Given the time frame of the performance decrement for OTS (usually several months[31]), physicians will only be able to diagnose OTS retrospectively. This is not a satisfying situation for athletes, coaches and medical staff.

The reviews listed above often mentioned the same causes for the lack of any diagnostic parameter in OTS. Over the years, the definitions, study methods, populations under study, as well as the statistical methods varied too much to enable straightforward comparisons of results. This has been one of the primary arguments to redefine the concept of the overtraining process in the European College of Sports Science position statement by Meeusen et al.[31].

Moreover, all reviews stress the multicausal character of the process of overtraining, thereby referring to the various regulatory processes that are involved in the development of OTS. Despite the apparent understanding of the complexity of OTS, most studies focused on a single regulatory system, and very often, potentially predictive parameters were judged using simple univariate statistical methods instead of a multivariate approach.

PREVENTION OF OVERTRAINING (OTS)

This thesis aims at increasing the knowledge to help prevent the damage due to sport activities. Evidently, this also applies to OTS. Because theoretically the stage of NFO precedes that of OTS, an early recognition of NFO and proper actions accordingly should be able to prevent the development of OTS.

The transition between FO and NFO shows a marked resemblance with the development of overuse injuries. Both phenomena are characterized by physical overload with an accumulation of tissue damage in muscles, tendons, bones, and periost. However, there is one important difference. The accumulation of damage in an overuse injury leads to a macro trauma that forces an athlete to lower or nullify the workload and prevents further damage. However, without excessive macro trauma, and with relatively mild complaints only, athletes are able to persist in their workload for a long period. This may lead to an increased (work)load in an attempt to compensate the reduced performance. In such cases, NFO or OTS may easily develop.

While the consequences of OTS, in terms of duration and severity as well as the additional signs and symptoms, are good reasons for a research focus on OTS, it is fortunate that incidence of OTS is only moderate. Furthermore, it is ethically unacceptable to manipulate athletes into a state of OTS. For research purposes this contrasts with the stage of NFO, which is more likely to occur than OTS. When applying a prospective study design, the natural development of NFO may be observed in specific cohorts without the requirement of a laboratory setting.

OUTLINE OF THIS THESIS

The central topic of this thesis is focused on the prevention of (physical and mental) damage as a result of sports participation. The first part of this thesis concentrates on the hypothesis that target groups for sports injury prevention can be derived from data acquired with a nationwide, retrospective survey. Methods to define target groups for sports injury prevention are presented, and existing registration systems for sports injuries are discussed.

In the second part, it is hypothesized that in young elite athletes non-functional overreaching (NFO) can be recognized by a set of distinctive parameters. The concept of NFO will be studied cross-sectionally, and for the first time, prospectively as well. NFO will be primarily linked to neuro-endocrine imbalances associated to the activity of the hypothalamic-pituitary-adrenal (HPA)-axis and the gonadal-axis, as well as to mood changes[37,39]. Instead of univariate statistical models, we will apply a multivariate approach to study the relationship between various parameters and NFO. The HPA-axis is closely related to the activity and production of several neurotransmitters (e.g., serotonin[2]). Neural network communication as measured by electroencephalogram (EEG) coherences will be linked to HPA-axis related hormones to test if the brain works differently in NFO athletes than in controls athletes.

In **Chapter 2**, data from the retrospective registration of sports injuries and sports participation (IPAN survey) during the 2000-2005 period are used to describe those types of sports contributing significantly to the sports injury problem in the Netherlands.
In **Chapter 3,** more detailed injury-related information is provided concerning a specific target group (outdoor soccer players) for injury prevention.
Chapter 4 describes the Dutch instruments used to evaluate the extent and severity of sports injuries with a future perspective to improve current methods.
Chapter 5 introduces the concept of NFO and the specific goals of the Chapters 6-8. This Chapter serves as a connection between the previous Chapters that address some aspects of the prevention of local injuries and the Chapters 6-8 that specifically focus on strategies that may be useful to prevent the development of OTS.
In **Chapter 6,** the symptoms of a reduced performance capacity and mood disturbances are analyzed, which are typical for athletes possibly trapped in the process of overtraining. Cross-sectional data collected from elite athletes at our sports medical department are used to connect mood, general well being, and performance (in training and competition) to serum hormone levels from the hypothalamus-pituitary-adrenal (HPA)- and gonadal axis in a multivariate way.
In **Chapter 7,** a cohort has been followed prospectively in order to link serum levels of HPA-axis related hormones and mood profile in NFO- athletes and control athletes using a multivariate design.
In **Chapter 8,** the link between HPA-axis related hormones (free cortisol levels), and neural network communication, as measured by EEG coherence, is investigated in NFO-athletes and controls.
Finally, **Chapter 9** provides a general discussion and conclusions with implications for future research, and some practical and clinical advices for prevention of sports injuries and OTS.

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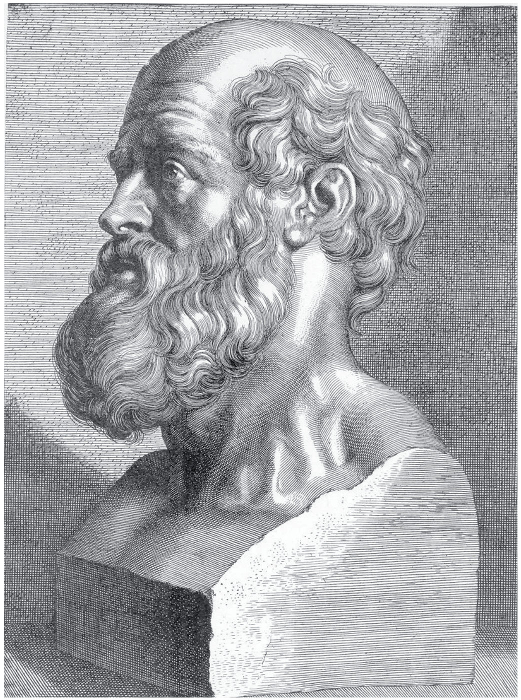
Epidemiology

In the ancient Greek language, the word 'epi' stands for 'upon', whereas 'demos' stands for 'people'. Epidemiology therefore refers to the study of 'what is or what falls upon people'. These principles were first introduced by Hippocrates (460-365 BC), who studied infectious diseases in specific populations. He considered the environment, nutrition and life style as causal factors of diseases.

In behavioural epidemiology, the causal factors of diseases are shifted towards human behaviour. Physical activity epidemiology is a specific branch of behavioural epidemiology. The goal of physical activity epidemiology is to find out how (in)activity can be altered to reduce the frequency and risk of diseases and injuries. Therefore, the epidemiology of sports injuries, as described in this chapter, is a part of the physical activity epidemiology.



Chapter 2

National survey on sports injuries in the Netherlands: target populations for sports injury prevention programs

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ABSTRACT

Objective: To define target populations for sports injury prevention programs.

Design: A computer-assisted telephone survey on sports injuries and sports participation during 2000–2005 using a 3-month recall period.

Setting: Data obtained from a representative sample of Dutch citizens.

Participants: Fifty–eight thousand four hundred five Dutch citizens aged older than 3 years.

Assessment of Risk Factors: Age, gender, and type of sports were used to distinguish subgroups with a substantial contribution to sports injuries.

Main Outcome Measures*:* The absolute number of sports injuries, the incidence of sports injuries per 10 000 hours, the severity, and costs of sports injuries.

Results: Sports participation was associated with 1.5 million injuries per year and 10 injuries per 10 000 hours; of these, 50% had to be treated medically. Two–thirds of all medically treated sports injuries were associated with 9 sports (representing 18 subpopulations, all younger than 55 years): outdoor soccer (males 4–54 years and females 4–17 years), indoor soccer (males 18–34 years), tennis (males/females 35–54 years), volleyball (females 18–54 years), field hockey (males 18–34 years and females 4–17 years), running/jogging (males/females 35–54 years), gymnastics (males/females 4–17 years), skiing/snowboarding (males 4–17 years and females 18–34 years), and equestrian sports (females 18–34 years). These groups showed more than average injury rates and covered two–thirds of all direct and indirect costs (€400 million).

Conclusions: The survey identified the most important (sports–, age–, and gender–specific) target populations for injury prevention programs in the Netherlands. Sports participants aged older than 55 years were excluded from these target groups because of their limited contribution to the total sports injury problem.

INTRODUCTION

In 1986, the Dutch Ministry of Welfare, Public Health and Cultural Affairs, postulated that 'health is the primary virtue in life', thereby actively stimulating a healthy lifestyle through sports. The government also stated that sports injuries, being the negative side effect of sports participation, should not be disregarded. To counteract this negative effect by means of preventive programs, the extent and nature of the sports injury problem need to be identified to define target groups for prevention.[1–3]

In general, to describe the extent of the sports injury problem, absolute numbers and relative risks and data on the severity and costs of sports injuries are used.[4] Age and gender (being intrinsic risk factors of sports injuries) are used to discriminate between risk groups. The nature of sports injuries focuses on the description of localization, diagnosis, and other characteristics of sports injuries. Furthermore, knowledge on causal factors from in-depth studies among specific cohorts within sports is used to define the content of intervention/ prevention programs.[5] The effectiveness of these programs should be judged by repeated estimation of the nature and extent of the injury problem using trend analysis, or based on randomized controlled trials.[6,7] To continuously monitor the nature and extent of sports injuries in the Netherlands, the Dutch government actively supports the documentation of sport injuries as part of an ongoing survey called Injuries and Physical Activity Netherlands (IPAN). This survey is primarily used to identify high-risk sports activities among age and gender groups; it is also used to evaluate the time trends of injury prevention campaigns.[8] The present study aimed to identify the high-risk age–, gender–, and sports-specific subgroups that would be eligible to receive special attention in sports injury prevention programs. Identification of high-risk subgroups is based on the absolute and relative contribution to sports injuries in the Netherlands. To achieve this, the most recent age–, gender–, and sports-specific estimates of the incidence and incidence rates in sports injuries are calculated. Medical treatment as an indicator of severity and the associated costs of medical treatment and work absence are also assessed with the data from the IPAN survey.

MATERIAL AND METHODS

Population

Data were obtained from the national survey IPAN, covering 6 years (2000–2005) of continuous registration. Using random digit dialing, each day during the evening a random sample of residential or undisclosed telephone numbers from the 2000–2005 Dutch population (average population size n = 16,119,000) was dialed to contact participants. Using this computer-assisted telephone interview method, the goal was to dial sufficient telephone numbers to achieve an average of 27 interviews each day. Three attempts were used before the number was listed as 'no contact'. Telephone numbers were excluded if during the initial contact they appeared to be associated with a company. A telephone number known to have provided a successful interview was excluded from the sample for a period of 2 years. A

random number, based on the number of persons within a family, was chosen by the computer to select 1 family member for the interview. Proxy interviews were made in case the family member was younger than 12 years. The exclusion criteria were institutionalization as a result of old age, physical or mental handicap, and language problems (5% of the Dutch population). The sporting population was divided into 4 age categories, which also distinguished between adolescents (4–17 years) and adults (18+ years). The latter group was further divided into 2 subgroups (about equal in size) split at the age when many adults decided to switch from competitive to recreational sports activities: 18–34 years and 34–54 years. Because of the specific attention given to seniors during nationwide physical activity and sports programs, the 55+ age category represents the fourth age group.
In the Netherlands, no approval is required from an ethics committee for this type of research.

Definitions
In the present study, the following definitions were used:

- Sports activity: physical activity, according to the respondent to be associated with the term ‘sports’. Mind sports are excluded.
- Sports participant: a respondent confirming that he/she had been active in any kind of sports activity at least once during the past 3 months.
- Sports injury: physical damage of a musculoskeletal nature, sustained in the recall period as a result of a sudden event during a sports activity or as a result of a gradual process related to sports activity.
- Medical treatment: an injury diagnosed and/or treated by any of the following persons involved in health care:
    - general practitioner, medical specialist, sports physician,
    - dentist, physical therapist, occupational physician and
    - ambulance personnel, or treatment at an emergency room (ER) of a hospital.

Analysis
With the first day of the recall period always set at the beginning of a month, the length of the recall period was (on average) 3.5 months. First, we estimated the annual number of their total time at risk to sustain an injury (n hours of sports per year derived from the average sports exposure per week). Subsequently, the sports injury incidence rates (SIRs) were calculated as follows:

$$\text{SIR} = (n \text{ injuries} \times 10{,}000)/n \text{ hours sports}$$

Injury statistics are presented only if cells contain at least 20 injuries. In each annual sample, deviations from the total Dutch population in terms of age, gender, educational level, family size, and urbanization were adjusted using weighting procedures. Sports participation was weighted at the respondent level to estimate the total sports participation. Respondents with multiple sports injuries were additionally weighted to obtain national estimates on sports injuries. The percentages of injured sports participants and SIRs are based on weighted data. Pearson χ^2 at a significance level of $P \leq 0.05$ was used within the ‘‘top 10’’ sports contributing most to sports injuries to test differences in the proportion of medical injuries. Similarly, the effect of gender and age categories and the effect of gender within age categories were tested on the proportion of medical injuries. Non-overlapping Poisson confidence intervals (CI) were used to test age-related and gender-related differences in SIRs. All costs associated with injuries were calculated using a model frequently applied in the Netherlands[9].

RESULTS

Of a total of 173,000 telephone numbers called, 29% did not lead to any contact to arrange an appointment for the interview. Of all initial contacts (N = 127,000), 3% were not available for an interview. Another 4% of the contacts were ineffective as a result of language problems. Due to old age and physical or mental handicap, 2% of the contacts did not lead to an appointment for an interview. Also, despite an appointment for the interview, 4% could not be contacted after all. At the start of the interview, 43% of the respondents refused to continue. During the interview, 2% did not wish to proceed or finalize the section about sports participation. Hence, 55% (N = 58,405) of the interviews were finalized completely. A total of 28,695 subjects were registered as being a sports participant. During the (approximately) 3.5-month recall period, one or multiple injuries were reported by 1,397 sports participants (957 males and 440 females). Using the weighted data, the population estimates indicate that each year an average of 1,507,000 (95% CI, 1,430,000–1,588,000) of the 7,950,000 sports participants were injured (ie, 19%); of these, the majority was male (68%).

Of all injuries, 50% needed medical treatment. Table 2.1 shows the age-specific distributions of injuries in males and females. The age category contributing most to the absolute injury volume was ‹18 years among the females and 18–34 years among the males; 7% of all injuries were registered among participants aged older than 54 years. Table 2.2 shows that the SIRs per 10 000 hours were highest in males aged 18–34 years and in females aged 4–17 years. Overall, the incidence rates in males were higher than that in females, but both males and females share the lowest SIRs in the 55+ age category. No age-specific difference in the percentage of medical treatment was found, but injuries were treated medically in females more often than in males ($P = 0.016$). This was mainly attributable to the fact that among females aged 35–54 years, 62% of all the injuries were registered as being medically treated compared with 47% among males ($P = 0.009$).

Table 2.1 Sample-based relative contribution of the four age categories (males and females separately) to the total number of sports injuries.*

	4-17 YEARS	18-34 YEARS	35-54 YEARS	55+ YEARS	TOTAL
Males N	269 (28%)	387 (40%)	238 (25%)	63 (7%)	957 (100%)
Females N	164 (37%)	134 (30%)	112 (25%)	30 (7%)	440 (100%)
Total N	433 (31%)	521 (37%)	350 (25%)	93 (7%)	1397 (100%)

** due to rounding effects row totals may add up to 100% exactly*

Table 2.2 Population-based age-specific sports injury incidence and incidence rate in Dutch males and females active in sports.

		4-17 YEARS	18-34 YEARS	35-54 YEARS	55+ YEARS	TOTAL
MALES	**No. of sports participants x 1000 (% injured)**	1,021 (28%)	1,127 (37%)	1,258 (20%)	588 (11%)	3,994 (26%)
	No. of injuries x 1000 (% medically treated)	290 (45%)	417 (51%)	257 (47%)	68 (48%)	1,032 (48%)
	Sports participation hours/week	3.9	4.7	4.1	4.8	4.3
	SIR per 10,000 hours (CI)	13.9 (12.3-15.7)	15.1 (13.7-16.7)	9.5 (8.4-10.8)	4.6 (3.6-5.9)	11.4 (10.7-12.2)
FEMALES	**No. of sports participants x 1000 (% injured)**	985 (18%)	998 (14%)	1,160 (10%)	763 (4%)	3,905 (12%)
	No. of injuries x 1000 (% medically treated)	177 (52%)	145 (54%)	121 (62%)	32 (48%)	475 (55%)
	Sports participation hours/week	3.1	3.5	3.1	3.2	3.2
	SIR per 10,000 hours (CI)	11.3 (9.7-13.2)	7.9 (6.7-9.4)	6.5 (5.4-7.9)	2.5 (1.8-3.6)	7.3 (6.6-8.0)
TOTAL	**No. of sports participants x 1000 (% injured)**	2,006 (23%)	2,124 (26%)	2,418 (16%)	1,351 (7%)	7,899 19%)
	No. of injuries x 1000 (% medically treated)	467 (48%)	562 (52%)	378 (52%)	100 (48%)	1,507 (50%)
	Sports participation hours/week	3.5	4.2	3.6	3.9	3.8
	SIR per 10,000 hours (CI)	12.8 (11.6-14.0)	12.2 (11.2-13.3)	8.3 (7.5-9.2)	3.7 3.0-4.5)	9.7 (9.2-10.2)

SIR: sports injury incidence rate; CI: 95% confidence interval

Table 2.2 shows that the SIRs per 10,000 hours were highest in males aged 18-34 years and in females aged 4-17 years. Overall, the incidence rates in males were higher than in females ($p \leq 0.05$), but both males and females share the lowest SIRs in the 55+ age category. No age-specific difference in the percentage of medical treatment was found, but injuries were more often medically treated in females than in males ($p=0.016$). This was mainly attributable to the fact that among females aged 35-54 years 62% of all the injuries were registered as being medically treated compared with 47% among males.

Table 2.3 Top 10 sports with the highest relative contribution to the total number of injuries (n=1,507,000): incidence, percentage of medically-treated injuries, and sports injury incidence rate (SIR).

	% OF ALL INJURIES	ANNUAL INCIDENCE (%)	% MEDICALLY TREATED INJURIES	SIR PER 10,000 HOURS	95% CONFIDENCE INTERVAL OF SIR
Outdoor soccer (n=386) *	28	11	53	20.3	(18.4 - 22.4)
Tennis (n=110)	8	5	54	9.6	(7.9 - 11.5)
Running/jogging (n=106)	8	8	45	16.0	(13.2 -19.4)
Field hockey (n=64)	5	11	42	20.2	(15.8 - 25.8)
Indoor soccer (n=59)	4	29	44	55.2	(42.7 - 71.3)
Volleyball (n=58)	4	8	52	16.1	(12.5 -20.8)
Skiing/snowboarding (n=53)	4	27	59	20.0**	(12.0 -33.0)**
Basketball (n=42)	3	17	44	32.0	(23.7 -43.2)
Fitness (n=42)	3	1	49	2.2	(1.6 -3.0)
Gymnastics (n=38)	3	5	49	10.5	(7.6 -14.4)
Total Top 10 (n=958)	69	7	50	12.7***	(11.9-13.5)***
Total in all sports (n=1397)	100	5	50	9.7	(9.2-10.2)

[*] n= number of injuries registered in the sample [**] Data available only for 2004/2005 [***] excluding skiing/snowboarding

Table 2.4 The percentage of injuries in one or more age categories within the top 3 sports, for males and females separately (excluding the 55+ age group)**.*

	MALES		
	4-17 YEARS	**18-34 YEARS**	**35-54 YEARS**
Outdoor soccer	28%	57%	13%
Tennis			51%
Running/jogging			59%
Indoor soccer		62%	
Skiing/snowboarding	47%		
Field hockey		73%	
Gymnastics	100%		
	FEMALES		
	4-17 YEARS	**18-34 YEARS**	**35-54 YEARS**
Tennis			69%
Volleyball		38%	27%
Outdoor soccer	72%		
Skiing/snowboarding		38%	
Equestrianism		53%	
Field hockey	75%		
Running/jogging			74%
Gymnastics	71%		

The top 3 sports consist of sports contributing most to the medically treated injuries within each age category, for males and females separately

** *Because the 55+ age category is not included in this table, the percentages in the horizontal cells do not add up to 100%*

Table 2.3 shows the 'top 10' sports that contributed most to the absolute number of sports injuries. These 10 sports accounted for 69% of all sports injuries, as well as for 69% of all medically treated injuries. Indoor soccer had the highest SIR with 55 injuries per 10,000 hours of sports participation; basketball came second with 32 injuries per 10,000 hours. Medical treatment was significantly more often associated with outdoor soccer, tennis and skiing/snowboarding ($p<0.05$).

Table 2.4 shows the ‘top 3’ sports contributing to medically treated sports injuries within our age and gender-specific categories. Because the 55+ age category made only a minor contribution to sports injuries in terms of the absolute numbers, as well as having low incidence, incidence rates and low percentages of medically-treated injuries (Tables 2.1, 2.2), we decided not to include that age category when defining target groups for injury prevention; therefore, the 55+ group is excluded from Table 2.4.
On average, 67% of all medically treated injuries were covered by the ‘top 3’ sports within each of the gender specific age categories. Among males in the 4-17 year old category outdoor soccer, skiing/snowboarding and gymnastics are considered as the top 3 sports.
In males, outdoor soccer is also part of the top 3 in the 18-34 years and 35-54 years categories. As a triple top 3 member, a total of 98% (28%+57%+13%) of the medically treated injuries is accounted for among male outdoor soccer. On the other hand, in gymnastics all medically treated injuries in males are confined to the 4-17 year old category.

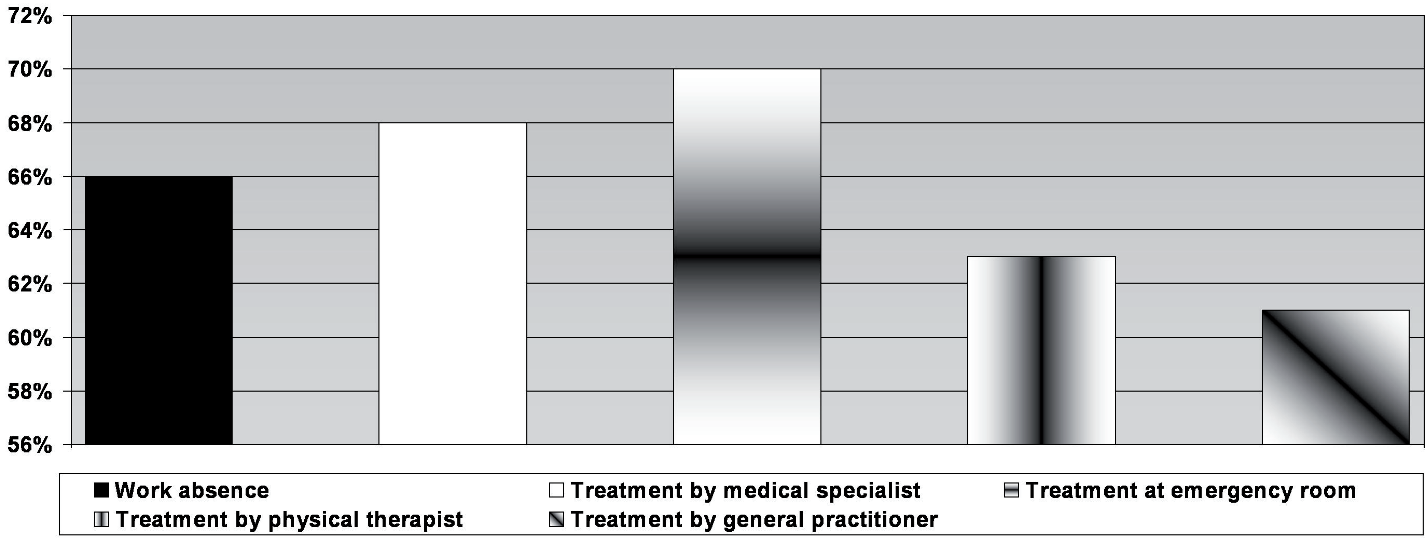

Figure 2.1 Relative contribution of the nine high-risk sports to the total costs associated with absence of work and the four options of medical treatment.*

* *Outdoor soccer, tennis, running/jogging, indoor soccer, skiing/snowboarding, field hockey, gymnastics, volleyball, equestrian.*

As can be seen, basketball and fitness do not rank high in any of the categories. Gymnastic injuries rank high only in the youngest age category; also, most of the gymnastic injuries were related to physical education (78% of all gymnastic injuries, and 85% of all medically treated gymnastic injuries). Direct costs associated with medical treatment were estimated at €170 million per year (at 2003 price levels). Indirect costs (related to work absence) were associated with 11% of all sports injuries and were estimated at an annual €420 million; 95% of these indirect costs were related to medically treated injuries. Of all costs associated with absence from work, 66% was accounted for by the following 9 sports from Table 2.4: outdoor soccer, tennis, running/jogging, indoor soccer, skiing/snowboarding, field hockey, gymnastics, volleyball and equestrian. These nine sports combined also accounted for about 70% of all direct costs (Figure 2.1).

DISCUSSION

The present study provides unique data on age and gender-specific sports injuries in different types of sports, collected during a continuous nationwide survey on sports participation injuries and sports injuries. During the 6-year survey, 51% of the total Dutch population reported to be active in sports. Almost one out five sports participants sustained a sports injury per year.

This study showed that a substantial part of (medically treated) injuries was confined to a specific subset of sports within certain age and gender cohorts (Table 2.4). Two-thirds of the injuries, two-thirds of the volume of medical treatment and work absence, as well as two-thirds of the total costs associated with the sports injuries were covered by 9 sports performed by males and females in 3 of the 4 defined age categories (i.e. excluding those aged 55+ years).

The results show that outdoor soccer, running/jogging, skiing/snowboarding, field hockey, tennis and gymnastics can be considered as target sports among both males and females. A specific subset of four sports from Table 2.4 (outdoor and indoor soccer, field hockey and volleyball) shared a more than average number of injuries per 10,000 hours of sports and accounted for 41% of all sports injuries. These findings offer good prospects for sports injury prevention programs within a restricted number of target groups. Some target groups can be characterized as participants in team-ball sports. Probably, they will share a similar number of risk factors. This offers many opportunities to apply efficiently similar prevention programs for both males and females within various types of sports. One example could be an intervention program on core stability; such an intervention will be tested on its cost effectiveness in soccer during the 2009-2010 soccer season.

In contrast to the ‘top 10’ listed in Table 2.3, the data in Table 2.4 do not define basketball and fitness as target sports. However, others have emphasised the importance of basketball in relation to sports injury problems because of its high incidence rates [1,3,10]. Although the present study also revealed high incidence rates in basketball, this sport (like fitness) did not emerge as one of the ‘top 3’ sports dominating the medically treated injuries within our population categories.

Equestrian sports, not appearing in the 'top 10' in Table 2.3, was included as the ninth sport in Table 2.4 because it showed a marked concentration of medically-treated injuries in the female age category of 18-35 years. Although equestrian is considered a low-risk sport, a substantial number of the equestrian injuries are of a serious nature. In the Netherlands, as much as 6% of all sports injuries treated at the ER are related to equestrian sports, ranking it the number 3 sports activity requiring ER-related treatment (Consumer Safety, LIS Report 2007, Amsterdam, The Netherlands; unpublished data).
In the age group <18 years, we have defined gymnastics as a target group for injury prevention. Most of these injuries are associated with physical education activities (as opposed to gymnastics at e.g. sports clubs); moreover, physical education ranks number 2 of those sports activities requiring ER-related treatment (Consumer Safety, LIS Report 2007, Amsterdam, The Netherlands; unpublished data). Both findings underline the importance of high-quality physical education.
Surveys are characterized by several advantages and disadvantages. The most prominent shortcoming is their retrospective nature, possibly causing recall bias. As a result, an underestimation of the number of less severe (and non-medically treated) injuries generally occurs. Nevertheless, a recall period of 1-3 months (similar to our selected period) is recommended for registration of non-fatal musculoskeletal injuries [11], and is certainly preferable to a longer period [12,13]. Also, compared to prospective studies, cross-sectional and retrospective studies using surveys are not suitable to detect risk factors in sports injuries [14,15]. However, with discriminating variables such as age, sex and type of sports, surveys are able to differentiate between high and low-risk or high and low-volume groups in sports injuries[2]. Nationwide surveys obtain data from a random sample of the entire population. Although our sample size (n=10,000 participants per year) is one of the largest among known surveys on sports injuries, it still suffers from a small number of registered injuries within some particular sports; important changes in these latter sports (both in an absolute or relative sense) may therefore remain (statistically) unrevealed.
Despite relatively large confidence intervals of the sports injuries treated at the ER, the annual estimates in IPAN (N=170,000) were consistently comparable to the estimates from the Injury Surveillance System (LIS) of the Dutch Consumer Safety Institute [4,9]. The LIS system is specifically designed to estimate the numbers of ER-treated injuries in the Netherlands. This comparison suggests that IPAN is a suitable instrument to identify target populations for sports injury prevention.
Recent large-scale studies on sports injuries suggest that injury incidence in sports declines with age [3,16]. In our survey this trend was particularly evident in females, but less so in males. Among women, the incidence and incidence rates per 10,000 hours of sports decreased with age, being five times higher among the youngest compared with the oldest women. Consequently, among females the youngest age category (<18 years) was also associated with most of the medically treated sports injuries; most of these injuries were associated with field hockey, volleyball and gymnastics. Nevertheless, among the injured females aged 35-54 years, the percentage of medically-treated injuries was remarkably high compared with males in the same age category (62% females vs. 47% males; p=0.026).

Among males, incidence and SIRs were highest in the group aged 18-34 years; this latter group had the highest percentage of medically treated injuries (51%) and most of these injuries were related to outdoor soccer (53%) and indoor soccer (8%).
Ueblacker et al.[17] reported a trend of rising numbers of sports participants in Germany, particularly because the elderly population is becoming more active in sports. We found a similar trend in the Netherlands, with the largest increase in the age category <18 years and in those aged 55 years and older (Figure 2.2). However, in the 55+ group, because of the relatively small contribution to the absolute number of sports injuries, the low percentage of medically-treated injuries and the low SIR, current sports participation in this older age group can be considered as 'safe' in relation to non-fatal musculoskeletal sports injuries. However, because this 55+ population may be at risk for cardiac problems during sports activities, various campaigns (e.g. 'Heart for Sports' of the Royal Netherlands Football Association) do promote the distribution of automated external defibrillators to sporting sites to reduce the number of fatal cardiac accidents in sports.

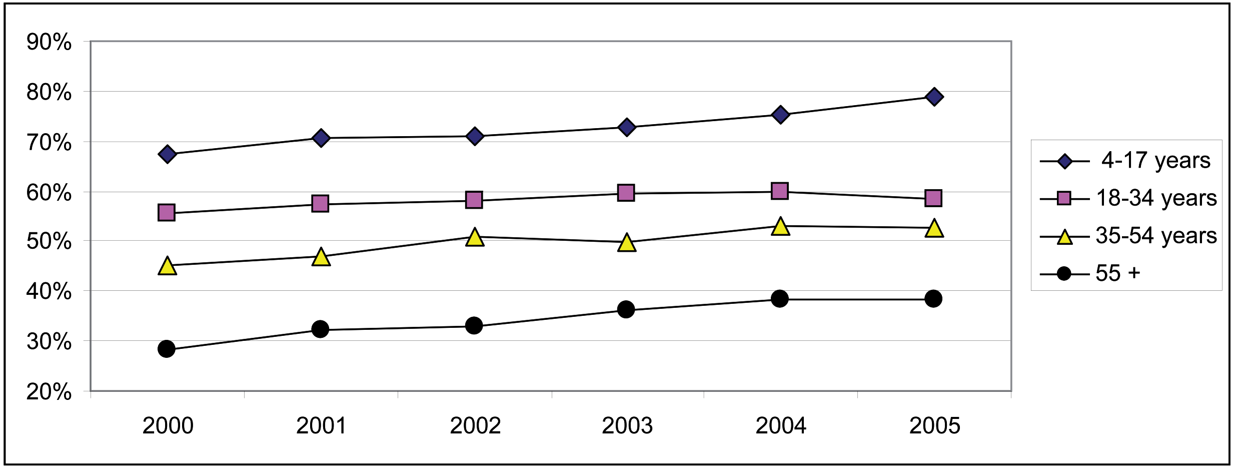

Figure 2.2 Trends in sports participation: proportion of the Dutch population registered as sports participant (in the four age categories) in the 2000-2005 period.

Studies on sports injuries have reported a higher incidence and SIRs among males than females [3,18-21]. Schneider et al. (using a 12-month recall period) also found males to be more at risk than females; they stated that prevention should mainly focus on male sports participants[16]. The common finding of an increased contribution of males to sports injuries despite the fact that methods vary significantly between studies (e.g. different duration of recall, prospective or retrospective, continuous or a one-time survey), is best described by Gabbe et al.[22]: " … *and reflects the nature of male sport/recreation activities, as well as the potential for increased risk-taking behaviour by men*." In the present study, similar results were found; on average, about two out of three sports injuries involved males. Also, the incidence and SIRs were about twice as high in males compared to females.

Although certain aspects are comparable, a detailed comparison between the published international surveys is difficult. For example, in a study from Finland the data were gathered by means of a repeated retrospective method[2]. From the Finnish data we were able to calculate a 46% annual incidence of sports injuries in a sports population older than 15 years; in our survey the incidence in this age group was only 19%. Calculating the Finnish gender-specific incidence, we found a three times higher incidence in their female population compared with a similar population of females in the Netherlands. In the Finnish study, SIRs in males and females were up to three times higher than those in the present study. Such large differences can probably be attributable to significant differences in the survey methods used[16,19,23-26]. In addition, historical, demographic, geographical and cultural differences may also influence various aspects of sports participation. Together, to some extent this could explain why such large differences in the overall injury incidence are reported in different countries.

In the present study, we focused on quantitative sport injury characteristics in specific target groups. Some qualitative characteristics of sports injuries in the IPAN survey, such as the type of injury, the injured part of the body, the circumstances and mechanisms (indoor vs. outdoor, contact vs. non-contact, etc.), as well as the extent and the precise nature of the injuries, still need to be investigated within each of the target populations.

CONCLUSION

Our results indicate that target groups for injury prevention programs are those sports that make a substantial contribution to the absolute number of injuries that have a high risk of injury and a high level of injury severity, among both male and female sports participants. In the present study, 66% of all sports injuries are accounted for by nine specific sports. These are: among men - outdoor soccer (4-54 years), tennis and running/jogging (35-54 years), indoor soccer and field hockey (18-34 years), skiing/snowboarding and gymnastics (4-17 years); and among women - volleyball (18-54 years), skiing/snowboarding and equestrianism (18-34 years), tennis and running/jogging (35-54 years) and outdoor soccer, field hockey and gymnastics (all 4-17 years). Of these nine sports, six are targets for both male and female sports participants. However, information that is more specific is needed about the cause of injury and the various options for prevention in order to make such programs specific enough to achieve the maximum effect. Such information can only partially be derived from surveys and should be obtained from well-designed prospective studies.

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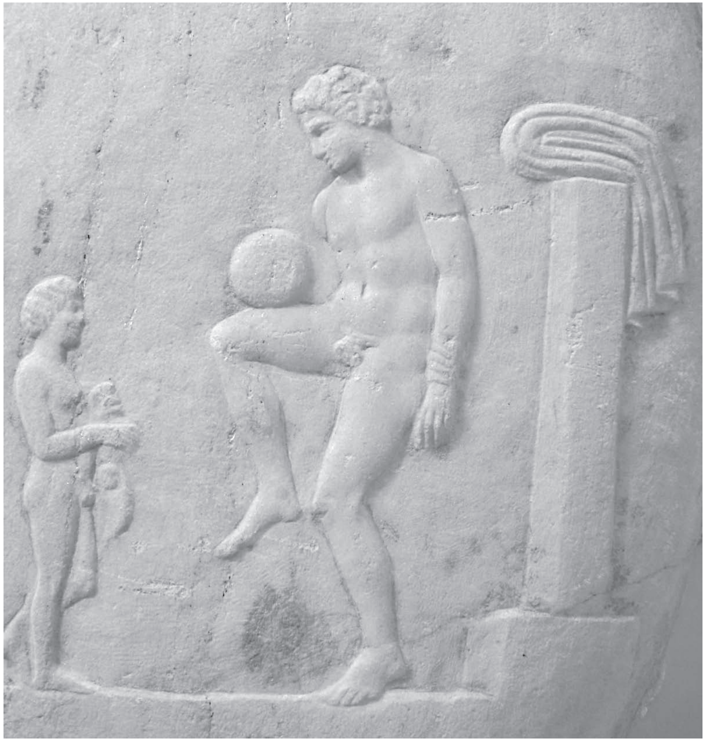

Ancient soccer

An early version of soccer is believed to be played by the ancient Chinese (2500 BC). The game, called Tsu Chu, was played with a stuffed ball, which was kicked by the feet.
The first game associated to soccer that was actually played with some kind of inflated ball, was named Episkyros. Although the game was initially played by the Greeks around 2000 BC with stuffed balls, later on the balls were made from inflated pig bladders wrapped in leather.
The image to the left was taken from a marble plate, on display at the Greek National Museum of Archaeology in Athens. The scene is considered an example of this ancient Greek game.
In the next chapter, all attention is centered on injuries in soccer.

Chapter 3

Injury prevention target groups in soccer: injury characteristics and incidence in male junior and senior players

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ABSTRACT

Objective: To identify target groups for injury prevention in male amateur soccer players under 35 years of age.

Design: retrospective*:* A computer-assisted telephone survey with a 12-month recall period for injuries in a representative sample of Dutch citizens from the Injuries and Physical Activity Netherlands (IPAN) -database.

Method: A comparison of the volume of soccer injuries , the incidence and the need for medical attention per level of exposure and age category.

Results: The incidence in seniors was twice that of juniors (17.5% versus 8.1%; odds ratio (OR=2.4). In juniors the overall incidence was lowest in the category with the least amount of soccer exposure time (0-3hrs: 2.9%; 3-5hrs: 13.0%; 5+hrs: 12.3%). A comparable result was found in seniors: (0-3hrs: 12.0%; 3-5hrs: 21.6%; 5+hrs: 21.5%). Within each level of soccer exposure, a different incidence was found in juniors and seniors (0-3hrs: OR=4.6; 3-5 hrs: OR=1.8; 5+ hrs: OR=1.9). Ankle, knee and upper leg injuries were most common (59.9%). Contusions, strains and sprains dominated (78.1%). Body region and type of injuries were similar in both age categories. Medical treatment for injuries was equally necessary in both age groups.

Conclusions: Senior male amateur soccer players and particularly the more skilled seniors (involved in soccer at least 3 hours per week), should be primarily targeted for studies on injury risk factors and prevention programs.

INTRODUCTION

Worldwide, soccer may be considered as the most popular organized sport with an estimated 240 million amateur players and about 200,000 professionals[1]. In the Netherlands, more than 1 million males, i.e. one in every eight Dutch male, participate in soccer. The incidence rate per 1000 hours and the percentage of medically treated soccer injuries have been among the highest of all sports[2]. A more recent epidemiological study of medically treated sports injuries in the Netherlands again substantiated this earlier finding, showing the high volume and severity of soccer injuries when compared to eight other high-risk sports representing 17 age and sex-specific target groups younger than 55 years[3]. Particularly the male soccer players under 35 years of age sustained a significant number of medically treated sports injuries, and showed a high contribution to the direct and indirect costs related to sports injuries in general. As a part of the first step in the prevention sequence[4,5], male soccer players under 35 years of age have been identified as an important high risk group, which stimulated both the Dutch government and the Royal Netherlands Football Association (KNVB) to put an effort into the development of injury prevention programs.

In the Netherlands, male soccer under 35 years of age represents a very large group of players (N=800,000; KNVB 2009 personal communication). This group may not be homogeneous in terms of incidence and injury characteristics and skill levels. Multiple target groups may exist, possibly demanding different preventive strategies. The group incorporates two major subcategories: junior players (4-17 years) and senior players (18-34 years). Therefore, the aim of this study was to identify homogeneous groups of soccer players at greater odds of sustaining an injury to be targeted in future injury prevention programmes.

METHODS

Data were obtained from the national survey Injuries and Physical Activity Netherlands (IPAN), covering 6 years (2000-2005) of continuous registration[3]. Out of 28,695 registered sports participants, 2,537 male soccer players ranging from 4-80 years of age were interviewed by telephone. The sub sample of under 35 years of age in this study consisted of 1241 junior soccer players (4-17 years) and 801 senior soccer players (18-34 years). The study was approved by the medical ethics committee of the University Medical Center Utrecht.

A soccer injury was defined as “physical damage or physical hinder related to soccer training or soccer competition games within one year preceding the interview”. Medical treatment was registered if an injury was diagnosed and/or treated by any of the following persons involved in health care: the general practitioner, medical specialist, sports physician, dentist, physical therapist, occupational physician, ambulance personnel, or physician in the emergency department of a hospital. Exposure time was derived from the IPAN records containing the average time spend for training and matches per week. The lowest exposure level (0-3 hrs/week, Table 3.1) described soccer players active up to one match and one training session. One match with two training sessions amounted up to a total exposure of

3-5 hrs/week. Three training sessions or more, and possibly multiple matches per week were typical for the highest exposure level (5+ hrs/week). In soccer, it is common that the total exposure time increases when skill levels[6] increase as well. Therefore, the different skill levels were based on the three different levels of exposure time. Time loss related to sports, school and/or work was specified by the number of days unable to participate in sports, the number of days unable to attend school, and/or the number of days absent from work. Because junior players may have paid jobs as well, work absence was also registered in the junior group. Statistical analyses were performed using SPSS 16 (SPSS Inc., Chicago, IL). Except for exposure time, all data were categorical (ordinal or nominal). Group averages are expressed as (M) and 95% confidence intervals as (95% CI). Differences in exposure time between juniors and seniors were tested using a T-test. For further analysis, the ordinal variable of exposure time representing the three different skill levels (0-3hrs; 3-5hrs; 5+hrs) was used. Multivariate logistic regression was applied to verify if both age categories and exposure levels were related to the injury incidence Wald statistics (W) are provided to indicate the strength of the association between the injury incidence and age or exposure. Chi-square analyses provided odds ratios (OR) for differences between age categories and exposure levels. The significance level was set at $p< 0.05$.

RESULTS

The average exposure time in male soccer players under 35 years was 4.3 hrs per week for training sessions and matches (Table 3.1). Junior and senior players showed similar weekly soccer exposure times (juniors: M=4.2 hrs, 95% CI=4.0-4.4 hrs versus seniors: M=4.4 hrs, 95% CI=4.2-4.6 hrs; $p>0.05$). Seniors were overrepresented in the 5+ hrs category ($\chi^2=22.9$; $p<0.001$, Table 3.1, 4th column).

A multivariate logistic regression showed that age categories and exposure levels were significantly related to the incidence of soccer injuries ($\chi^2= 37.1$, $p<0.001$; age category: W=36.5, $p<0.001$; exposure levels: W=44.6, $p<0.001$).

Compared to juniors, the incidence of soccer injuries in seniors was twice as high (Table 3.1, 2nd and 3rd columns). This difference was consistent across each exposure level (Table 3.1, 5th column). Exposure time was associated with the incidence of soccer injuries, mainly because of a reduced incidence at the lowest level of exposure (Table 1, 5th column). This effect was consistent in juniors and in seniors.

The proportion of the injuries treated medically (54.8%) in both age groups did not differ. However, the proportion of medically treated injuries increased with every exposure level (0-3hrs: 41.7%; 3-5hrs: 51.4%; 5+hrs: 67.0%; $\chi2=10.1$, $p <0.01$).

Only in the lowest two exposure levels, the incidence of medically treated injuries was significantly higher in seniors than in juniors (0-3hrs: OR=9.5, 95% CI=3.2-28.0; 3-5hrs: OR=2.5, 95% CI=1.5-4.5). At the 5+hrs level, seniors only showed a borderline higher incidence compared to juniors (OR =1.8, 95% CI=1.0-3.2, $p=0.06$, Figure 3.1).

Table 3.1 Injured players, multi response injuries, exposure time, and incidence per exposure level in Dutch junior and senior soccer players (n=2042).

	INJURED PLAYERS IN 12 MONTHS	INJURIES IN 12 MONTHS	EXPOSURE	INCIDENCE PER EXPOSURE LEVEL
Juniors : 4-17 years (n=1241, M=10.9 (CI=10.7-11.0)	n=100; 8.1%; 95% CI= 6.9%-9.6%	n=104*	0-3 hours: 48.4% 4-5 hours: 33.1% 5+ hours: 18.5%	2.9% # § 13.0%§§ 12.3%§§§
Seniors : 18-34 years (n=801, M=25.8 (CI= 25.4-26.1)	n=140; 17.5%; 95% CI=14.9%-20.1%	n=148	0-3 hours: 42.9% 4-5 hours: 29.6% 5+ hours: 27.5%	12.0%## 21.6% 21.5%
Total : 4-34 years (n=2042, M=16.7 (CI=16.5-16.9)	n=240; 11.8%; 95% CI=10.4%-13.2%	n=252	0-3 hours: 46.2% 4-5 hours: 31.8% 5+ hours: 22.0%	6.2%### 16.1% 16.8%

**Higher incidence in seniors compared to juniors: OR=2.4; 95% CI=1.8-3.1; p <0.001*
Lowest incidences in the lowest exposure group: #: χ^2=41.1; p<0.001 ##: χ^2 =12.4; p<0.01 ###: χ^2 =51.2; p<0.001:
Higher incidence in seniors compared to juniors: §: OR=4.6; 95% CI= 2.6-8.3; p <0.001 §§: OR=1.8; 95% CI=1.2-2.8; p ≤0.01 §§§: OR=1.9; 95% CI=1.2-3.2; p <0.01

Absence from sports occurred more often in juniors than in seniors (32.7% versus 14.2%, OR = 2.9, 95% CI=1.6-2.9, p≤0.001), but the duration of sports absence was similar in both groups: 18 days (95% CI=12.7-23.3 days; median=14 days). Work absence, reported by 15.5% of the seniors, was negligible among juniors. The average duration of work absence in seniors was 9.4 working days (95% CI=4.1-14.6 days; median=5.5 days, missing n=1). School absence among juniors was rare (6.7%), and lasted an average 4.3 days (95% CI=0.9-7.7 days; median=3 days).

Acute injuries dominated (89.6% of all injuries) with gradual and insidious onset injuries accounting for the remainder. A contact mechanism was a causal factor in 56.3% of the injuries, with the remaining injuries covered by non-contact. Most injuries were new (81.5%) but re-injuries still accounted for 18.5% of the total. As opposed to training injuries, most of the injuries occurred during competition matches (74.2%, n=27 missing). The distribution of these etiological factors was similar in juniors and seniors as well as in the three exposure levels.

Competition-related injuries caused medical treatment more often than training-related injuries (OR=1.8, 95% CI=1.0-3.4, p<0.05). Re-injuries showed a tendency to be treated medically more often than new injuries (OR=1.8, 95% CI=1.0-3.6, p=0.05).

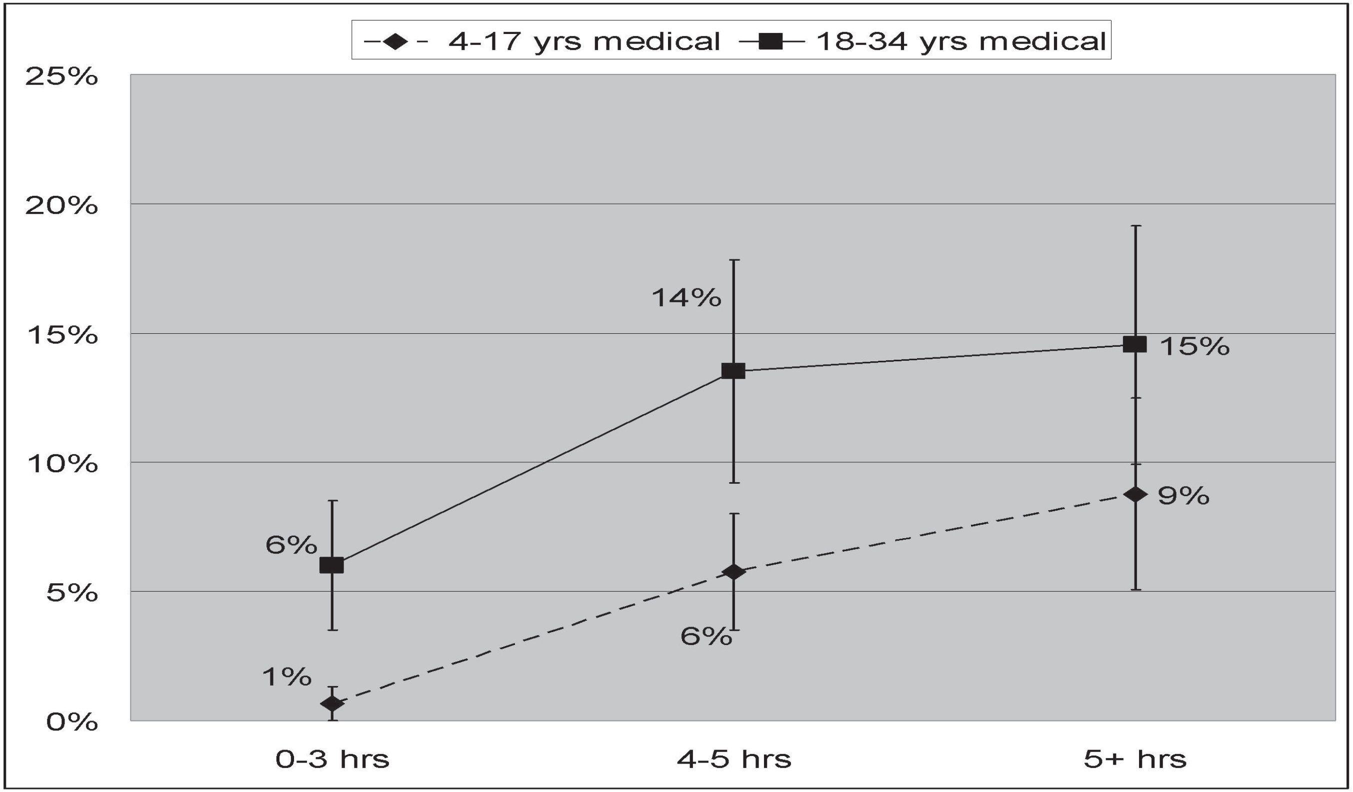

Figure 3.1. Significantly different incidences of medically treated injuries between juniors (4-17yrs) and seniors (18-34yrs) acting at the first two exposure levels, but not at the highest 5+hrs exposure level.

Two hundred-and-sixteen players (26 players missing) reported an injured body region (multiple injury responses =228) as well as a specific type of injury (multiple injury responses =235). Lower extremity injuries (ankle, knee and upper leg) were registered most often (Figure 3.2).

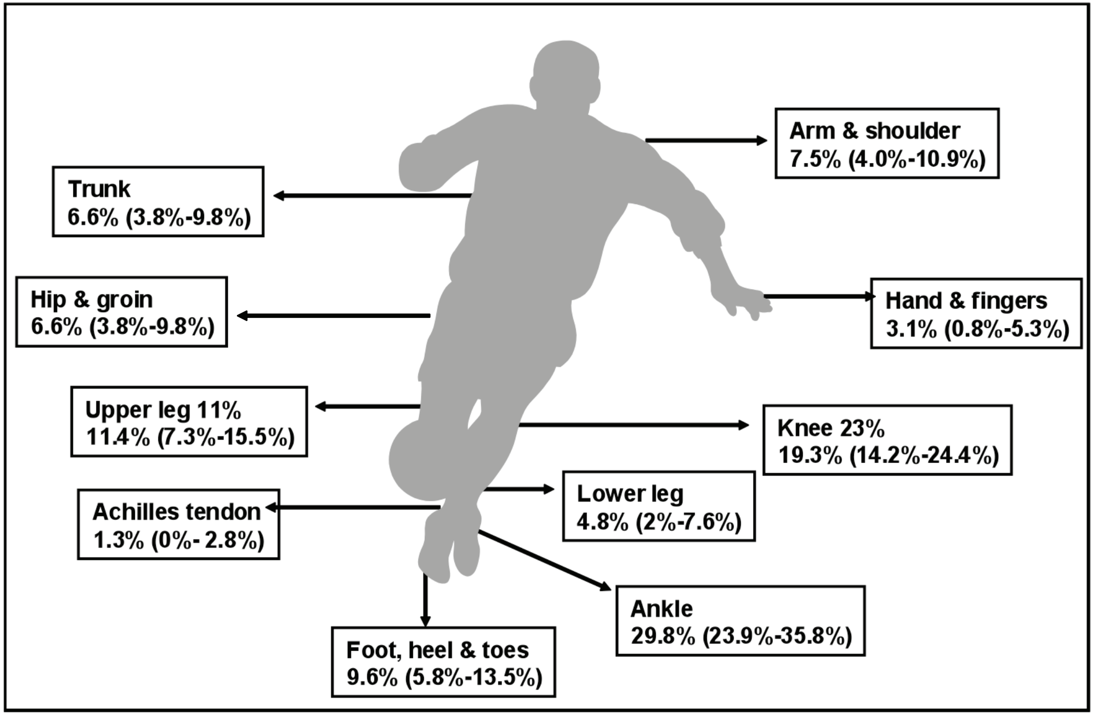

Figure 3.2. Proportions and 95% confidence intervals of 228 injured body regions (n=24 missing) in male soccer players younger than 35 years of age.

Arm and shoulder injuries (n=17) were more likely to be treated medically than non-medically (82.4% medically treated; OR=4.0, 95% CI=1.1-14.3, p≤0.05). Upper leg injuries and ankle injuries were less likely to receive medical treatment (upper leg: OR=0.3, 95% CI=0.1-

0.7, $p<0.01$; ankle: OR=0.5, 95% CI=0.3-1.0, $p<0.05$). Achilles tendon injuries were rare (n=3), only seen in juniors and treated medically. Forty percent of the injuries to the hip and groin were described as a reinjury (OR=3.1, 95% CI=1.0-9.3, $p<0.05$).
Contusions, strains (both 27.2%), sprains (24.6%), fractures (6.1%) and overuse injuries (3.9%) were reported most often. Contusions were reported more frequently by juniors (OR=1.9, 95% CI=1.1-3.5, $p<0.05$). No other type of injury showed a preference for juniors or seniors, or for any of the three different levels of soccer exposure time.
Fractures were mainly medically treated (OR=5.1, 95% CI=1.1-23.3, $p<0.05$), which contrasted with sprains (OR=0.4, 95% CI=0.2-0.7, $p\leq0.01$). All dislocations (2.2%) and cartilage-related complaints (1.8%, including meniscal injuries) were treated medically.

DISCUSSION

In this study, we focused on identifying specific sub-groups that would benefit most from targeted injury prevention programmes within a population of male soccer players under 35 years of age. To identify such groups we calculated the incidence in junior and senior soccer players within three different exposure levels. It was shown that seniors had a consistently higher incidence than junior players. The group of senior soccer players active at least during two training sessions and one game per week (3-5 hrs, and 5+ hours), represents the primary target for soccer injury prevention in the Netherlands. This target group resembles players who are active in the first or second senior team of clubs, playing in the higher amateur leagues of the Royal Netherlands Football Association.
Figure 3.1 shows a clear trend of an increasing incidence of medically treated injuries with every level of exposure in juniors, but not in seniors. It also shows the effect of the smaller number of players in the 5+hrs groups, causing larger 95% confidence intervals to overlap. Hence, the incidence of medically treated injuries in seniors and juniors in the 5+ hrs groups is no longer significantly different. This may indicate that the juniors, who are active for more than 5 hrs/week, should be second specific target group for injury prevention in soccer.
In the Netherlands, juniors under 13 years of age play their soccer game with significant rule adjustments. A comparison of the incidence and characteristics of injuries between juniors under 13 years of age and those who are older may therefore be relevant. However, the number of injuries in the IPAN junior sample was not large enough for a comparison between more specific age categories.
The relatively small number of injuries in the IPAN junior sample may be related to some of the limitations in IPAN. Up to 12 years of age, the Dutch law allows surveys to use proxy methods only. Generally, surveys apply a retrospective, self-reporting method that introduces memory bias. The proxy method may introduce some extra reliability issues, for instance in the specific characteristics of the injuries such as body region and type. However, it could also cause an increased underreporting of injuries, particularly of minor injuries[7]. IPAN also underreports the number of immigrants, but a weighting procedure is used to address this issue. Finally, and much less relevant in the case of junior soccer players, IPAN has limited access to the Dutch population living in institutions (e.g. in psychiatric centers). Therefore, a new study is advised with a sufficiently large sample of junior soccer players to further differentiate the incidence and

characteristics of soccer injuries between the age categories 4-12 years and 13-17 years of age. A prospective instrument to register the injuries is preferred to help overcome some of the above-mentioned limitations of survey methods in junior players.

In spite of the limitations in IPAN, many similarities were found in the type and body region of soccer-related injuries compared to several prospective studies in amateur or professional soccer[6,8,9] . The same holds true for the percentage of contact and non-contact injuries[8,10-13]. In our study, almost 19% of the injuries were re-injuries. As expected with a retrospective instrument, the mainly prospective studies showed a somewhat higher incidence of re-injuries, varying from 30% to 45% depending on the specific injury and the study population[14]. Nevertheless, similar to the other studies most of the re-injuries were muscle strains and particularly ankle sprains. Almost 20 years ago, soccer injuries were studied prospectively in two top-level amateur soccer clubs in the Netherlands[15]. Inklaar et al.[15] reported similar injury characteristics compared with our study. They emphasized at that time the prevention of ankle, knee and upper leg injuries in soccer. The current results about the dominant types of soccer injuries (Figure 3.2) would have provided similar advice on the prevention of specific injuries.

Inklaar et al.[15] also postulated that in the Netherlands highly trained subgroups were associated with the highest injury risks. Although not unanimously [3], other studies supported the view that higher level players sustain more injuries compared to lower level players[16,17]. Such a lack of consensus may be related to differences in methodology, ranging from injury definition to the methods used to register the injuries. Furthermore, some studies used an injury index with exposure time as a denominator[7,8,14,15], or a denominator derived from the size of the population at risk, or the number of athlete's exposures[12,13]. Also, less obvious differences may exist between apparently similar samples. A different distribution of skill levels may coincide with differences in intrinsic and extrinsic risk factors, hence explaining some of the differences found in various studies on soccer injuries.

In our previous study[2], we used the incidence per 10,000 hours of exposure time as one of the injury indices to compare the injury problem across different types of sports. In this study, within a single type of sport (outdoor soccer) and with identical exposure times in the two major subgroups (juniors and seniors), we have chosen to use the proportion of injured players as the main injury index. There were two important reasons to apply the current method. First, exposure time was used primarily for stratification. The relation between exposure time and skill levels [6,17] enabled us to identify subgroups with different skill levels. Second, prevention in the Netherlands is initiated mainly from a public health perspective. This perspective focuses on minimizing the negative impact of sports on health, and calls for a focus on the reduction of costs. Sports injury-related costs are highly dependent on the volume of sports injuries, as well as on the risk of medical treatment and time loss (school or work). Therefore, in our perspective, in this specific study the arguments related to volume and costs to define target groups for injury prevention are more important than the number of injuries per time unit.

CONCLUSION

Senior amateur players active in soccer for three hours or more each week, usually playing in the first or second senior teams, represent the primary target group for soccer injury prevention in the Netherlands. When specifically using the incidence of medically treated injuries to determine target groups, junior soccer players active for at least five hours per week, are the second most important target group.

PRACTICAL IMPLICATIONS

- Nation wide retrospective surveys on sports injuries can deliver valuable information to set the agenda of sports injury prevention if they provide data about the population at risk and exposure time.
- In soccer, the lower extremities are affected most. More than half of the lower extremity injuries are contact-related. Prevention could opt to focus on minimizing contact actions with a high injury risk
- Inadequate recovery can be an important causal factor in re-injuries. ‘Return to play’ protocols, to be used by coaches, physical therapists and sports physicians, should be tested to identify their utility in the reduction of the incidence of soccer injuries.

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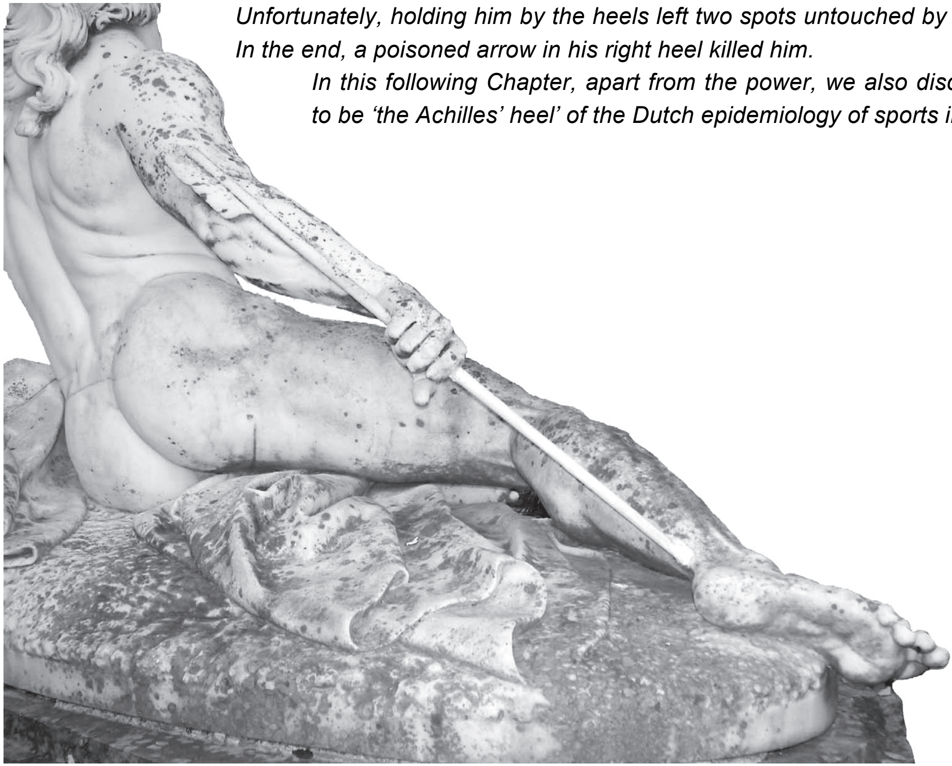
Achilles

The meaning of the phrase 'the Achilles heel' refers to the weakest spot of a famous warrior during the Trojan Wars, named Achilles. According to the Greek mythology, Achilles was supposed to survive any damage to his body because he was dipped in the water of the river Styx by his mother, Thetis.

Unfortunately, holding him by the heels left two spots untouched by the magic water: his heels. In the end, a poisoned arrow in his right heel killed him.

In this following Chapter, apart from the power, we also discuss what we can consider to be 'the Achilles' heel' of the Dutch epidemiology of sports injuries.



Chapter 4

A quarter of a century of nationwide registration of sports injuries in the Netherlands: to count, to measure and to evaluate

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ABSTRACT

Sports stimulation by the Dutch government for over 30 years has resulted in both positive and negative effects. In order to review the negative consequences of participation in sports, measurement of sports injuries was initiated. Sports injuries in the Netherlands have been registered over the years by different institutions and in many different ways. Moreover, government policy behind the registration of sports injuries has changed frequently in the past 25 years. Such changes have had their impact on the content and methods of registration and therefore, on the comparability and compatibility of results from the national survey entitled ‘Accidents and Physical Activity in the Netherlands’.

After presenting a historic overview of the effects of these changes, some major differences between various population estimates are explained. Also, a new perspective on the registration of sports injuries is presented which will enable the collection and use of straightforward, non-conflicting injury data.

FROM PROMOTION OF SPORTS ACTIVITIES TO SPORTS INJURIES

During the 1970s sports participation and physical activity was promoted to the entire Dutch population (Trim U Fit, 1968; Sport Real, 1976[23]). This originated from the idea that sports participation improves both mental and physical health [16]. Initially, the research focused on establishing how many Dutch citizens became active in sports. It was shown that the promotion policy with nationwide campaigns had a positive effect, and there was indeed a substantial increase in the number of sports participants in the Netherlands[14,15,24].

In their book on injury prevention, Snellenberg and Kuipers (1981) discuss the downside of this supposedly healthy activity:"*If someone has been inactive for years it certainly isn't healthy to imply start playing soccer with the veteran players. Sports participation might be healthy but ruthlessness often leads to injuries*." At that time, it was also known that in Germany, after 1950 about 10% of the injuries treated in hospitals were sports-related[7]. However, until the early 1980s, no data on sports injuries in the Netherlands were available.

In 1978, a small-scale inventory of sports injuries was held among general practitioners (GPs), company medical services, and hospitals in the Arnhem area[2], but the analyses failed to provide information on the nationwide topic of sports injuries. Nevertheless, the impact of the reported numbers of injuries was enormous. After an attempt to extrapolate the results to the total population, the numbers became so high that the government realised a reliable nationwide estimate of the type and severity of sports injuries was necessary in order to develop appropriate policies for healthy sports participation.

This article presents an overview of the methodological aspects in the Dutch registration systems of sports injuries. Using the largest nationwide registration systems as an example, historical perspective is used to discuss how the selected methods affect the results of the various registrations systems, and what effects these methods have on the interoperability and compatibility with other registration systems. Finally, an overview is given of the largest nationwide registration systems, and the future of sports injury registration is discussed.

DESIGN OF SPORTS INJURY REGISTRATION SYSTEMS

Registration systems may be of a transversal or longitudinal type. Transversal systems (cross-sectional studies) present information on the extent and type of injuries at a specific point in time. Aggregated data from repeated transversal studies, whether or not retrospectively obtained, can be used to study trends.

Cross-sectional data on sports injuries can be collected by addressing the sports participants directly (injured or not injured) or when he/she seeks medical attention. The frequently used statistics from health insurance companies[7] in international reports are not available in the Netherlands. The injured Dutch sports participant can seek medical help from several medical services. Apart from hospitals, other options include the general practitioner (GP), physical therapist (PT), first-aid assistant in sports (FA) and the sports physician at Sports Medical Advice Centers (SMA). In the hospital, sports injuries are mainly treated in the Emergency Room (ER), the Sports Medical

Department (SMD), or at other hospital clinics (Figure 4.1). Trends on sports injuries treated in the ER have been studied using the Private Accidents Registration System (PARS, in Dutch: *Privé Ongevallen Registratie Systeem,* PORS) and the *Injury Information System (IIS: in Dutch Letsel Informatie Systeem*, LIS), often referred to as PORS/LIS[22].

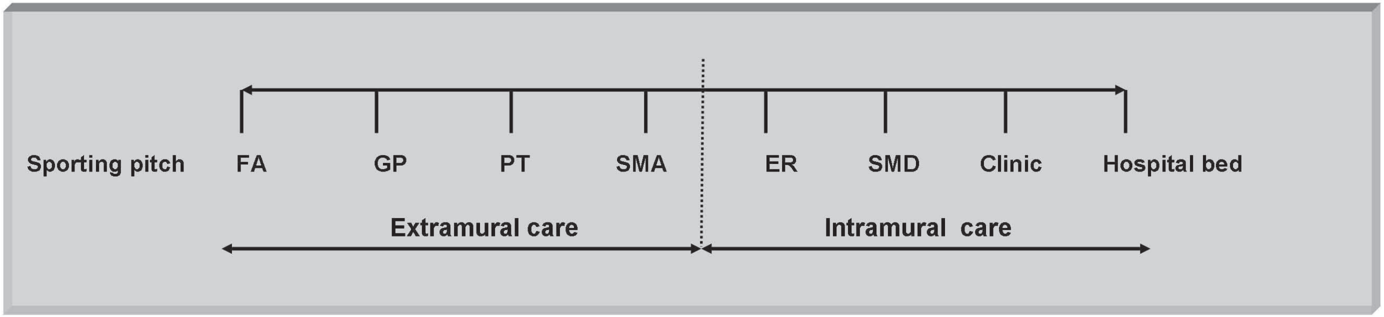

Figure 4.1. Continuum of medical care in sports injuries in the Netherlands.

FA first-aid assistant in sports *GP the general practitioner* *SMA Sports Medical Advice Centers*
ER Emergency Room *PT physical therapist* *SMD Sports Medical Department*

Depending on the point of entry in the medical care system and its usual routing through the medical system, injuries may be registered by various systems. Examples of care-specific registration systems include those of the GPs (GPR, in Dutch: *Huisartsen Peilstations /Continue MorbiditeitsRegistratie*, HP/CMR), the ER's, and registrations at SMA's.

In nationwide surveys on sports injuries, the injured sports participant is always contacted directly and independently from the treatment location to gather data. Over the past 25 years, three such systems have collected sports injuries data covering the entire medical care system: the Health Inquiry (HI, in Dutch: *de GezondheidsEnquête/Permanent Onderzoek LeefSituatie*, GE/POLS), Accidents in the Netherlands (AiN, in Dutch: *Ongevallen in Nederland*, OIN) and the successor of AiN, the Injury and Physical Activity Netherlands (IPAN, in Dutch: *Ongevallen en Bewegen in Nederland*, OBiN). Table 4.1 presents an overview of all Dutch registration systems. All the systems that were operational in 2005 (i.e. IIS, GPR and IPAN) are placed in the care continuum, each covering its own area (Figure 4.2).

The initial data emerging from the nationwide registration systems on sports injuries (HI, GPR, PARS/IIS, Table 4.1) did not sufficiently cover the entire Dutch population. Data were either restricted to age (older than 16 years[13]), or they only registered treatment by the GP [10] or by the ER[4]. At that time, AiN/IPAN was the only registration system that produced statistical data with a broad enough scope (i.e.

including medically/non-medically treated, mild to severe, and prevention) to produce national estimates of the total numbers of sports injuries.

Table 4.1. Registration systems for sports injuries in the Netherlands.

REGISTRATION SYSTEM	GOAL	TARGET POPULATION	**RECALL PERIOD**	**SAMPLE**	**TYPE OF DATA**	**CARE TAKER**	**INJURY TYPE**
GPR ('79-'83, '92)[10]	Estimate of the number of sports injuries treated by the GP	Dutch population	None	Cases from 46 GPs covering GP care of ca.1% of Dutch population.	Health care consumption	GP	Medically treated, acute and overuse
PARS/IIS ('83-'96 / '97-today)[22]	More leisure time injuries occurred than expected, new system necessary to provide reliable estimates that was: - Limited in size but reliable in volume and severity of accidents; - Suitable for priority analyses; - Starting point for in-depth research; - Able to evaluate seasonal effects and effects of prevention programs.	Dutch population	None	Cases at 14 hospitals (n = ± 15,000 injuries/year)	Health care consumption	ER	Medically treated, severe, acute
AiN ('86-'98)[18]	Provide complete coverage of injuries in the Netherlands.	Dutch population	'86-'87 (4 weeks) '92-'93 (4 weeks) '97-'98 (3.5 months)	Random selection from Dutch Community Administration (DCA) n=5,600 per month	General data, and specific data on (sports) injuries and sports participation	All	all
IPAN ('99-today[11,25]	Continuation of the AiN, with additional monitoring of Physical Activity and Health	Dutch population aged > 4 years	3.5 months	Random Digit Dialing (n= ± 2500/3 months)	General data, and specific data on (sports) injuries and sports participation	All	all
SMA[1] ('88-'89)	To provide data to determine methods of quality control and quality improvement.	Dutch population	None	Cases at 20 SMAs and SMCs	Health care consumption	SMA	Medically treated, overuse
HI ('81-'96 / '97-today)[22]	Description of health, medical consumption, lifestyle and preventive behaviour in the Netherlands	Dutch population aged > 12 years and > 16 years	1 year	81-85/ sample drawn from known addresses (n=±13,300/year) /97- sample from DCA (n=±13,300/year)	General data, and specific data on (sports) injuries and sports participation	All	All

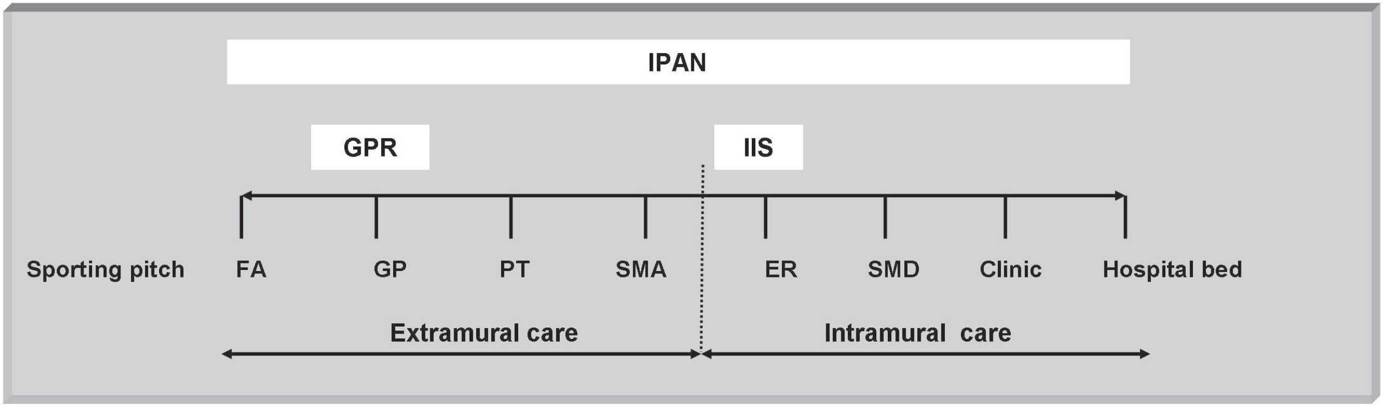

Figure 4.2. Coverage of sports injury registration by IIS, GPR and IPAN systems.

Using AiN/IPAN as an example, the following section discusses how the quality of data and results are affected by changes in policy on injury registration.

AIN/IPAN AND CHANGES IN SPORTS POLICY 1980-2005

The beginning

To evaluate the success of governmental policy to stimulate sports participation, in the early 1980s the government needed nationwide data on the type and extent of medically/non-medically treated sports injuries. This was the start of the nationwide registration of sports injuries (AiN) in 1986 and 1987. In addition, sports participation was registered [6,18]. However, government policy on sports changed rapidly in the late 1980s/early 1990s. Initially striving for absolute growth in the number of sports participants, the aim was revised to focus on quality and safety. In the 1988-1992 period, safety in sport was actively promoted by the National Institute for Sport and Health with an injury-prevention campaign called *Mastering sports injuries* (In Dutch: Sportblessures blijf ze de baas). However, the content of this campaign did not reflect the results of the first nationwide survey on sports injuries. The first AiN data were not presented until 1990 (considerably later than the start of the campaign) and showed 2.7 million medically and non-medically treated sports injuries each year[6]. The former Minister of Welfare, Public Health and Culture (period 1989-1994, Drs. H. d'Ancona) decided to use the original report as a tool to make decisions regarding future goals and targets in sports injury prevention.

Evaluation of prevention campaigns

Therefore, the second AiN in 1992-1993 had to evaluate the general effect of the ongoing prevention campaigns. For instance, information was needed about changes in preventive measures in sports. Unfortunately, as in 1986-1987, this information was only collected when the participant actually reported a sport injury. No information about preventive measures by the uninjured sports participant was available. Therefore, the effect of the injury prevention campaign *Mastering sports injuries* was mainly calculated by using an estimate of the injury risk per 1000 hours of sports participation (incidence rate); this type of evaluation is still used today. In the government policy document *Sports, Physical Activity and Health* (the Ministry of Health, Welfare and Sports), a goal was set to reduce the incidence rate by the year 2010. As a result, the nationwide registration of sports injuries was now permanently linked to the necessary registration of sports participation, and, specifically, to the registration of the exposure time in sports. It was also stated that the next AiN should be extended to provide information on preventive measures in all sports participants.

Responsibility and financial burden

At the end of the 1980s/early 1990s the socio-economic aspects of sports injuries had become more prominent. Taking into account the extent of sports-related absence from work and the ‘considerable’ number of sports injuries, it was questioned whether the sports participant should be held responsible for all societal consequences of a sports injury, or whether employers should carry the burden of sports injuries [3]. As result, more attention was paid to the costs of sports injuries, and to the relative risk of several diseases, complaints and accidents in sports participants and in non-sports participants. This was the onset of the first cost-effectiveness study on the health effect of sports participation[26].

In order to collect the ever-increasing amount of information needed, more and new content was required in the registration systems of sports injuries. The systems had to provide adequate estimates of the costs of sports injuries by registration of medical care and work absence. Moreover, a clear distinction was needed regarding differences in risks/effects of diseases/ailments between sports participants and non-sports participants.

In fact, none of the systems (not even the AiN 1997-1998) was suitable or capable to provide the required information. This made it necessary to connect data from different registration systems, even though each had its own specific goal. Unfortunately, these connections proved difficult due to the large differences in registration methods and the populations under study. As a result, a considerable amount of information was unavailable, and the results often lacked validity and reliability.

Healthy physical activity

During the 1990s, sports injuries were used as an argument to promote physical inactivity with a 'less dangerous' lifestyle approach. After presenting the Dutch Guideline on Healthy Physical Activity (NNGB)[12], it was decided that, as of 2000, an activity monitor should be added to the AiN (Figure 4.3). From that point onwards, the name of the system changed to IPAN.

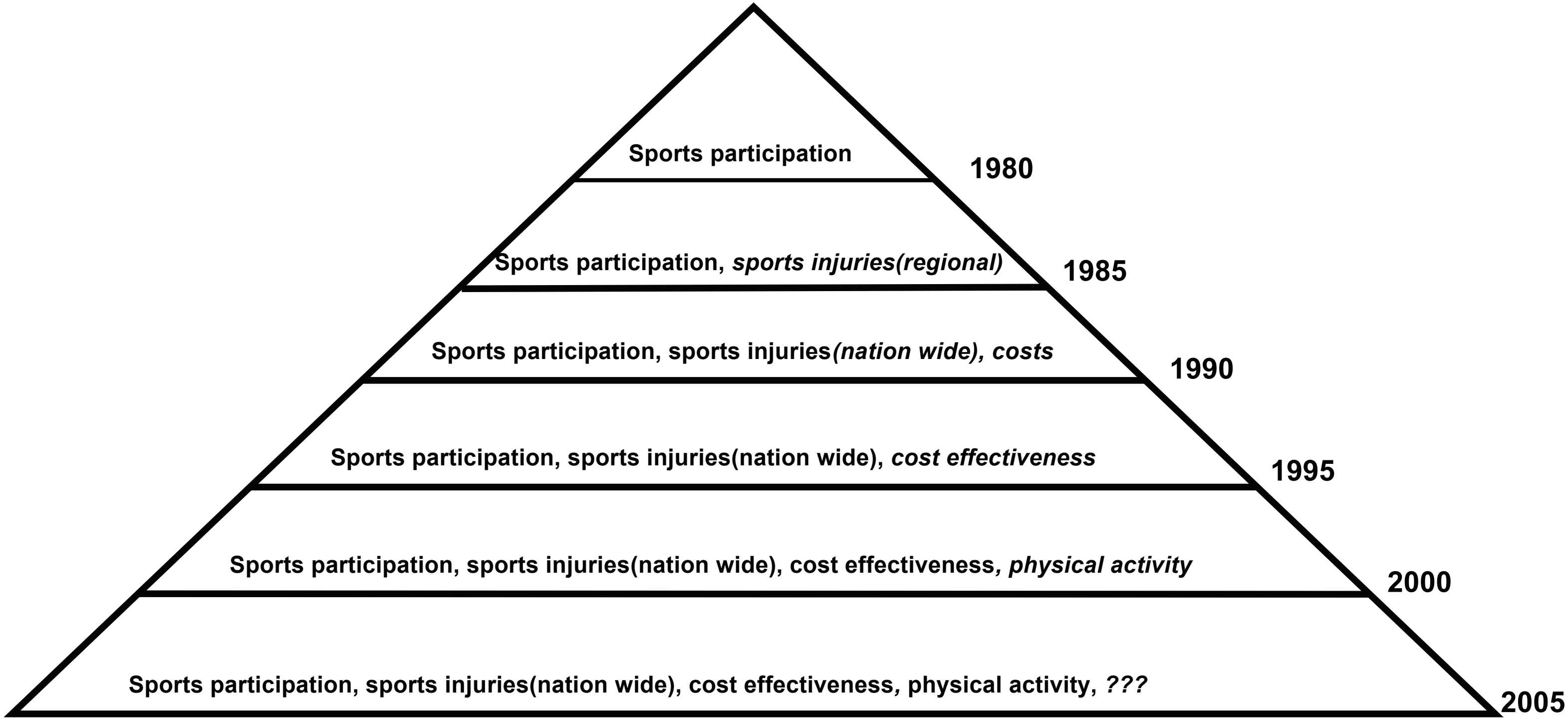

Figure 4.3 IPAN: the development of research topics with additions (in italics) over a 25-year period.

CONSEQUENCES OF CHANGES IN GOVERNMENT POLICY

As explained above, in the Netherlands the registration of sports injuries has become a part of a much wider inventory on physical activity and health. Changing definitions and methods, combined with financial cutbacks imposed by the government, left few options to maintain a consistent and reliable registration of sports injuries. The statistical data from several systems, and even from a single system, were difficult to compare and interpret because of the changes in policy. For instance, in 1986-1987 AiN estimated 2.7 million sports injuries each year, but 10 years later the estimate was only 1.5 million. This huge reduction was 'hidden' by the recall bias in the AiN 1997-1998 data, because financial cutbacks forced an increase in the recall period from 4 weeks to 3 months. In addition, due to methodological issues, nationwide estimates were available for acute injuries only[8]. It was shown in the Trendreport *Physical Activity and Health 2000-2001*[19] that a correction for these methodological issues almost completely deleted the differences, i.e. 2.4 million acute injuries in 1986-1987 versus 2.3 million acute injuries in 1997-1998 (Figure 4.4). Reporting of uncorrected numbers, and unfamiliarity with the methodological causes of the resulting differences, is a well-known source of misunderstanding and problematic interpretation of nationwide statistical data, even today.

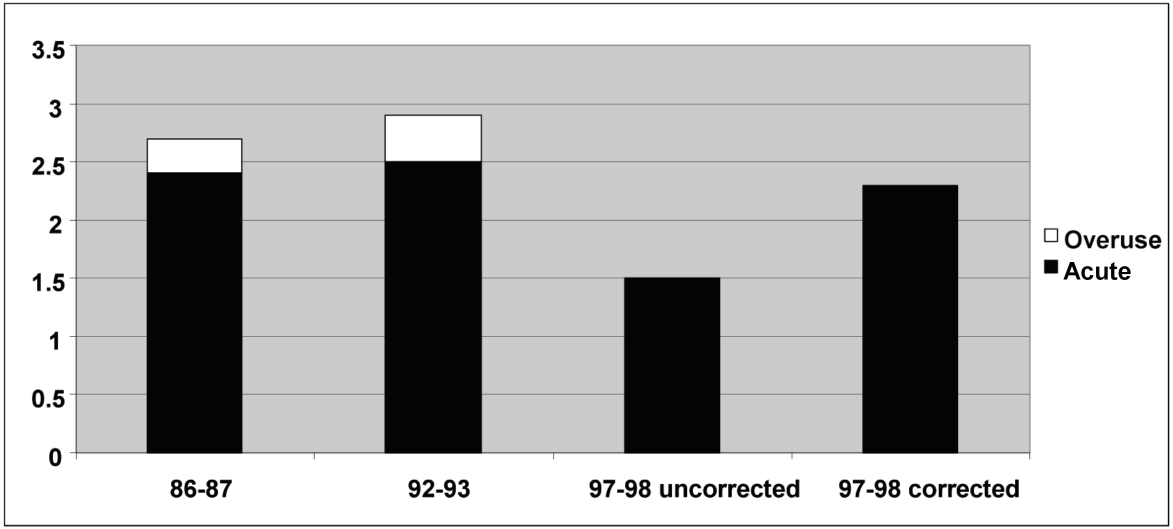

Figure 4.4 Annual numbers of sports injuries (in millions) in the Netherlands based on data from the AiN and IPAN (1986-1998).

The only registration system less affected by changes in government policy over the last 25 years was PARS/IIS. Its consistent method of registration and high level of accuracy made it possible to describe the injury problem starting from the 1980s. The main problem with the PARS/IIS statistical data was that it was limited to ER-treated injuries of an acute nature only, which revealed only the tip of the 'injury iceberg'. Annually, approximately 160,000 injuries are treated at the ER[9]. However, compared with the ER, GPs are visited 2.5 times more often by injured sports participants, physical therapists treat twice as many injured sports participants, and medical specialists treat a similar number injured sports partcipants [27].

RECOMMENDATIONS FOR FUTURE REGISTRATIONS

In 2005 (the year this study took place), reduction of sports injuries was still an important priority in government policy, with emphasis on the development of safe sports for those at increased risk and implementation of effective injury-prevention measures[17]. Also, sports specific injury prevention gained increasing attention. Sports federations were encouraged to assist with the development of a sport-specific registration system, called the Injury Registration and Information System (in Dutch: Blessureregistratie en InformatieSysteem; BIS, by TNO Delft). Moreover, some sports associations had already taken steps to address the most common injuries within their specific line of sport.

The national registration systems, such as the LIS, IPAN and the periodic GPR, were used to evaluate the effects of policies implemented in the previous years, and to provide insight into the development and extent of injuries related to so-called fad sports or new sports (e.g. snowboarding)[17].

The current registration systems differ from each other on some essential points. Consistency, clarity and mutual consensus regarding the registrations and estimates are essential to enable them to be properly used to evaluate the effects of policy. The Handbook Epidemiology of Sport Injuries (in Dutch: Handboek Epidemiologie Sportblessures[5]) addresses these problems. This handbook outlines the most important characteristics of a registration system that effectively contribute to the estimation of the extent and nature of the sports injury problem.

Care-specific registration

Similar to the registrations made by GPs and in the emergency departments there is also a need for registrations by physical therapists and policlinics of hospitals. The National Medical Registration (in Dutch: De Landelijke Medische registratie; LMR) [20] collects medical and administrative data on patients treated in a hospital or as a day-patient in the Netherlands. In 2005, reasons for hospital admissions were not registered, and therefore, a breakdown by sport injuries was not possible. If such a registration would have been made together with a registration by physical therapists, then almost all (para)-medical treatments of sports injuries would be covered. What applies to the

National Medical Registration, also applies to the so-called Diagnosis-Treatment Combination (in Dutch: Diagnose-Behandeling Combinatie: DBC registration). The DBC is the total set of activities and procedures provided by hospitals and medical specialists, resulting from patients consulting a medical care unit in the hospital. Also, in this type of registration the reason for medical care is not yet routinely recorded. When changed, the DBC could be used to register all sports injuries treated in Dutch hospitals.

Random population-wide injury registration

A random population-wide injury registration system (such as the IPAN) will still be required for national estimates of sports injuries because of inevitable duplications (e.g. patients may visit multiple caregivers for the same injury), or because the care-specific systems cannot provide the actual numbers. Moreover, IPAN is necessary for a complete picture of the routing in the medical care system, and for statistical data from a random sample of athletes to determine e.g. (cohort and sport-specific) risk indices.

Non-medically treated sports injuries (50% of all sports injuries) are only recorded with the IPAN system. As a result, this nationwide random survey can provide insight in changes of the accessibility of the current health care system. For example, treatments with physical therapy have partially disappeared from the basic health insurance package. Visits to other care providers (such as the GP) are discouraged. Because of these changes, it is conceivable that sports injuries might unjustly fall outside the (para)-medical circuit.

A consensus on the definitions and methodology in various registration systems enables large-scaled national registration systems (such as the IPAN) to link with other care-specific systems in an ‘umbrella-like’ structure. In this case, IPAN may serve as the ‘cover’ under which independent registration systems will function. This allows optimal use of the specific strengths of each individual registration system. Moreover, the often larger number of injuries registered in the care-specific systems are better suited for detailed research than the often small numbers of cases in non-care-specific nationwide registration systems. When linked with eachother, this avoids the need to register lots of details about sports injuries in large-scale systems similar to the IPAN.

We already stated that sports injuries have become a part of the general topic on (in)activity and health in the Netherlands. Various government policies may lead to the registration of a single type or a compatible type of data, whether or not with an umbrella-like structure with a survey-type registration system and with various sub-registrations. For example, multiple systems monitor mobility, traffic accidents, industrial accidents and/or health. An overview of all the registrations systems is necessary to help prevent that various policy issues will lead to a financially undesirable double registration, or to different registration methods of a similar phenomenon with different statistical outcomes. An optimal use of registration systems with various compatible topics, when linked, will offer substantive, organizational and financial advantages. However, sometimes highly specific information and/or statistical data are required and double recording will remain practical, or even necessary.

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A cure against fatigue?

Pedianus Dioscorides (40-90 AD) was a Greek physician from Cilicia (now Turkey). He worked as a surgeon in the Roman army. During many trips with the army he gathered information about a large number of plants and herbs with medicinal characteristics. He wrote down all this information in the Materia Medica. In this book, he was the first one to describe the positive effects of the roots of a specific plant for patients suffering from fatigue related disorders: Rhodiola Rosea, currently also known as Sedum rosea.

Nowadays, substances from the roots of this plant have been proven to be effective in depressive disorders. It also shows activating qualities in patients with stress related chronic fatigue, whereas in healthy subjects it appeared to increase concentration but not physical performance.

Chapter 5

Introduction to non-functional overreaching in athletes

NON-FUNCTIONAL OVERREACHING

In 2006, the theoretical concept of non-functional overreaching (NFO) was extensively described in the position statement of Meeusen et al. [15] concerning prevention, diagnosis and treatment of the overtraining syndrome (OTS). NFO occurs when athletes do not preserve an adequate balance between physical and psychological load and recovery. It leads to a decrease in performance instead of an increase; it causes signs and symptoms; and requires several weeks or months to recover (see Figure 5.1).

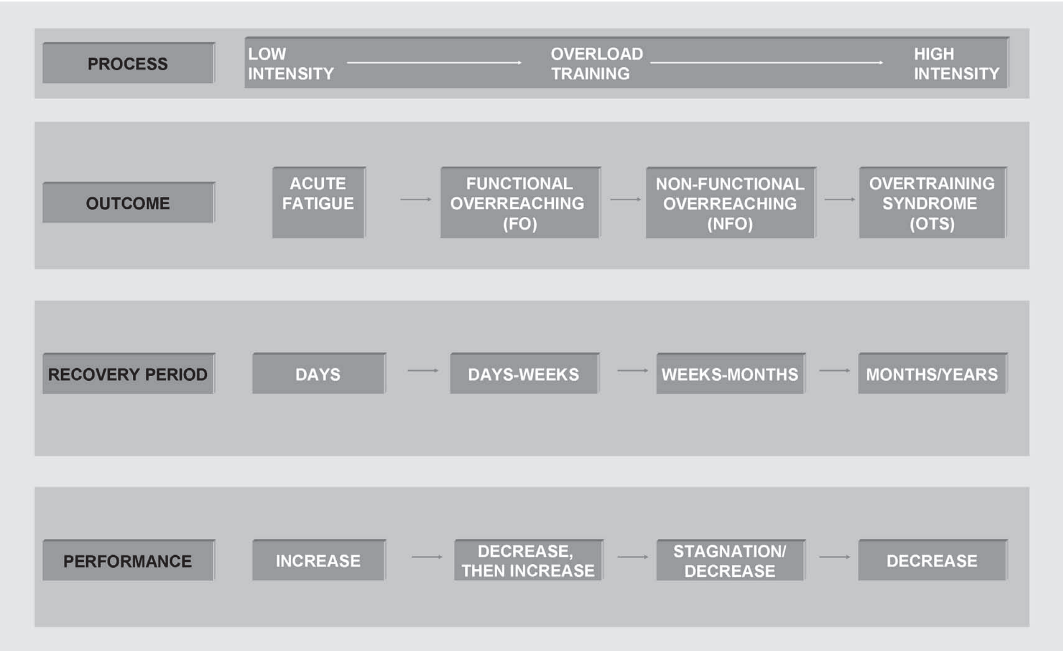

Figure 5.1 Characteristics of three different stages in the overtraining process[15]: functional overreaching (FO), non-functional overreaching[*] (NFO) and the overtraining syndrome (OTS).

This statement was developed for physicians, coaches, psychologists, and physical therapists who needed to handle the issues of overtraining. In this statement NFO referred to very practical questions: *When will overreaching (OR) lead to supercompensation*, *and when will it evolve into a state of extreme OR that will lead to a stagnation or decrease in performance for several weeks or months?*.
The role of the new term NFO was basically to replace the phrase “extreme OR”, thereby marking not only the boundary between proper and improper overload training, but also the start of a process that may ultimately lead to the development of OTS.
In the literature, there is no consensus about the duration of symptoms in NFO or OTS. In earlier studies[10,18], athletes suspected of OTS were diagnosed if symptoms persisted for at least 2-3 weeks. However, in recent studies on NFO [16,19] the duration of symptoms of about one year was allowed, and OTS required symptoms for more than one year.

Signs and Symptoms

The signs and symptoms in NFO are often similar to those in OTS[15]. Prior to the introduction of NFO in 2006, the lack of obvious differences between overreaching (OR) and OTS forced Halson and Jeukendrup[5] to question the basis of any difference at all between OR and OTS. Essentially, this explains the title of their review: ‘Does overtraining exist ?’

Table 5.1 Signs and symptoms in two types of OTS, according to Hackney and Battaglini[3].

HYPER AROUSAL (SYMPATHETIC OTS)	HYPO AROUSAL (PARA-SYMPATHETIC OTS)
Impaired physical performance	Impaired physical performance
Easily fatigued	Easily fatigued
Restlessness, hyper excitability	Feelings of depression, phlegmatic
Disturbed sleep	Sleeps easily
Anorexia, weight loss	Normal appetite and body weight
Increase resting heart rate	Low rest heart rate and quick recovery
Increase resting blood pressure	Hypoglycemia during exercise
Slow heart rate recovery	Decreased libido, amenorrhea in women
Loss of motivation	Loss of motivation
Increased incidence of infections	Increased incidence of infections
Decreased maximal lactate after exercise	Decreased sub maximal and maximal lactate after exercise
Postural hypotension	

It has been postulated that OTS may be characterized by two distinct substates: the hyper arousal and hypo arousal state[3]; (see Table 5.1). These states are similar to the Basedowian-sympathetic and Addisonoid-parasympathetic types of OTS, as previously described by Israel [6,7].

The two types of OTS have been a topic of debate for more than 50 years. Nowadays, there is consensus about the presence of impaired physical performance and fatigue in both types. Consensus also exists on the relatively low incidence of the hyper arousal type, as well as on the interaction of hyper arousal with external stressors, although there is no real scientific evidence for the latter interaction [1,3,4,7,11,12,13,15].

Israel (1976) stated that the Addisonoid type of OTS (i.e. the hypo arousal state) occurs most frequently in endurance athletes, while the Basedowian type of OTS (i.e. the hyper arousal type) is more often associated with athletes in team and power sports, such as sprinting or weight lifting.

However, Kuipers [11] suggested that the hyper arousal state would precede that of the hypo arousal state. A hyper arousal state effectively addresses the bodily needs to cope with an extended period of stress. When this period is stretched for a relatively long time, the sympathetic activity will be reduced, and a relatively dominant parasympathetic tone will result in a hypo arousal state. The analogy with transitions from FO into NFO and finally into OTS, as described in the model in Figure 5.1, becomes apparent.

Table 5.1 also depicts some mood characteristics in both states. The irritable mood on the one hand, and the phlegmatic and depressed behaviour of athletes on the other, has been recognized by many trainers and coaches. Both mood profiles have led to a wealth of scientific reports on mood changes related to the overtraining process. Several questionnaires have been used in research and sports practice to monitor mood and affective states in athletes who are suspected to suffer from OR or OTS:

- Profile of Mood State: POMS [18,20,21,22]
- Total Quality Recovery: TQR [9]
- Recovery-Stress Questionnaire: RestQ-Sport [8]
- Daily Analysis of Life Demands of Athletes: DALDA [4]
- Self-Condition Scale [23]
- French questionnaire of overtraining [14]

However, it was evident that mood changes also occurred in athletes without any hint of developing NFO or OTS at all [5]. Therefore, it is advised to monitor mood parallel to decreases in performance in order to evaluate an ongoing process of NFO or OTS in athletes [15].

In Chapter 7 of this thesis, the POMS questionnaire was used to test mood difference between two groups: athletes with a prolonged reduction of performance, and healthy control athletes with normal performance profiles.

Studies on non-functional overreaching (NFO)

Prior to the introduction in the literature of the term 'NFO' in 2006, all studies on the overtraining process used some kind of profile to characterize athletes suspected for OR or OTS. Characteristics were obtained by clinical evaluation, or evoked by trials (overload studies). In general, between-group differences were used to test various potentially diagnostic parameters, but some parameters were also evaluated by their changes over time (within-group analysis). As stated in Chapter 1, none of the parameters of these studies could be used as a valid and reliable diagnostic parameter.

Table 5.2 Studies on non-functional overreaching (NFO) published after the introduction in the European Journal of Sport Science of the position statement on the prevention, diagnosis and treatment of OTS[15].

Authors	Study population	Age in years	Research type*	Study objectives	Recovery period*	Main outcome parameters	Instruments	Results
Moore and Fry, 2007 [17]	9 American college football players ♂	?	Tr	Diff. NFO/FO	NFO: ? FO: ?	T, C, performance	4 wks IT (1), 5 wks IT (2), 6 wks normal load	IT (2) T↓↓
Coutts et al., 2007[2]	18 rugby players, ♂ N (IT)=9 N (CL)=9	IT: 24.4±2.6 CL :22.4±2.6	R, CL, Tr, F	Diff. NFO/FO	NFO: ? FO: ?	Various biochem/immunol/physiol/ psychol. markers, performance	6 wks IT versus normal, 7 days TA	IT: max VO_{2max} ↓, Gln/GgluTA ↓
Nederhof et al., 2008[19]	3 speed skaters ♀	Range:16-19	CS, F	Diff. NFO/FO	NFO: 3-4 months FO : none	RESTQ, POMS, C, ACTH, PRL, GH, RT	2-bout maximal exercise	NFO: ΔACTH at bout 2 ↑, RT↑, mood↓
Meeusen et al., 2010[16]	10 athletes; 8 ♂	Range:17-46	CS, F	Diff.NFO/ OTS	NFO: 3 (5) months OTS: 29 (36) months	C, ACTH, PRL,GH, Lac	2-bout maximal exercise	OTS: max.L↓, rest C/ACTH/PRL ↑ NFO: ΔACTH/PRL at bout 2 ↑

*time to recover used in diagnosis; ()= including pre-visit symptoms period; ?=not known

Abbreviations: Population/Age/Research type/Results: N=number, CL=controlled, IT= intensified training
Research type: CS=cross-sectional, F=follow-up, R=randomized, Tr=trial/intervention
Study objectives/Recovery period/Results: Diff=difference, FO= functional overreaching, NFO=non-functional overreaching, OTS=overtraining syndrome
Main parameters/Results: ACTH=adrenocorticotrophic hormone, C=cortisol, GH=growth hormone, Lac=lactate, POMS=profile of mood states, PRL=prolactin, RESTQ= recovery stress questionnaire, RT= reaction time, T=testosterone
Instruments/Results: Gln/Gglu=glutamine/glutamate ratio, max VO_{2max} =maximal oxygen uptake, TA=taper

After 2006, some studies on the overtraining process focused on the new concept of NFO. Table 5.2 summarizes all recent studies on NFO published after the position statement on prevention, diagnosis and treatment of OTS [15] without presenting any inclusion or exclusion criteria. The studies will be evaluated on possible new predictive parameters.

Moore and Fry[17] studied NFO by introducing an overload period lasting for 9 weeks (pre-season). At the end of the overload period, no differences were found with pre-overload performance levels or cortisol levels and cortisol/testosterone ratios. The only difference was a reduced serum testosterone level immediately after the overload period. However, the testosterone levels were normalized within two weeks after ending the overload period. A consecutive four-week period with normal training showed no changes in hormone levels. The lack of a decrease in performance rules out a NFO state at the end of the overload period. We conclude that this study does not provide sufficient evidence that the participants reached a state of NFO.

In the study by Coutts et al.[2] performance improved after a six-week overload phase on the parameters $VO_{2\ max}$ and vertical jump. All rugby players recovered within a week after the period of overload. All post-taper measurements were at least equal to pre-overload measurements. However, a reduced glutamine/glutamate ratio in blood, obtained immediately after a six-week overload period, may be a promising characteristic of the NFO state. Nevertheless, we conclude that this study typically describes the profile of FO athletes, and not of NFO athletes.

Nederhof et al.[19] described differences between one healthy female athlete and two female athletes suffering from NFO or recovering from NFO. Both NFO athletes were characterized by sufficient durations of performance decrement and long-lasting signs and symptoms (SAS), as they did not recover 'within a few days or weeks' (similar to the model in Meeusen et al[15]). It should be noted that the maximal duration of SAS in NFO in this study was set at one year, theoretically indicating that OTS should be present only if the SAS and performance decrement last for more than one year. Nederhof et al.[19] suggested elevated serum ACTH levels after the second maximal exercise in a two-bout exercise protocol to be a hallmark in NFO athletes when compared to the healthy control athlete. However, with only 3 subjects in this study, any interpretation of the data is open to debate.

Meeusen et al.[16] shifted the focus to differences between NFO and OTS athletes. Thus, no information was provided about parameters that could distinguish FO athletes from NFO athletes. Nevertheless, serum ACTH and prolactin responses to a second maximal exercise in a two-bout exercise protocol were more obvious in NFO athletes than in OTS athletes. Meeusen et al.[16] interpreted the boundaries of NFO and OTS in a similar way as in the study of Nederhof et al. [19]. Consequently, any athlete who suffered from a serious performance decrement with sign or symptoms, which causes a loss of an entire year or season, should now be classified as suffering from NFO instead of suffering from OTS.

FOCUS OF CHAPTERS 6, 7 AND 8

Comparable to the studies on OR/OTS before 2006, the methods used in the four studies on NFO (Table 5.2) relied on short periods of overload training and on cross-sectional instruments in clinical settings with retrospectively obtained data from small samples. They shared a univariate approach. Such methods are not able to study the natural changes that take place when athletes find themselves trapped in the overtraining process. In addition, as the parameters used in studies on FO/NFO/OTS are part of complex psychological, endocrine, physiological, metabolic, or neurological systems, it is obvious that a focus on the (inter)relationship between various parameters from different regulatory systems is lacking. We again conclude that no scientific evidence has been provided to qualify any parameter as having diagnostic properties of NFO.

Therefore, in the second half of this thesis the focus is on three aspects:

- multivariate testing using the relationship between potentially predictive parameters of OR from different regulatory systems (Chapter 6)
- multivariate testing, using the relationship between potentially predictive parameters of NFO within a single regulatory system (Chapters 7, 8)
- prospective methods to identify NFO in a natural environment with the usual time course without a specific intervention (Chapters 7, 8)

As an example, the study by Meeusen et al.[6] concluded that the sensitivity of resting serum ACTH and cortisol levels was too low to differentiate between NFO and OTS athletes. Considering a simplified model of the HPA-axis in Figure 5.2, it is clear that an interaction between ACTH and cortisol exists: ACTH levels directly stimulate the production of cortisol, which then suppresses the ACTH production directly and indirectly by means of a negative feedback to the pituitary and the hypothalamus. Therefore, to differentiate between athletes, an interaction effect between ACTH and cortisol (i.e., a multivariate approach) must be evaluated instead of separately testing the sensitivity of ACTH and cortisol.

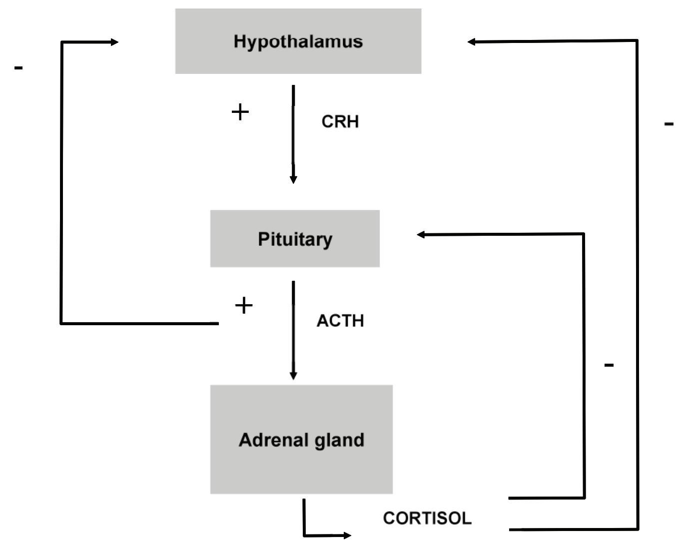

Figure 5.2 Production and control of corticotropin-releasing hormone (CRH), adrenocorticotropic hormone (ACTH) and cortisol.

A multivariate approach is the central theme in Chapter 6. In a large number of elite athletes, potential markers of OR were used to define a multivariate model that could be used to distinguish underperforming athletes from controls.

In the Chapters 7 and 8 the focus is on prospective methods. To monitor the onset of NFO in the studies of Chapters 7 and 8 we strictly interpreted the 2006 model, described in figure 5,1, by using a one-month boundary of SAS between NFO athletes and healthy controls (or FO athletes). Using the one-month inclusion criterion of reduced performance to distinguish NFO from FO athletes, mood profiles and hormonal parameters (ACTH, cortisol) at rest and after a two-bout exercise protocol [15,16, 20] were measured in a cohort of elite athletes. Multivariate aspects of mood differences, as well as their connection to the hormones, were measured. In Chapter 8, resting brain activity as measured by electroencephalography (EEG), as well as free (salivary) cortisol levels were used in an explorative study to evaluate their potential contribution to distinguish between NFO athletes and control.

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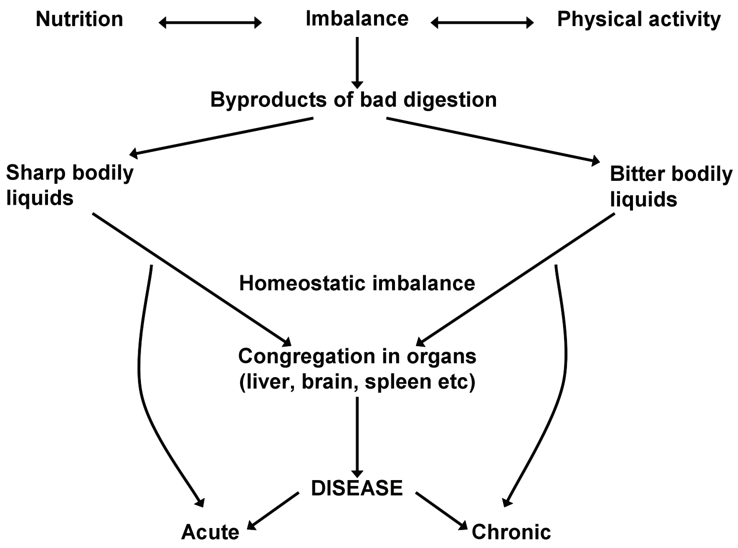
The first sports physician

Herodicus was a physician of Selybria or Selymbria in Thrace who lived in the fifth century B.C. He worked as a doctor-physician and dietician. However, he started his professional career as a gymnastics trainer. In those days, physicians were not allowed to enter a gymnasium. But as a trainer he was, and this enabled him to learn the role of physical exercise and diet to protect health. By combining both disciplines, sports and medicine, he is considered the first sports physician ever.

Herodicus developed a theory about diet and exercise. Food would not be properly digested when consumed without corresponding physical activity. Improper digestion would lead to by-products, which generated two different 'bodily liquids': a sharp and a bitter. As shown in the figure below, he explained this as the basics of homeostatic imbalance. The imbalance explained why chronic and acute diseases occurred.



Herodicus was a firm believer of his own theory, and his behaviour resembled his principles. He was a disciplined athlete, and restricted himself to a sober diet. Rigid as he was in his methods, so he was with his advice to patients. The diets were 'unpleasant', as one of his pupils Hippocrates wrote in Rhetorica: ''Many men are in good health, for example Herodicus, but no one would congratulate them on their health, because they abstain from all or most human pleasures.''

Ironically, Herodicus was also accused of having killed some of his patients because of excessive exercise: ''Herodicus have killed fever patients by running exercises, many bouts of wrestling and vapour baths.''

In the next Chapter, data from elite athletes who were treated by our modern- day sports physicians, were analysed to find a multivariate explanation of an imbalance between load and recovery as a cause of underperformance.

Chapter 6

Prediction of subjectively rated performance capacity in elite male endurance-, interval- and resistance exercise athletes

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ABSTRACT

Introduction: Overreaching is marked by a deteriorated performance without a clear aetiology. Until now, no definite set of parameters identifying overreaching is known.

Aim of the study: To develop a multivariate factorial model derived from single measurements of Hb, Ht, red blood cell count (RBC), ferritin, cortisol (C), cortisol-binding protein (CBG), testosterone (T), sex hormone-binding protein (SHBG), free C (FC) and free T (FT), that is capable of classifying male athletes with or without a performance drop.

Methods: From 78 healthy elite male athletes (mean age: 25.4 yrs, range 17-34 yrs), who were involved in different endurance, interval and high intensity sports, venous blood was sampled under resting conditions for measurements of Hb, Ht, RBC, ferritin, C, CBG, T, SHBG, FC and FT (cross-sectional design). In addition, the athletes were asked to rate their performance capacity (PC), training work load, injury free status, and feelings of general well being during the week preceding blood sampling. Misfits of the model, defined by serious over- or underestimations of the data, were used to predict a low PC.

Results: Three independent factors could describe the O_2 transport capacity and anabolic/catabolic activity. These factors explained 84% of the total variance in all parameters. Overestimation of SHBG levels and underestimation of Ht levels coincided with low PC ratings (R^2= 0.48). Inclusion of Hb to the regression model increased R^2 to 0.55.

Conclusions: The internal consistency of the selected parameters from a composite group of athletes was sufficient to construct a three-factorial model. This model could be used to classify elite male athletes with or without a performance drop. The model should be tested in prospective studies on it’s predictive power of overreaching-related performance decrements.

INTRODUCTION

Studies in athletes with the aim of finding diagnostic parameters of overreaching/overtraining have suffered from poor statistical power and evidence. This is mainly caused by the relatively small number of athletes with overtraining, the fact that signs and symptoms of overreaching/overtraining vary considerably between individuals and definitions of overreaching/overtraining have changed over time[1]. Moreover, regarding the potential markers of overreaching/overtraining, Halson and Jeukendrup[2] concluded that nearly every marker was based on small studies that have induced overreaching but not overtraining. In practical sense, this implies that sports physicians and scientists are mainly dealing with markers of overreaching rather than markers of overtraining. These markers consist of a wide range of biochemical, haematological, psychological and hormonal parameters[3,4-22]. In almost all cases, associations with overreaching/overtraining were based on univariate regression or anecdotal evidence[3, 9,10,18,20,21,23]. Because relatively large inter-individual variations in many overreaching/overtraining-related parameters have been found[4,5,7,10,11,17,19-23], it is not likely that such an approach will lead to strong predictive markers.

Assuming that overreaching is potentially a pre-stage or reversible first stage of overtraining[1,2,9,24], and sports physicians are dealing mainly with athletes suffering from overreaching, our major concern as scientists should be the state of overreaching. As Dal Monte[25] stated: *“Failure on the part of athletes and coaches to recognise overreaching can lead, as a direct consequence of a poor competitive performance, to an inappropriate increase in the training loads, which, rather than sustaining the intended performance improvement can actually result in the onset of overtraining”.* Various authors have used a training or exercise continuum, ranging from under- to overtraining, to explain how training load is associated with overreaching/overtraining and as a result, to deteriorated performances[1]. Using this continuum, a recent consensus statement on the diagnosis of overtraining syndrome has defined functional (FO) and a non-functional phase (NFO) in overreaching[26], both preceding the state of overtraining (OTS). Furthermore, the statement contains a myriad of possible markers of OTS, based on the principles that absolute values of these markers or changes in the processes associated with these markers might identify OTS in athletes. Compared to OTS, NFO is characterised by a shorter duration of the performance decrement and less severe symptoms. This implies, that identifying athletes at high-risk for overreaching (NFO) in time, may prevent a further deterioration into OTS.

Thus, the goal of this study is to find patterns of markers that discriminate athletes with a performance decrease associated with the NFO state from athletes without any performance decrease.

Haematological and hormonal parameters of elite male athletes who visited our hospital for a regular health screening, were used to study patterns of potential markers. The patterns were defined by means of a multi factorial model, basically describing the relationship between the parameters in healthy athletes. Then we hypothesized that serious statistical misfits of the model–thus not adequately representing the original values of these parameters - indicated the existence of deviating regulatory mechanisms in these athletes.

Assuming that such misfits were not symptomatic to any random error of the model, the model was tested by its potency to predict a reduced performance capacity. Regarding the mixture of sport activities of our athletes, a single test to objectively assess performance capacity could not be applied. Therefore, we quantified this performance capacity by means of a subjective rating, based on its validity in monitoring exercise tolerance.

MATERIAL AND METHODS

Subjects

We analysed a database of 78 healthy male elite athletes (mean age: 25.4 yrs, range 17-34 yrs; mean height: 178 cm, range 165-197cm; mean body weight: 77 kg, range 60-95 kg), who visited our hospital for the first time. The athletes came to our hospital for various reasons, such as monitoring baseline levels before the competition season, seasonal evaluation, participation in research programs, or occasionally previous injury-related complaints. Athletes with prevalent injuries were excluded from the study. The athletes were involved in different high performance sports at national and international levels. Forty-four athletes (56%) participated in endurance and long distance sports, mainly track and field, ice speed skating and cycling. Sixteen athletes (21%) participated in sports activities with a duration between 2 and 6 min, such as middle-distance track and field, ice skating and cycling. Twelve athletes (15%) were active in short distance track and field and short time power sports, such as sprinting and weight lifting. Finally, six athletes (8%) participated in interval sports, such as tennis or badminton. All subjects signed an informed consent before inclusion, and institutional review board approval was obtained for this study.

Blood sampling

Under resting conditions, venous blood was collected into K_3EDTA tubes between 8.00-9.00 hr a.m. after an overnight fast. At the previous day subjects refrained from intensive training. As part of our clinical evaluation protocol a selected number of haematological and hormonal parameters were measured. Blood for hormone measurements was immediately centrifuged (3000 RPM, 20 min at 4°C) and stored at -20°C until assayed within 4 wk. Hemoglobin (Hb) was measured by HiCN-method, hematocrit (Ht) by micromethod, red blood cell count (RBC) by coulter counter, and ferritin by immunometric assay. Serum cortisol (C) was measured by fluorescence polarization assay, cortisol-binding protein (CBG) and testosterone (T) by radio immuno assay (RIA), and sex hormone-binding protein (SHBG) by immunoradiometric assay (IRMA). Albumin was determined by immunochemical method to calculate free cortisol (FC) and free testosterone (FT) according to a mass action formulation model. FC was calculated from total C, albumin, CBG, and the association constants of the protein-cortisol complex, and FT according to Vermeulen et al. (27). The intra- and inter-assay coefficients of variation for all analyses were less than 10%.

Ratings

Subjects were asked to rate performance capacity (PC) with performance capacity: 1 = a very low performance (i.e., "not at all in a good shape") and 5 = an optimum performance (i.e., "in a very good shape"). Similarly, they rated training workload (TL), injury free status (IS) and feelings of general well being (WB) on a five-point scale (Likert technique (28)) during the week preceding the blood sampling. Low scores were related to problems and high scores to optimum conditions.

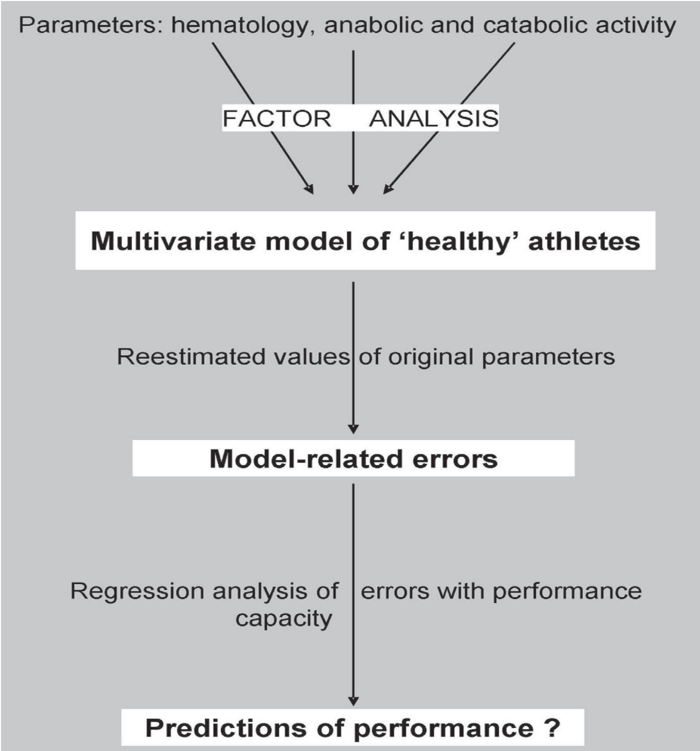

Figure 6.1 A step-by-step description of the data analysis

Statistical analysis

Statistical analyses were carried out using SPSS for Windows Release 11.5. Mean values ± SD for blood parameters were calculated. Normality of distribution was examined using Kolmogorov-Smirnov statistics and a Lilliefors test. We used a Principal Component Factor Analysis with Varimax Rotation to extract independent factors from these parameters[29]. The number of independent factors was based on eigenvalues larger than 1. To assess how well the model fitted the data, we required a minimum goodness-of-fit (R^2) of 70%, independent of the number of factors. Factor loadings of parameters represent the magnitude of the correlations between relevant parameters and the extracted factors. Each factor was represented by factor scores, indicating the impact of each factor on an individual athlete. These scores were used to reproduce the original blood levels by a multivariate linear regression technique. The residuals ($X_{original}$-$X_{predicted\ by\ factor\ scores}$) were used to identify athletes with an extreme misfit of the model, defined by cases in which residuals represented one of the 5 largest over- or underestimations by the model. As a result, for each original parameter ten (2x5) athletes could be marked as "deviated". Under-and overestimation were then saved into binary variables, with “deviated” athletes labeled as '1' and others as ‘0'. Finally, univariate regression and analysis of variance, as well as multivariate regression were used to test the link with PC. Statistical significance was defined as P ≤5%. A step-by-step description of the data analysis is shown in Figure 6.1.

RESULTS

Univariate analysis of blood- and performance-related parameters

The values of the parameters (Table 6.1) showed a normal distribution. A correlation matrix between these parameters is shown in Table 6.2. Within three distinct sets of parameters, strong correlations were found 1) Hb, Ht, RBC; 2) T, FT, SHBG; and 3) C, FC. CBG did not correlate with any parameter. Table 6.3 shows a correlation matrix of the performance-related parameters obtained using a Likert scale. Regarding these relationships, a decreased performance capacity will appear in a number of cases in athletes with previous injury-related complaints, loss of well being, or a reduction in training volume and intensity.

Table 6.1 Obtained values of blood-related parameters from a database of 78 male elite athletes.

	MEAN ± SD
Hb (mmol/l)	9.4 ± 0.6
Ht (l/l)	**0.45 ± 0.03**
RBC ($x10^{12}$/l)	5.0 ± 0.4
Ferritin (ng/ml)	**127 ± 77**
C (μmol/l)	0.39 ± 0.12
CBG (mg/l)	**47.0 ± 10.4**
FC (nmol/l)	20.7 ± 10.5
T (nmol/l)	**23.6 ± 7.4**
SHBG (nmol/l)	38.0 ± 12.7
FT (pmol/l)	**510 ± 154**

Hb=hemoglobin; Ht= hematocrit; RBC= red blood cell count; C= cortisol; CBG=cortisol-binding protein; FC= Free cortisol; T= testosterone; SHBG= sex hormone-binding protein; FT= Free testosterone

Table 6.2 Correlation matrix (Pearson's correlation coefficient R) of blood-related parameters in male athletes (N=78).

	Hb	Ht	RBC	FERRITIN	C	CBG	FC	T	SHBG	FT
Hb		.91**	.80**	.09	.03	-.12	.08	.17	-.17	.28*
Ht			.84**	.06	.05	-.02	.07	.12	-.18	.22
RBC				.00	.02	-.08	.05	.21	-.12	.29*
FERRITIN					-.07	.12	-.11	.25*	.18	.23*
C						.11	.88**	-.01	.07	-.13
CBG							-.28*	-.18	-.08	-.18
FC								.07	.05	.10
T									.51**	.88**
SHBG										.07

*** significant at P < 0.01 (2-tailed)*
**   significant at P < 0.05 (2-tailed)*
For abbreviations, see legends Table 6.1

Table 6.3 Correlation matrix (Pearson's correlation coefficient R) of feelings of well being, injury free status, training workload, and performance capacity in male elite athletes (N=78).*

	WELL BEING	INJURY FREE STATUS	TRAINING WORKLOAD	PERFORMANCE CAPACITY
Well Being		.53	.35	.55
Injury Free Status			.54	.56
Training workload				.44

**all correlations are significant at P<0.001, except for the correlation between Well being and Training workload at P< 0.01.*

Multivariate factorial analysis

Using all parameters from Table 6.2 the Principal Component Factor Analysis extracted a maximum of three independent factors, representing O_2 transport capacity in blood, anabolic activity and catabolic activity. Ferritin and CBG levels did not fit in this three-factorial model very well, and the model did not reach the minimum required goodness-of-fit of 70%. After removal of ferritin and CBG levels from the analysis, a new three-factorial model could explain 84% of the total variance. The first factor, covering Oxygen Transport Capacity, explained 37% of the variance (eigenvalue=3). The second factor, covering anabolic activity, explained another 24% of the variance (eigenvalue=1.9). The last factor, related to catabolic activity, explained the remaining 23% (eigenvalue=1.8). Cumulative variances for parameters explained by the three factors (communalities) are shown in the last column of Table 6.4. Factor loadings of parameters are shown in the middle three columns of Table 6.4. Apart from the moderate loading of SHBG on the anabolic activity-related factor, factor loadings were high (≥ 0.82). For example, a factor loading of 0.91 for RBC indicated that the O_2 transport capacity-related factor explained 83% (= 0.91^2) of the variance in RBC. Because the cumulative explained variance in RBC was 84%, the remaining anabolic and catabolic activity-related factors could only contribute 1% to the variance of RBC (84-83%).

Table 6.4 Factor loadings of relevant parameters, and cumulative variance explained by three factors for all parameters separately (N=78).

	O2 TRANSPORT CAPACITY	ANABOLIC ACTIVITY	CATABOLIC ACTIVITY	CUMULATIVE VARIANCE (%)*
Ht	.96			92
Hb	.95			90
RBC	.91			84
T		.99		99
FT		.82		77
SHBG		.62		45
C			.97	94
FC			.97	94

** R^2 explained by the three-factorial model*

Prediction of PC :Univariate

From all haematological and hormonal parameters used in the study, only Hb levels showed a significant positive Pearson's correlation with PC (R=0.24; P<0.05). A non-parametric Spearman rank correlation revealed small but significant positive correlations of Hb and SHBG levels with PC (R=0.24; P<0.05 and R=0.23; P<0.05). An analysis of variance on these parameters showed mean differences between PC groups on T and FT levels, with highest values in both the lowest and highest PC group.

Such an analysis also showed that a model-overestimation of SHBG levels ($R = -.43$, $F = 16.9$; $P<0.001$), as well as a model-underestimation of FT levels ($R = -0.29$, $F=6.9$; $P<0.01$) were significantly related to PC. Therefore, if the factorial model either predicted higher levels of SHBG or lower levels of FT than actually found, a lower than average PC was found. Additionally, four athletes with underestimated FT levels also belonged to a group of five athletes with overestimated SHBG levels ($\chi2=48.2$; DF =1; $P<0.001$). In latter group, the average FT-level (734 pmol/l) was about 48% higher than that in the athletes without overestimated SHBG levels ($t=-3.6$; $P<0.001$, Mann-Whitney test: $U=53.0$; $P<0.05$).

Prediction of PC: Multivariate

The upper panel of Table 6.5 showed that PC was associated with a combination of an overestimation of both SHBG and Ht levels. The proportion of the explained variation (R^2) was 0.48 ($F=11.5$; $P<0.001$). After inclusion of the original Hb levels (in mmol/l) in the regression model, the proportion of the explained variance increased to 0.55 ($F=10.6$; $P<0.001$, lower panel of Table 6.5). Based on these results, the following regression equation could be obtained, in which the constant (–1.4) was no longer significant:

Performance Capacity = -1.6 – (2.2 x overestimation SHBG) + (1.2 x overestimation Ht) + 0.5 x Hb

Table 6.5 Regression model of subjective performance capacity (PC) without (top) and with inclusion of Hb (bottom).

PARAMETER	REGRESSION COEFFICIENT	SIGNIFICANCE
Constant	3.1	P<0.001
Overestimated SHBG*	-2.2	P<0.001
Overestimated Ht*	1.1	P<0.05
Constant	-1.4	non-significant
Overestimated SHBG*	-2.2	P<0.001
Overestimated Ht*	1.2	P<0.01
Hb**	0.5	P<0.01

** Overestimated SHBG and Ht as binary parameters: 1 = overestimated, 0 = non-overestimated, Performance Capacity PC ranges from 1-5*
***Hb in mmol/l*

DISCUSSION

In this study in a composite group of elite male athletes, data of haematological and hormonal parameters were considered suitable for developing a three factorial model that could adequately describe deviating parameters. We hypothesize that athletes with an extreme misfitting to the model may represent a group with deviating regulatory mechanisms. This study has shown that such a misfitting can be used to classify elite male athletes with or without a subjectively rated performance drop; hence supporting the concept that subjectively rated underperformance does seem to have a real physiological background. Because a reduced performance capacity is a key symptom in overreaching, this result may help to develop a toolkit that identifies athletes at a high-risk of overreaching.

Regarding the mixture of sport activities of our athletes, we have chosen to quantify their PC by rating. Kenntä & Hassmén[32] postulated that 'a physical effort is best conceptualized as a complex psychobiological construct'. Such a construct validates the use of ratings, such as the rating of perceived exertion (RPE), as a valuable and reliable indicator in monitoring an individual's exercise tolerance[33]. The observed associations between the scores of the rated parameters (see Table 6.3) showed that a reduced PC may coincide with an impact on the athlete's well being and may not always represent a 'minor issue'. This supports the construct validity of the scores, and the concept that underperformance is related to more problems than purely physical overload only. Unfortunately, because of the retrospective character of the data, it was impossible to describe the nature of the reduced performance as e.g. injury- or disease-related, or simply due to voluntary undertraining. Of course, future studies have to address further the validity and reliability of the PC-scores by comparing those scores with more objective data, as obtained by field or laboratory tests.

Three-factorial model and PC

The data used in the factorial analysis can be considered as representative for elite male athletes involved in various endurance, interval and high intensity sports, as the average values of the selected parameters were consistent with data obtained from the literature[1,4-6,8,9,13,14,18,19,21-26,30,31].

The three-factorial model is very robust. The internal consistency of the selected parameters was more than sufficient to construct this model, with factors explaining 84% of the total variance in all parameters. However, regarding the anabolic activity-related factor, SHBG data fitted only moderately. This was as expected because FT levels were not correlated with SHBG levels, although T levels correlated with SHBG levels (Table 6.2). This suggests that the underlying construct of this factor did not cover the typical function of SHBG, being binding of T and controlling FT. Similar conclusions could be drawn for the data of CBG. As CBG data did not fit into the model, the catabolic activity-related factor only represented C and FC levels. Therefore, both factors seem to point at constructs that describe net hormone levels that are based on the balance between production and degradation, rather than the dynamic status of hormones with feedback mechanisms.

The interaction of an overestimated SHBG with high T and FT values in the prediction of PC posed the question how androgen levels respond to training and overtraining. Fry et al.[34] studied a group of weight-trained athletes during an overtraining period and compared them with controls. They found no significant drop in FT after an overtraining period. They also concluded that SHBG levels simply followed the changes in T levels, implying that FT and SHBG levels were not related to each other. This is a similar result as we obtained from our factorial model based on a cross-sectional sample. However, the lack of a correlation between SHBG and FT could be expected because of the highly non-linear relation between both[35]. A simple linear correlation between SHBG and FT is also obscured by a feedback loop at the pituitary level. The pituitary increases LH (luteinizing hormone) as a reaction to increasing SHBG levels. This effectively stimulates the testes to produce more T [36]. Reviews also confirmed the lack of proof for decreased androgen levels in overreaching or overtraining [1,2]. Recently, a prospective study with middle-aged to older men following a 12-month aerobic exercise program again did not show any change in androgens[37]. However, a recent cross-sectional study by Maïmoun et al.[38] showed that endurance athletes had reduced T levels compared to controls. Another prospective study by Safarinejad et al.[39] showed similar results. Finally, a prospective study on the effects of aerobic training by Grandys et al.[40] revealed that improved local muscle endurance after a 5-week training period coincided with increased T, decreased SHBG, and of course, increased FT levels. But in spite of a drop in average SHBG levels, the highest increases in T and FT levels were achieved in athletes who had the highest SHBG levels . They reported no linear relation between performance and T or FT levels. In our study, we also did not find a linear correlation between performance and T or FT levels, but indeed a correlation between performance and SHBG levels.

This intriguing similarity between the results of the intervention study of Grandys et al.[40] and our cross-sectional study triggered us to verify the reason for a lack of a relationship between performance and T or FT levels in our data. One should keep in mind that the study of Grandys et al.[40] used an objective performance index, whereas our study used a subjective one. In our study a highly overestimated SHBG-level coincided with the lowest PC rating. SHBG-levels in the overestimated group were significantly lower, and showed a narrower range compared to the non-overestimated group (mean SHBG: 27.2 versus 38.7 nmol/l; range: 21-33 versus 14-71 nmol/l, respectively). Although average T levels were not significantly different between the groups, the overestimated group again showed a narrower range in T than the non-overestimated SHBG group (range: 19-36 versus 10-42 nmol/l, respectively). However, FT levels were 1.5 times higher in the overestimated group ($F=13$ $P<0.01$), and the range was also smaller than in the non-overestimated group. Such a finding makes it tempting to suggest that in the SHBG-overestimated group with poorly rated performances, FT levels were highest of all. But such an interpretation is not correct, because FT levels in the non-overestimated group with a maximal performance rating (PC=5) were equally high. A similar pattern was found in T. Therefore, the average T and FT levels showed a type of U-shaped curve with performance, and no linear relationship. This may also explain why Glandys et al.[40] only reported a positive correlation between SHBG levels and performance, but not between T or FT levels and performance.

Our results suggest that there was simply less SHBG available to bind T in the overestimated SHBG group with a poor performance rating. This caused relatively high FT levels. In the non-overestimated SHBG group with the highest PC values, absolute levels of T were highest. However, these athletes also had more SHBG to bind T compared to athletes in the overestimated SHBG group. This resulted in marginally lower FT levels in the non-overestimated SHBG group compared to the overestimated SHBG group with the lowest performance rating.

There maybe several reasons why androgen studies in athletes have revealed more or less conflicting results. In our study, both low and high performance athletes showed similarly high FT levels, but different T/SHBG ratios. More importantly, a direct comparison of androgen levels between different studies is very difficult, because methods to obtain T and SHBG, as well as methods to measure or calculate FT vary substantially between studies[35,36].

Multivariate regression analysis revealed that an underestimated Ht *(low predicted values of Ht compared to the actual levels)* was linked with a relatively low PC. The blood viscosity is relatively high in those cases, which may limit the blood flow to the muscles. Monitoring of Ht has been mentioned as an important factor in early detection of overtraining in elite sportsmen[5]. It should be noted that both RBC and Hb levels were not significantly different in the overestimated and non-overestimated Ht-group. The inclusion of Hb in the regression model as a positive predictor of PC is in line with the experience that low levels of Hb, indicating a low binding capacity for O_2, may contribute to a low PC.

In summary, a relatively low PC was predicted if 1) FT levels were high because SHBG levels were relatively low, 2) lower than actual levels of Ht were predicted by the model, and 3) low Hb levels were found.

CONCLUSIONS

A multi-factorial model in healthy male elite athletes that describes the regulatory systems of O_2 transport in blood, the anabolic and catabolic activity, appears to provide sufficient information to detect those athletes who might not be 'in good shape' according to their misfit to the model. The strongest misfits, associated with parameters of O_2 transport and anabolic activity, were capable of predicting a subjectively rated low performance capacity. However, the cross-sectional design of this study demands that the predictive power of this multivariate model approach must also be studied prospectively, before its application can be helpful for the early detection of overreaching. Finally, additional parameters, such as insulin or IGF-1, must be explored to improve the potency of the factorial model further.

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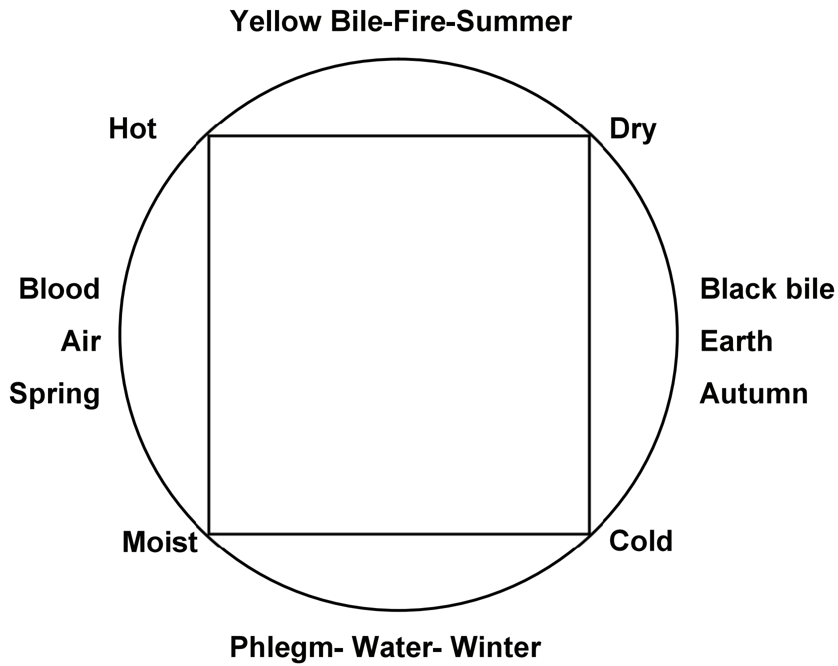
Four humors

Mood has been linked to the functioning of the body for ages. In the fourth century BC, the ancient Greeks believed human health was based on the balance between four liquids (humors). The liquids were black bile, yellow bile, phlegm and blood. An imbalance between the fluids occurred if any of the fluids dominated, causing health problems specific to the dominating fluid. This is clearly a more elaborate approach compared to the older concept by Herodicus, but compatible to concepts of health in other cultures during that time. Interestingly, the fluids are also associated with behavioural characteristics. Blood was connected to amorous and courageous behaviour. Black bile was thought to cause a depressed mood and insomnia. On the other hand, a dominance of yellow bile caused irritability, anger, aggression and dominance. Phlegm however was associated to a lack of emotion, calmness and pragmatic or cowardly behaviour. This concept has been altered to a certain extent by Galen (131-201 AD), but it remained the fundaments of medicine and psychology until 1858 when Rudolf Virchow's published his theories of cellular pathology.
Today, we are still searching for the 'bodily fluids' that are associated to our health. In the next chapter, hormones as the 'modern liquids' and mood are used to distinguish between adolescents with and without an unexpected decrease in elite athletic performance.



Chapter 7

Can we detect non-functional overreaching in young elite soccer players and middle-long distance runners using field performance tests?

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ABSTRACT

Objective: To study whether field performance tests can make a valid distinction between non-functionally overreached (NFO) athletes and control athletes.

Design: Monthly field performance tests were used to determine a performance decrement throughout a season. Athletes with a minimum of one month performance decrement (PD) were compared with control athletes without a performance decrement on mood characteristics and resting levels of stress hormones.

Setting: Sporting field and sports medical laboratory.

Participants: 129 young elite athletes, 77 soccer players and 52 middle-long distance runners, were followed prospectively during the 2006-2007 season. Fifteen of them were invited to the laboratory. Eight athletes showed a performance decrease lasting longer than one month and seven athletes without a performance decrease acted as their controls.

Main outcome measures: Performance changes over time were measured using field tests. Profile of mood states and resting levels of adrenocorticotrophic hormone (ACTH) and cortisol in blood were measured in the laboratory.

Results: PD athletes showed several symptoms typical of the non-functional state of overreaching. The PD group scored higher on depression and anger than controls. They also showed a specific pattern of correlations between negative mood subscales (Tension, Fatigue and Depression), which was absent in controls. ACTH levels at rest were similar, but lower cortisol levels in PD athletes pointed at a blunted cortisol response. Only in PD athletes cortisol levels were decoupled from ACTH levels.

Conclusions: Implementing performance-related criteria in field tests can help coaches and sports physicians to distinguish NFO-athletes from athletes with balanced workload and recovery.

INTRODUCTION

According to the consensus statement of the European College of Sport Science (ECSS) on the prevention, diagnosis and treatment of the overtraining syndrome (OTS) a gold standard for diagnosis of this syndrome is still lacking[1]. The statement characterizes OTS as long-term performance decrease with a multi factorial etiology in athletes. The statement comes with a checklist that does provide a diagnosis per exclusionem. Similar to previous checklists[2,3], it helps physicians to determine whether or not athletes might suffer from OTS and exclude other possible causes of a long-term underperformance.

The ECSS statement defines the term “overtraining” as a process of intensified training that may result in short-term or functional overreaching (FO), non-functional overreaching (NFO) or OTS. The distinction between FO and NFO is based on the duration of the symptoms until performance returns to normal levels. Recovery to normal performances should incur within days to weeks in FO, whereas in NFO it may take several weeks to months. OTS will last several months or years. As a consequence, a follow-up of athletes is necessary to finalize the diagnosis per exclusionem.

The estimated incidence of OTS is low to moderate[4-6]. Simply inducing OTS for research purposes is however ethically unacceptable for many reasons. Thus, many studies attempting to explore the early signs of the overtraining process rely on inducing a state of overreaching by means of short periods of intensified training. Such studies, however, rarely match the normal situation of athletes. In addition, many studies have been conducted without a proper indication of performance changes as an outcome[7]. Cross-sectional studies focussing on the diagnostic parameters of OTS, generally include samples of athletes from sports medical clinics where athletes suffering from overtraining have a high representation[8-11]. These studies do not reveal any information about the early development of overtraining because the focus of these studies is on the end stages of the process. Longitudinal studies within sports environments to evaluate the onset of the overtraining process by monitoring training load and performances, combined with cross-sectional case-control studies to identify markers of overtraining are scarce. Consequently, only experience-based, non-specific and open-ended advice to coaches can be provided by monitoring physical performances, mood, training load and diseases[1,2,3].

Despite the process of intensified training, performance will only improve if both excessive overload and incomplete recovery are avoided. Within the process that initiates a general state of overreaching (OR), athletes and coaches will most likely stress the importance of an unwanted transition from a state of functional overreaching (FO) into a state of non-functional overreaching (NFO). The latter state is characterised by performance decrements, and psychological and hormonal disturbances[1,7].Hypothalamic-pituitary-adrenal (HPA)-axis related plasma levels of ACTH and cortisol, as well as GH levels have been shown to be reduced in overreaching[12-15]. Ronsen et al.[14] and Meeusen et al.[15] developed double maximal physical exercise tests that could differentiate between responses of these hormones in healthy and overtrained athletes. It would be of great help to sports physicians, coaches and athletes if a field monitor validated by these parameters could identify the onset of the overtraining process.

Although the time to recover from a performance drop is a key criterion to help distinguishing FO- athletes from NFO-athletes, the duration of this time frame is an element of constant debate[16]. Based on the assumptions in the model introduced by Meeusen et al.[1], we hypothesize that the transition from FO to NFO will take place if the underperformance period exceeds the duration of one month. Therefore, we tested cross-sectionally if such a performance decrement in young elite athletes (PD athletes hereafter) marks the onset of additional symptoms typical to the non-functional state of overreaching, i.e., deteriorated mood and altered hormone profiles.

METHODS

Subjects

Out of 77 young elite soccer players (mean age: 16.5 years, range 15-18 years) and 52 young elite middle and long distance runners (mean age: 17 years, range 16-21 years), 15 athletes (8 PD athletes and 7 controls) were included in this study during the 2006/2007 season. Selection of these athletes during one competitive season took place on a monthly basis, using performance changes measured in sport-specific field tests. PD-athletes were invited to the laboratory if they showed a persistent performance decrease lasting at least one month, i.e. measured at two consecutive field tests. Control athletes were invited to the testing laboratory if they did not show a performance decrease for at least one month. The study was approved by the Dutch Central Committee on Research Ethics involving Human Subjects (CCMO). All participants, and both parents if participants were younger than 18 years of age, provided written informed consent.

Field Performance tests: *Interval Shuttle Run Test for soccer players*

To determine performance in soccer players, a submaximal Interval Shuttle Run Test (ISRT) was used[17,18]. During the entire season submaximal intensity was set at 70% of the maximal number of runs achieved at the start of the season. An elevated heart rate response indicated a state of overreaching[3,19]. During the outdoor ISRT's, players alternately ran for 30 seconds and walked for 15 seconds. Running speed increased from 10 $km \cdot h^{-1}$ every 90 seconds up to 15 $km \cdot h^{-1}$ depending on baseline maximal running performance. Heart rate (in $b \cdot min^{-1}$) was recorded at 5-s intervals (Polar, Kempele, Finland; Suunto, Vantaa, Finland). The tests were performed every month at the start of a training session as a substitute for the warm-up.

Atletes with an elevated heart rate response of ≥ 5 $b \cdot min^{-1}$ [20], and a relative heart rate increase of at least 5% persisting for at least one month (and measured at consecutive field tests) were included as overreaching related[3,19] performance decreased athletes (PD athletes).

Field Performance tests: Zoladz Test for runners

The Zoladz test proved to be a reliable and valid method of measuring performance capacity in track and field[21]. During the test, athletes ran for 6-minute in 4 heart rate zones (zones 4, 3, 2, and 1 at respectively 20, 30, 40 and 50 $b \cdot min^{-1}$ below maximal heart rate). Maximal heart rate was determined using an all-out 400 meter run at the start of the season. Between the 6-minute runs, subjects walked for two minutes. The total distance in each zone was measured[21], but for further analysis the distance obtained in submaximal zone 3 was used. To include track and field PD athletes similar to the method used in soccer players, a runner's performance had to drop a minimum of 5% at two consecutive (monthly) tests compared with a previous test[22].

Profile of Mood States

Validity and reliability of a Dutch translation of the original 65-item, 6 subscales version of the POMS has been evaluated in a previous study [23]. Participants respond on a 5-point Likert scale ranging from 0 (not at all) to 4 (extremely).This validated version contains 32 items and 5 subscales: "Tension", "Depression", "Anger", "Fatigue" and "Vigor". The five-factor model again showed to be adequate. In a second study, the one-factor model (Total Mood Score) was rejected[24]. Hence, in this study we used the shortened version of the POMS, consisting of 5 subscales and 32 items. The POMS was administered to subjects in the laboratory before lunchtime (11.30-12.30 h).

Hormones

At least two hours after a standardized meal (approximately 71% CHO, 19% protein, 10% fat), that was planned between 11.00 AM and 12.00 AM**,** blood samples were drawn under resting conditions in supine position from an antecubital vein in Dickinson vacutainer tubes (Becton Dickinson, Franklin Lakes, NJ, USA). SSTII tubes were used for cortisol, and K2E EDTA tubes for ACTH. Samples were immediately stored on ice and transported to the hospital for subsequent analysis. Plasma cortisol levels were determined by radio-immuno-assay and plasma ACTH levels by chemiluminescence-immuno-assay.

Statistical Analyses

Statistical analyses were performed with SPSS 16 (SPSS Inc., Chicago, IL). Differences in mood scores and hormone levels between PD and control athletes were tested using ANOVA. Pearson's correlation coefficients (R) were used to verify the coherence between the mood subscale scores, and to test the linear relationship between ACTH and cortisol, i.e., the coupling of ACTH to cortisol levels. Because of the small numbers of participants, non-parametric equivalents (Mann-Whitney U test and Spearman's rank correlation (*r*) were also applied. The significance level was set at $p < 0.05$.

RESULTS

Subjects and field performance

A total of 8 PD athletes were invited to the laboratory: one long distance runner and seven soccer players (age (years):16.9 ± 1.1, height (cm) 174.6 ± 6.5, body weight (kg) 70.4 ± 6.4, (mean ± SD). The control group consisted of 7 athletes: four middle-long distance runners and three soccer players (age (years): 18.7 ± 1.6, height (cm) 183.0 ± 9.4, body weight (kg) 68.7 ± 6.5 (mean ± SD). Controls were slightly, but significantly older than PD-athletes (Mann-Whitney U=8.5, P=0.023).

PD-soccer players showed an average 6% increase of their submaximal heart rate response (10 b· min^{-1}; S.D.= 5) during the ISRT, compared to their mean reference submaximal heart rate of 172. b· min^{-1}. The PD-long distance runner was tested in heart rate zone 1 instead of zone 3 because of excessive fatigue. He showed an 8% performance decrease in zone 1 (1050 meters at baseline and 970 meters after 2 consecutive monthly tests), compared to a 3% increase in the control runners.

Mood States

The average subscale scores indicated an unfavourable mood state in PD-athletes (Table 7.1). The differences with controls were only significant for Anger (F=12.8, DF=14, P=0.00) and Depression (F=3.0, DF=14, P=.049). This was confirmed non-parametrically (Anger: Mann-Whitney U=5.5, P=0.01, Depression: Mann-Whitney U=10.5, P=0.04).

Table 7.1 Mean scores and mean rank scores of five mood subscales.*

		DEPRESSION	ANGER	FATIGUE	VIGOR	TENSION
Controls (N=7)	Mean	1.3 (5.5)	3.9 (4.8)	3.6 (6.8)	13.1 (7.4)	3.9 (7.2)
	SD	2.6	2.8	3.0	3.2	11.8
PD (N=8)	Mean	6.3** (10.2)	10.3** (10.8)	5.8 (9.1)	12.4 (8.4)	5.4 (8.7)
	SD	7.1	3.9	3.8	2.8	4.8
Total (N=15)	Mean	3.9	7.3	4.7	12.7	4.7
	SD	5.9	4.7	3.5	2.9	3.7

** average mean rank scores between brackets*
***significant difference between OR and controls at P<.05 (non-parametrically)*

The correlations between the five mood states in Table 7.2 are specified by significance or borderline significance. As expected, Fatigue and Vigor were negatively associated in both groups. In the PD-group depression was associated with Fatigue and Tension. Also, Fatigue and Tension correlated highly in the PD-group.

Among the controls Anger, but not Depression, was associated with Fatigue and Tension. In contrast with the PD-group, Fatigue and Tension did not correlate in the control group.

Table 7.2 Pearson's correlation coefficient and Spearman's rank correlation between POMS-scales in PD-athletes** and controls***.*

	DEPRESSION	ANGER	FATIGUE	VIGOR	TENSION
Depression		.43 (.34)	.72+ (.81+)	-.26 (-.24)	.93+ (.94+)
Anger	.39 (.49)		.40 (.19)	.13 (.23)	.39 (.33)
Fatigue	.12 (.14)	.73++(.74++)		-.69++(-.67+++)	.81+ (.81+)
Vigor	-.18 (.00)	-.59 (-.60)	-.78+ (-.74++)		-.30 (-.21)
Tension	.55 (.53)	.63 (.73++)	-.05 (.09)	.03 (-.13)	

+ significant at P=0.05, ++ significant at P=0.06, +++ significant at P=0.07

**Spearman rank correlation between parentheses, ** PD-athletes; N=8, above diagonal, ***Controls; N=7, below diagonal, grey colour*

Table 7.3 Mean levels of ACTH and cortisol (mean rank scores in brackets).

		ACTH (NG/L)	CORTISOL (μMOL/L)
Controls (N=7)	**Mean**	27.0 (9.1)	.35 (10.9)
	SD	16.2	.15
PD (N=8)	**Mean**	20.1 (7.1)	.20 + (5.4)
	SD	10.3	.07
Total (N=15)	**Mean**	23.3	.27
	SD	13.4	.13

+ significant difference between OR and controls at P<0.05

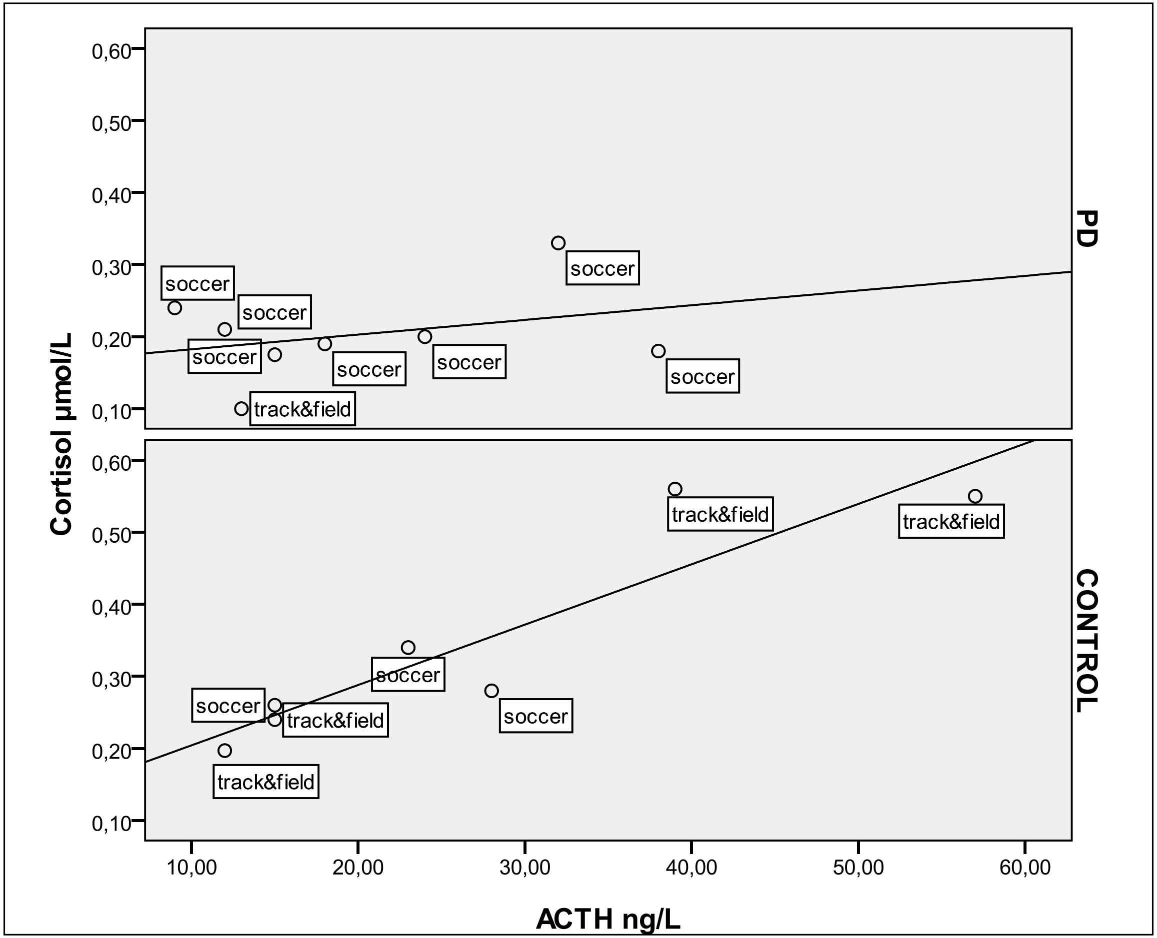

Figure 7.1 The relationship between ACTH and cortisol in PD athletes and control athletes.

Hormones

Table 7.3 shows the hormone levels of the participants. No significant differences in ACTH levels between PD and controls could be found. Only cortisol showed a significant difference between both groups (F= 6.2 P=0.03), with lower values in the PD-group. Non-parametrically tested, this difference was confirmed (Mann-Whitney U=7.5, P=0.01).

Relation between ACTH and cortisol

No significant linear relationship between ACTH and cortisol levels was found in the PD-group (see top part of Figure 7.1), indicating no coupling between the levels of these hormones. In contrast, control athletes showed a linear relationship between both hormones (see bottom part of Figure 7.1). ACTH accounted for 83% of the variance in cortisol (R= 0.91, P=0.00 (2-sided); *r*=0.92, P=0.00 (2-sided)). Even when leaving out the two top right track and field athletes from the control group, the explained variance in cortisol by ACTH was still 81%.

DISCUSSION

In this study, we found that a performance decrease in young elite athletes of at least one month coincided with a worse mood state, and lower resting cortisol levels in blood being decoupled from ACTH levels.

We used sports-specific field testing as key indicators of a structural performance drop in athletes. The ISRT [17,18] is based on the interval performance resembling the physical workload in soccer with frequent acceleration and short but frequent periods of (relative) rest. The sports- Zoladz test[21] mainly relies on aerobic performances with the ability to recover from a steadily increasing work load that is typical for middle-long distance runners. To evaluate performance changes we tested at a submaximal level. Testing at submaximal level greatly increased support from the coaches to facilitate ISRT or Zoladz tests because the tests were less time consuming and did not interfere with the intensity and training frequency of up to 6 times a week in both sports. Submaximal field tests could however have been one of the explanations for the small number of players included with performance decrements because such tests are considered as less sensitive to performance changes than maximal tests[7]. Furthermore several athletes suffering from a performance drop of at least one month could not participate in the laboratory study because of international matches, test matches, school exams and injuries. With some athletes a performance decrement could not be confirmed a second time because the coaches sent them on leave to recover from fatigue and poor performance. Unfortunately, small numbers of subjects in overtraining and overreaching studies are not uncommon[10,11,25-28].

The POMS has been used in many studies to monitor mood state in athletes, and several reviews have reported consistent results[3,7,29]. In the taper-study by Hooper et al.[30] high scores on the subscales Depression, Tension, Anger, and Fatigue measured with the extended

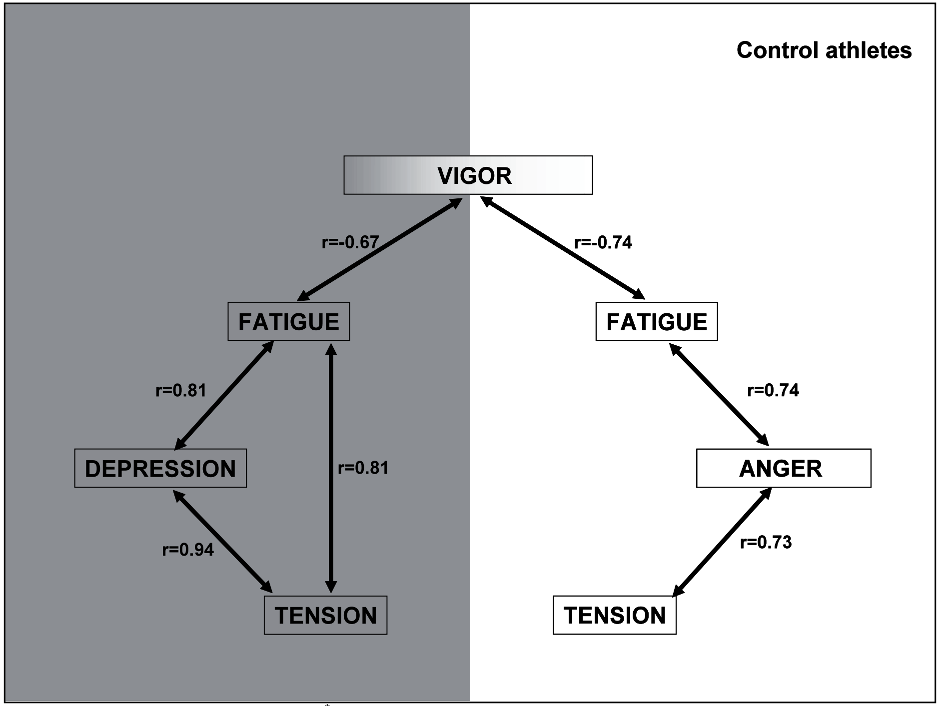

Figure 7.2. Spearman rank correlations * *between POMS subscales in PD-athletes and control athletes.*
** Non-significant Spearman rank correlations from Table 6.2 are ommited from this figure.*

version of the POMS[31] were considered as markers of "staleness" (a synonym for overreaching or overtraining). Halson et al.[32] found a clear increase of the total mood score of the POMS- 65 (the extended variant of the POMS) with the introduction of a two week intensified training period, and subsequently, a drop after two weeks of recovery. However, mood state could be worsened during overload phases without leading to a performance decrement[33-35]. Consequently, in overreaching and overtraining research the use of the POMS should be combined with performance assessment[7].

We also observed a worse mood state in PD-athletes compared to controls, as shown by significantly higher anger and depression scores (Table 7.1). Nuissier et al.[36] reported a 5 times higher anger score and a 8 times higher depression score in physical education students with the highest negative mood scores than their colleagues with the lowest negative mood scores. Therefore, although statistically significant, the differences in mood scores between our PD- and control athletes were not as dramatic as seen in other studies.

Our study is unique in using the coherence of the different mood subscale scores to distinguish PD-athletes from controls. Based on the concept of the POMS it is expected that the subscales Anger, Depression and Tension share a common factor with fatigue. This common factor contrasts with the subscale Vigor. Thus, a negative correlation between Fatigue and Vigor could be expected. Such a correlation was present in controls and PD-athletes, although in the latter group it was borderline significant only (see Table 7.2). Anger and Depression not only scored higher in the PD group compared to controls, they also seemed to be the starting point in a cluster of associations typical to either PD-athletes or controls (Figure 7.2). This creates psychological profiles of both groups, seemingly mirrored yet very distinct if, among other things, we consider the lack of an association between tension and fatigue in controls.

As ACTH levels in PD-athletes did not differ from ACTH levels in controls, the lower levels of cortisol in the PD-subjects may indicate a blunted response to ACTH stimulation. Handziski et al.[37] studied ACTH and cortisol profiles in 30 elite soccer players during a six weeks preparation period, prior to the start of the season. This period is considered as physically the most demanding one, and coincides with a high injury risk[38]. Despite the fact that our PD-athletes were well advanced into the season, the general hormone levels resembled that of athletes shortly after the 6 weeks heavy overload phase in the Handziski-study[37].

The blunted response to ACTH resulting in low resting levels of cortisol in the PD-group has not been observed in previous studies with overreached athletes[39-41]. Nevertheless, Schnyder et al.[42] reported lower resting levels of cortisol level in endurance athletes (cyclists) after a short period of intensified training, although a generally reduced performance was not found. Urhausen et al.[13] also reported reduced cortisol levels in short term overtrained athletes, with a markedly reduced performance.

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The diurnal rhythm of cortisol parallels the release of ACTH from the anterior pituitary. Both physical and mental stress increase the release of ACTH and consequently, will lead to higher levels of cortisol. In healthy subjects, ACTH and cortisol are correlated positively[43], but in depressed patients this correlation is non-existent[44]. In a study on high and low risk alcoholism, the low risk group showed a high correlation between ACTH and cortisol, whereas ACTH and cortisol showed a decoupling because both hormones were not correlated in the high risk group[45]. Decoupling of cortisol and ACTH levels in our PD-athletes was found as well (see figure 7.1). The decoupling was not dominated by soccer players, nor did the two extreme track and field athletes have a decisive influence on the strong correlation between ACTH and cortisol in controls. We also checked if the type of sports had a decisive overall effect on the decoupling phenomena. Without any of the track and field athletes and after adding 11 soccer players without a performance decrease from the same study population but tested during the 2007-2008 season, we analyzed 14 soccer players in the control group and the remaining 7 PD-soccer players. Again, in the control group ACTH correlated significantly with cortisol ($R= 0.72$, $P=0.00$ (2-sided); $r=0.75$, $P=0.00$ (2-sided)). No correlation was observed in the PD-soccer players. Evidently, our data are not suited to fully explain at which level of the HPA-axis the decoupling of ACTH and cortisol originates. But we hypothesize that a reduced overall sensitivity of the adrenal cortex to ACTH is the most likely explanation.

Considering the mood and hormonal differences between the control and PD-athletes, we postulate that characteristics of PD-athletes adequately fit the description of non-functionally overreached (NFO) athletes as described by Meeusen et al.[1]. Compared to athletes without a lengthy performance drop (controls), we found higher levels of anger and depression in athletes with an underperformance period exceeding the duration of one month. Depression scores were associated with fatigue and tension scores. In the underperforming athletes, cortisol levels were reduced and decoupled from ACTH levels. These results support the assumption that field performance tests can be useful in distinguishing non-functionally overreached (NFO) athletes from athletes with a proper load and recovery balance, thereby preventing athletes from developing the overtraining syndrome (OTS).

What is already known on this topic

Recently, non-functional overreaching (NFO) was presented as the pre-stage of the overtraining syndrome. In contrast with athletes characterized by functional overload symptoms and temporary performance decrements, NFO athletes share prolonged periods of reduced performance, psychological distress and hormonal disturbances. No screening instruments for NFO are available in the sports practice.

What this study adds

Repeated field performance tests showed that a prolonged reduction of performance coincided with worsened mood scores, different mood profiles, a blunted cortisol response and a decoupling of ACTH to cortisol levels. Field performance tests may develop into valid screening instruments of NFO in athletes.

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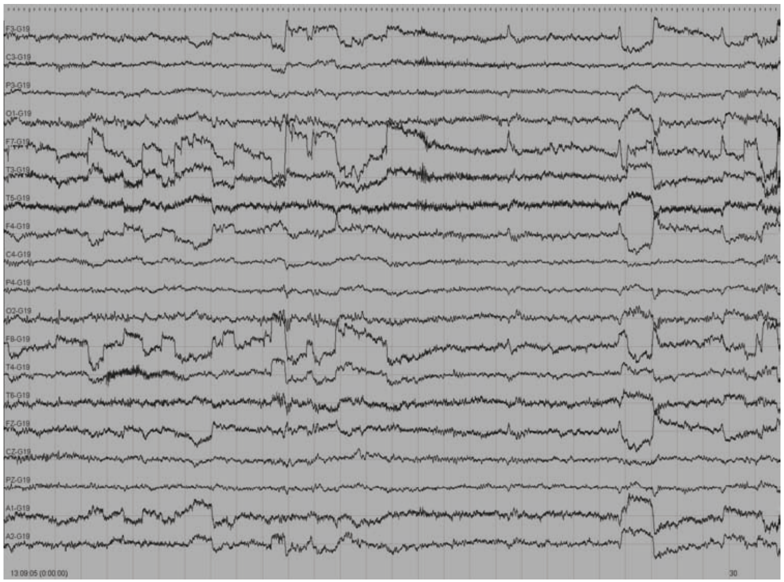
Brain activity

In 2003, on the Aegean Island of Chios archaeologists discovered evidence going back to 250 BC of a successfully performed procedure called 'trepanning' - a process that involves carefully drilling into the brain. Ancient Greek traditions prohibited physicians to open up a human body for further study. Thus, although they were able to perform very complex and dangerous operations on the human skull, many Greek physicians were unaware of what was underneath it.

In the sixth century BC, Pythagoras suggested: "the brain served as the organ of the mind and the temple of the soul". However, this view was not supported throughout the Ancient Greek history. Aristotle, a Greek philosopher and a former student of Plato, considered the center of intelligence and emotion to be in the heart. This was in agreement with the view of Hebrew and Chinese philosophers. The brain was considered merely as a cooling device of human blood. This view was more or less adopted by Galen in the second century AD.

It took a Flemish anatomist Andreas Vesalius to break the spell of these old believes in 1543 AD. After Descartes' mistake about the function of pineal gland with the human brain 300 years ago, scientists rapidly gained more knowledge about the anatomy and functions of the brain. In 1920, the physiologist and psychiatrist Hans Berger studied the human EEG. The term EEG stands for electroencephalography, which is the measurement at the scalp of electrical activity caused by firing of neurons within the brain, and therefore associated to the activity of brain that is close to the skull.



This technique of EEG is used in the study presented in the next chapter. In the attempt to link young elite athletes with a status associated with a reduced performance, fatigue and poor mood, they were subject to measurements of stress hormones and EEG (see electroencephalogram on the left).

Chapter 8

EEG and cortisol: markers of non-functional Overreaching?

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ABSTRACT

The aim of this study was to verify if under resting conditions F3-P4 EEG coherence (EC) in the α and β frequency domains correlated negatively with free cortisol (FC) in non-functionally overreached (NFO) athletes and healthy controls. This negative correlation was observed previously in healthy non-athletic subjects. EC represents an index of neural network communication in cortical brain areas. In a prospective study, 8 NFO athletes and 7 healthy control athletes were included. Salivary free cortisol (FC) levels as well as EC values in the θ, α, β frequency domains with electrodes on positions F3, F4, P3, and P4 were obtained. No group difference in FC was found. F3-P4 EC (mean [95% confidence interval]) was lower in NFO: 0.19 [0.14-0.25] versus controls: 0.26 [0.22-0.30], $p=0.02$. In controls a significant negative correlation between α F3-F4 EC and FC was found ($r= -0.76$, $p=0.05$), but in NFO athletes θ F3-F4 EC correlated positively with FC ($r=0.88$, $p=0.00$). It is concluded that EC interacted differently with salivary cortisol levels in elite athletes and healthy non-athletic controls. This interaction also differed between NFO and controls, which may contribute to their distinction in future research.

INTRODUCTION

In 2009, Schneider and colleagues [1] referred to the growing interest in the changes of brain activity as a result of physical exercise. Assuming there was a positive effect of exercise on brain activity and mood, they studied the link between EEG activity and mood as a function of different of exercise intensities. They reported a positive effect on both EEG and mood after a preferred and high intensity exercise. In 2010, physical exercise was shown to lead to an improved mood among men in long-term confinement [2]. The mood improvement again correlated with changes in brain cortical activity.

Studies like these support the general opinion that physical exercise can have profound positive effects on mood, and that these effects may be related to changes in brain activity. Unfortunately, there are always two sides of the coin, meaning that exercise is not always good. The other side of the coin is represented by strenuous exercise described as ‘high intensity and high volume’ followed by insufficient recovery. Such imbalance between physical and mental load and recovery may induce a process called overtraining. This process is characterised by reduced performance levels, severe fatigue, endocrine maladaptation, immune deficiencies and a disturbed mood [3-10]. An underperformance lasting for months or more may eventually develop into a premature career ending. If no disease can be diagnosed explaining the characteristics, then the athlete is considered to suffer from the Overtraining Syndrome (OTS). Such a per exclusionem approach shows many similarities with other fatigue-related health problems like the chronic fatigue syndrome or burnout.

OTS is supposed to be preceded by a state of functional overreaching (FO) and a state of non-functional overreaching (NFO) [8]. Whereas in the former the athlete is able to recover within days without a serious performance drop and other symptoms, the latter state is characterized by a more prolonged loss of performance that may last for several weeks. Fatigue, deteriorated mood such as depression and anger, and first signals of endocrine dysfunctions are common in NFO athletes as well [e.g. 3,5,7,8,11]. Endocrine dysfunction is mainly focussed on hypo- or hyperactivity of the hypothalamic-pituitary-adrenal (HPA)-axis or the sympatho-adreno-medullary (SAM)-axis.

The impact of OTS on athletes explains why prevention of this syndrome is one of the priorities in elite sports. Therefore, monitoring the onset of the symptoms associated to NFO-state is very relevant. Apart from a prolonged performance decrease, depression may be an important symptom in monitoring the process of overtraining [8]. Morgan et al. [9] reported that up to 80% of athletes with OTS showed significantly elevated levels of psychological depression. Recently, we reported elevated depression and anger scores in NFO athletes compared to healthy control athletes [12]. Robson [13] introduced the possibility of sharing etiological pathways in depression and in overtraining, suggesting that interleukin-6 (IL-6) would be involved in both syndromes. IL-6 has been linked to depression in other studies as well, for instance in studies using the arousal theory of depression [14,15]. Armstrong and VanHeest [3] also proposed the shared etiological pathways by presenting an elite long distance runner who suffered from OTS for several years. When treated with fluoxetine, a selective serotonin reuptake inhibitor (SSRI), his mood and running performance improved within days. It is also known that overreached and overtrained athletes often suffer from a lack of concentration and reduced technical skills as well [3,5,6,7,8]. The possible effect of an SSRI on performance and skills was supported by studies of Loubinoux et al. [16] showing the impact of serotonin in the activation of brain motor pathways during specific tasks. These authors explained that performance improvement was a result of increased efficiency in cerebral motor processing. Support for this explanation in athletes was provided by studies that linked functional efficiency of the brain network, as measured by electroencephalogram (EEG) coherences, with intellectual performances and sports specific skills [17,18,19]. EEG coherence (EC) can be interpreted as an electrophysiological method to measure the synchronised activation of groups of neurons and an indicator of information transfer between two parts of the brain [20].

Like the neurotransmitter serotonin, the stress hormone cortisol may be associated to the efficiency of the brain network. Increased cortisol secretion down-regulates serotonin neurotransmission leading to clinical depression in vulnerable subjects [21]. Corticosteroids crossing the blood brain barrier reduced cellular excitability in the brain [22], and it also affected the communication between various parts of human brain [23]. The latter finding received support from a study of Schutter et al. [24]. They showed that even in a group of healthy male and female subjects lower left frontal - right parietal scalp (α and β F3-P4) EC were associated with increased salivary cortisol levels.

In this study, we hypothesized that in the same elite athletes as in our previous study [12] neural network communication under resting conditions and quantified with EC, was reduced in NFO athletes, whereas EC was also negatively associated with salivary cortisol. First, we tested if EC values differed between healthy adolescent athletes and their NFO counterparts. Second, we tested the negative correlation between EC and salivary cortisol in both groups.

MATERIAL AND METHODS

Participants

Out of 77 young male elite soccer players (mean age: 16.5 years, range 15-18 years) and 52 young male elite middle and long distance runners (mean age: 17 years, range 16-21 years), 15 athletes could be included in this study. On the average, soccer players were involved in 5 training sessions per week as well as in one or two matches per week. A single training and match lasted about 1.5 hours, with the exception of the 15-16 year old juniors whose matches lasted 80 minutes. Each week, the elite runners exercised during 6 training sessions, each lasting about 1.5 hours. However, the time spent in competition was much less then in soccer players, because races never took more than an hour and the frequency was less than an average of 2 races per month.

Selection of these athletes during one competitive season (2006/2007) took place on a monthly basis, using performance changes measured in sport-specific field tests. NFO suspected athletes (hereafter NFO athletes) were invited to one of our two laboratories (in Groningen or Utrecht), if they showed a persistent performance decrease lasting at least one month, i.e. measured at two consecutive field tests. Control athletes of identical elite skill level and of similar age were invited to the laboratory if they did not show a performance decrease for at least one month.

The study was approved by the Dutch Central Committee on Research Ethics involving Human Subjects (CCMO). All participants, and both parents if participants were younger than 18 years of age, provided written informed consent.

Procedure

All athletes refrained from exercises at the day of the laboratory measurements. The day prior to the measurements only mild recovery exercises were allowed. Athletes arrived at the laboratory before lunch time. All athletes were medically screened using a per exclusionem diagnostic protocol [8] to exclude diseases that might cause the reduced performances, or hinder the athletes from being tested. At least one hour after having received a standardized meal (approximately 71% CHO, 19% protein, 10% fat), and 10 minutes prior to EEG-measurements saliva was collected for assessment of cortisol levels. Subsequently, athletes were placed in a sound-attenuated testing room and asked to sit quietly, resulting in 2 minutes of visually artifact free baseline eyes closed EEG recordings.

Field Performance tests

a) Interval Shuttle Run Test for soccer players

To determine performance in soccer players, a submaximal Interval Shuttle Run Test (ISRT) was used [25,26]. Submaximal intensity was set at 70% of the maximal number of runs obtained at the start of the season. A fixed number of runs was used for every individual during an entire season assuming that an elevated heart rate response indicated a state of overreaching [3,27]. During the outdoor ISRT's, players alternately ran for 30 seconds and walked for 15 seconds. Running speed increased from 10 $km \cdot h^{-1}$ every 90 seconds up to 15 $km \cdot h^{-1}$ depending on baseline maximal running performance. Heart rate (in $b \cdot min^{-1}$) was recorded at 5-second intervals (Polar, Kempele, Finland; Suunto, Vantaa, Finland). The tests were performed every month at the start of a training session as a substitute for the warm-up.

Since on an individual level the biological variation in heart rate response is 2-4 $b \cdot min^{-1}$ [11]), any player with a change within this range was considered as a control. Only players, who showed an absolute heart rate increase of ≥ 5 $b \cdot min^{-1}$ and a relative heart rate increase of at least 5% during the last run, persisting for at least one month (and measured at two consecutive field tests) were included as NFO players.

b) Zoladz Test for runners

The Zoladz test proved to be a reliable and valid method of measuring performance capacity in track and field [28]. During the test, athletes ran for 6 minutes in 4 submaximal heart rate zones (zones 4, 3, 2, and 1 at respectively 20, 30, 40 and 50 $b \cdot min^{-1}$ below maximal heart rate). Maximal heart rate was determined using an all-out 400 meter run at the start of the season. Between the 6 minute runs, subjects walked for two minutes. The total distance in each zone was measured [28], but for further analysis the distance obtained in heart rate zone 3 was used.

To include track and field NFO runners similar to the method used in soccer players, a runner's performance had to drop a minimum of 5% at two consecutive (monthly) tests compared with a previous test [29].

Salivary Cortisol

At least two hours after the standardized meal and 10 minutes prior to EEG-measurements, 1.0 ml of saliva was collected in a Salivette. Saliva was then stored by -22°C until final analysis. Salivary cortisol concentrations (in nmol/l) were measured without extraction using an in house competitive radio-immunoassay (RIA) employing a polyclonal anti-cortisol antibody (K7348) and [1,2-3H(N)]-Hydrocortisone as a tracer. The lowest limit of detection was 0.5 nmol/l and inter-assay variations were less than 6%.

Electroencephalographic (EEG) recordings

At the laboratory in Groningen EEG was recorded from 19 electrode sites using BrainLab with a sampling rate of 500 Hz. EEG data were online referenced to the average signal of 17 electrodes (F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, O2). In Utrecht, EEG was recorded from 32 electrode sites using the ActiveTwo system (BioSemi, Amsterdam, The Netherlands) or BrainVision Recorder with a sampling rate of 256 Hz or 500 Hz, respectively. The reference electrode was placed on the right mastoid.

EEG analysis

EEG data during the eyes closed condition were analyzed using BrainVision Analyzer software (www.brainproducts.com). EEG data were filtered using a band-pass filter of 1-30 Hz. The sampling-rate was changed to 256 Hz. For the participants in Utrecht, EEG signals were referenced off-line to the average signal of the 17 electrodes similar to the participants in Groningen (see Fig. 8.1). Then, the data were segmented into 4-second epochs. Epochs were rejected from further analyses if data exceeded +/-50 μV. Subsequently, segmented data were Fourier transformed (Hamming window length of 10%). To compute coherence between inter- and intrahemispheric electrode sites (F3-F4; P3-P4; F3-P4; F4-P3), cross-spectra for the different frequency bands (theta (θ), 4-7 Hz; alpha (α), 8-13 Hz; beta (β), 14-30 Hz) were calculated and normalized by the autospectra [30].

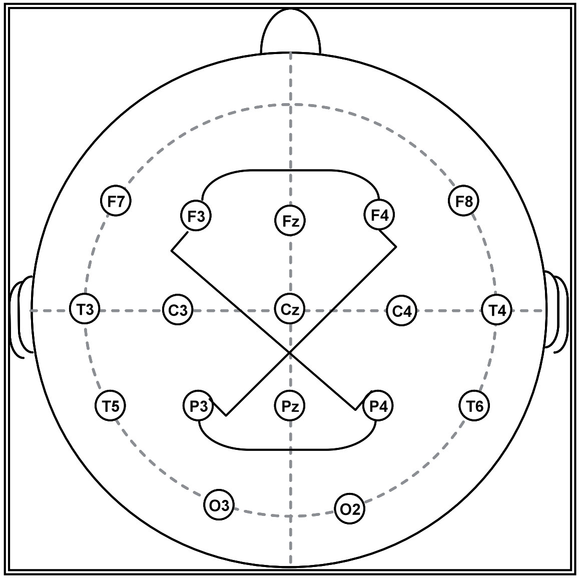

Figure 8.1. Seventeen electrode sites used for the electroencephalogram (EEG) measurements with solid lines between two electrodes selected for the calculated coherences.

Statistics

Statistical analyses were performed with SPSS 16 (SPSS Inc., Chicago, IL). Descriptive statistics of the subjects are presented as mean ± standard deviation.

Group values of parameters used in the statistical tests are presented as a mean and the 95% confidence interval (mean [95% CI]). Group differences were tested using the non-parametric Mann–Whitney U test using exact significances. Non-parametric Spearman rank correlation coefficients (r) were used to test the relation between salivary cortisol and coherence values. The significance level was set at $P < 0.05$.

RESULTS

Subjects

A total of 8 NFO athletes were invited to the laboratory: seven soccer players and one long distance runner (age (years):16.9 ± 1.1, height (cm) 174.6 ± 6.5, body weight (kg) 70.4 ± 6.4). The control group consisted of 7 athletes: three soccer players and four middle-long distance runners (age (years): 18.7 ± 1.6, height (cm) 183.0 ± 9.4, body weight (kg) 68.7 ± 6.5). Controls were slightly, but significantly older than NFO-athletes (Mann-Whitney U=8.5, P=0.02). Age, however, did not correlate with hormone levels and EEG coherence values.

NFO-soccer players showed an average 6% increase of their submaximal heart rate response (10 b· min^{-1}± 5) during the ISRT, compared to their average submaximal heart rate of 172. b· min^{-1}. The NFO-long distance runner was tested in heart rate zone 1 in stead of zone 3 because of excessive fatigue. He showed an 8% performance decrease (1050 meters at baseline and 970 meters after 2 consecutive monthly tests), compared to an average increase of 3% in the control runners.

Group differences on salivary cortisol and coherence

Salivary cortisol levels were not significantly different in both groups (NFO: 6.4 nmol/l [4.0-8.4] versus controls: 8.9 nmol/l [5.1-12.0]).

A significantly lower θ F3-P4 coherence was found in NFO athletes: 0.19 [0.14-0.25] versus controls: 0.26 [0.22-0.30] (Mann-Whitney U=8, P=0.02).

Correlations between coherence and salivary cortisol within groups

In NFO athletes θ F3-F4 coherence correlated positively with salivary cortisol levels (r=0.88, P=0.00, see Fig. 8.2), whereas θ F3-P4 coherence correlated positively with salivary cortisol levels without reaching statistically significance (r=0.67, P=0.07).

In the control group α F3-F4 coherence was negatively correlated with salivary cortisol levels (r= -0.76, P=0.049; see Fig. 8.3). F3-P4, P3-P4 and P3-F4 coherences in the α frequency domain were also negatively correlated with salivary cortisol levels, however, without reaching statistically significance (r= -0.70, P=0.08; r=-0.56, P=0.19; r=-0.45, P=0.31, respectively).

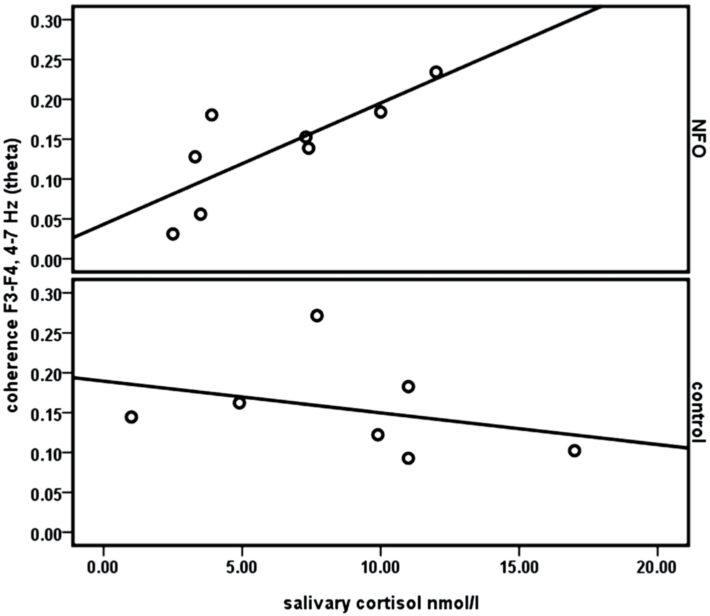

Figure 8.2. Linear relationship between salivary cortisol and θ F3-F4 coherence[*] in eyes closed condition in NFO athletes (N=8) and controls (N=7).

[*] Non-parametric correlations: NFO r=0.88 P=0.00; control r=-0.45 P=0.31

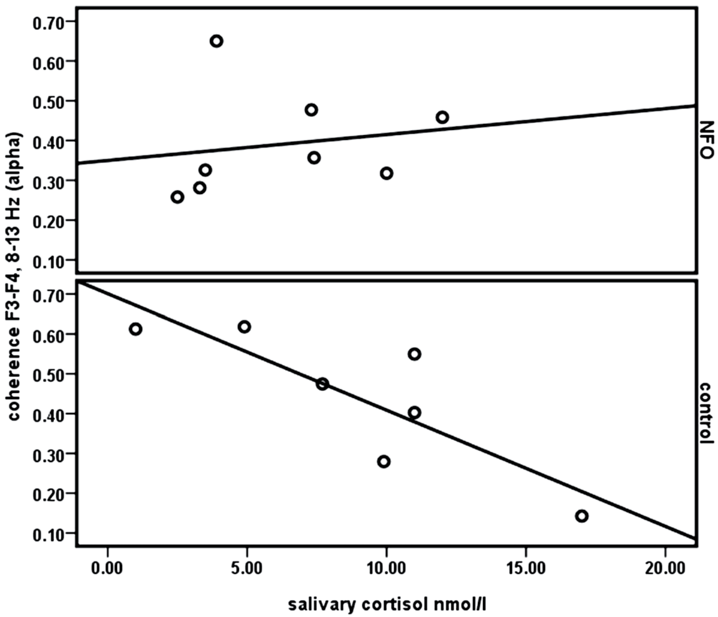

Figure 8.3. Linear relationship between salivary cortisol and α F3-F4 coherence[*] in eyes closed condition in NFO athletes (N=8) and controls (N=7).

[*] Non-parametric correlations: NFO r=0.5 P=0.21; control r=-.0.76 P=0.049

DISCUSSION

Results of this study showed a negative correlation between prefrontal interhemispheric EEG coherence values in the α-band and salivary cortisol levels in healthy controls. However, in NFO athletes prefrontal coherence values in the θ-band correlated positively with salivary cortisol levels (see Fig. 8.2 and 8.3). Furthermore, θ F3-P4 coherence values were significantly lower in NFO athletes compared to controls with similar salivary cortisol levels.

We compared the results in our control athletes with a study of Schutter et al. [24], who reported data of EEG coherences and salivary cortisol in males and healthy females. We could not confirm their observation of negative correlations between α and β F3-P4 coherences with salivary cortisol. The brain regions involved were different (left-right prefrontal in stead of left prefrontal and right parietal). Gender difference might be put forward as a possible explanation for these results. However, salivary cortisol levels at rest did not differ between males and females [24], and no gender differences were found in EEG coherence values in similar age cohorts [31,32]. Another explanation may be linked to the differences in skill status between athletes and non athletes. Possibly, neural network communication patterns in healthy athletes at rest are more efficient than in healthy non-athletic controls. This may be related to skills-specific functional qualities of the brain in athletes as discussed extensively in a review by Yarrow et al. [19]. Some studies using EEG coherence values and power spectra already confirmed the functional difference of synchronized neural network communication between elite athletes and non-athletes or less skilled athletes [17,33]. However, these data were obtained during specific tasks such as balance exercises or rifle shooting, and not during resting conditions as in our study. Therefore, more research is necessary to test if neural network communication in elite athletes under resting conditions differs from non-athletic controls, with the specific task to evaluate if this difference is also reflected in the interaction of neural network communication with stress hormones.

The positive correlation between salivary cortisol and θ F3-F4 coherence in NFO athletes contrasted with the negative correlation of α F3-F4 coherence in our controls. A negative correlation between this stress hormone and neural network communication was also observed in patients with Cushing's syndrome (i.e., chronic excess of glucocorticoids) and explained by increased brain atrophy, and a state of depression [34]. Interestingly, previously we reported increased levels of depression and anger in our group of NFO athletes [12]. But apparently, the premise of a negative correlation between neural network communication and salivary cortisol levels is lacking. No differences in salivary cortisol levels between NFO athletes and controls were found and salivary cortisol levels were too low to be associated with hypercortisolism [35]. We postulate that the mood state of our NFO athletes did not follow the classic pattern of increased levels of salivary cortisol in depression. This is in line with studies showing that several depression-related disorders (major depression, dysthymic-, cyclothymic-, bipolar and unipolar depression) did not coincide with a consistent presence of hypercortisolism [36-39]. Also, hypercortisolism in patients with depression may disappear at a later stage without substantial changes in the depressed mood [40].

Moreover, our NFO–athletes with mild depression scores never gave the impression of being clinically depressed patients. At most they showed a dysthymic mood state.

Maybe even more relevant was the fact that anger scores differentiated much better between NFO and controls than depression scores [12]. We also showed that within the NFO-athletes anger was not associated to depression. Therefore, the depressive mood in NFO athletes was more likely a secondary symptom of long term physical exhaustion. If anger is a dominant feature in our NFO athletes, then a link to prefrontal neural network communication (i.e., F3-F4 coherence) may be expected. Anger is a very strong emotion, and the regulation of emotions is often associated to the activity of prefrontal regions. For instance, negative mood, emotion handling and feelings of disgust have been associated to the F3-F4 frontal activity [41]. To improve motivation and to reduce symptoms in bipolar disorders and depression, patients were treated with neurofeedback training to increase the dominance of α F3-F4 activity [42].

Shibata et al. [43] found that event-related EEG coherence (ErCoh) was very specific in a visual Go-NoGo test, particularly in the θ F3-P4. High θ F3-P4 was associated with a NoGo-decision, whereas a various pairs to F3 and F4 in the α band were associated to the inhibition of the motor cortex. Although not event-related, we showed different associations in NFO-athletes and controls in exactly the same two frequency band-specific coherences with stress hormones: θ F3-P4 increased with stress hormone levels in NFO-athletes, but remained uninfluenced in the controls. This may lead to the hypothesis that increased stress levels could influence the decision taking process after visual cues (for instance, during sports activities) in NFO-athletes, whereas in controls it would not.

To our knowledge, this is the first study that focussed on the connection between endocrine adaptations and actual measurements of neural network communication in the overtraining process. Given the small number of subjects we prefer to present our results as explorative and indicative. For this reason we decided not to apply type 1 error corrections for multiple comparisons (Bonferroni or Sidak correction). We conclude that there is no pattern of generally reduced coherences (between F3, F4, P3 and P4) in NFO athletes. Only θ F3-P4 coherence was reduced in NFO athletes, which is in line with observations of Davidson et al. [44]. We also did not find a generalized, negative correlation between coherence levels and free cortisol in either two groups. The high correlations, found between free cortisol and θ or α F3-F4, in NFO-athletes and controls respectively, need to be reproduced and clarified. Possibly, this will help us we to find specific patterns of neural network communication, typical for well-trained, healthy athletes that are susceptible for the process of overtraining.

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The battle

In this thesis, the battle against injuries and overtraining is a major topic in modern sports. But nowadays, many other battles are fought. Apart from the violent ones that kill too many people, we for instance are also fighting the modern diseases caused by an inactive lifestyle. Ironically, sports is supposed to bring people together and serves as tool against inactivity. Although we must except that the damage in sports will never be fully 'out of the game', the next chapter rounds up what could be learned from a number of studies about the battle against sports injuries and overtraining.

Sports, however, is also a battle. It is a battle against your opponents and against yourself, but also against the circumstances and the rules of the game. This is actually the beauty of sports.

Chapter 9

General discussion and recommendations

FOCUS

The objective of this thesis was to provide additional knowledge and tools, which can contribute to adequate prevention of the physical and psychological damage caused by local injuries and overtraining as a result of sports participation.
The thesis addresses two hypotheses:
1) Target groups for sports injury prevention can be derived from data acquired with a nationwide, retrospective survey.
2) In young elite athletes, non-functional overreaching (NFO), which is considered an early stage in the process that may lead to the overtraining syndrome (OTS), can be recognized by a set of distinctive parameters.

The first part of this thesis (Chapters 2-4) focuses on topic 1: aiming to define target groups for the prevention of local injuries based on their contribution to the extent and severity of the sports injury problem in the Netherlands. These investigations and analyses were aimed at quantitative support of the policies of the Dutch government and various sports organizations.
In the second part of this thesis, the aim was to supply tools for preventing OTS. Currently, the damage in sports due to systemic overuse leading to NFO or OTS, suffers from a lack of proper diagnostic tools. Therefore, Chapters 5-8 focus on the search for practical diagnostic parameters to distinguish NFO athletes from healthy control athletes, as well as possible explanations for the ongoing process of overtraining.

TARGET GROUPS FOR INJURY PREVENTION

A general analysis

Because sports participation is considered a relatively inexpensive instrument, the Ministry of Health, Welfare and Sports (Dutch Ministry of VWS) promotes sports participation to achieve a healthy lifestyle. This includes the promotion of ‘low-risk sports’ and physical activities in order to obtain maximum health benefits [31,32]. However, some sport activities are not characterized by a low risk of injury. Therefore, to enhance the net health benefit in sports, prevention of sports injuries has become an additional and important goal.
This thesis aims at facilitating the prevention of damage in sports. Amongst others, it describes topics an approach to select specific sports activities that are most eligible for sports injury prevention campaigns. As shown in Chapter 2, the method of selection relies on a combination of the absolute contribution of a sports activity to all sports injuries and the incidence rate (injuries per 10,000 hours of sports participation). Sport activities with a large impact on sports injuries were then further selected based on their contribution to medically-treated injuries within age and gender-specific cohorts. We concluded that for sports participants under 55 years of age (both males and females), target groups for injury prevention programs in the Netherlands could be restricted to a total of nine sport activities: outdoor and indoor soccer, tennis, running/jogging, skiing/snowboarding, field hockey, gymnastics, volleyball, and equestrian (see Chapter 2, IPAN

data). In the Netherlands, indoor/outdoor soccer with the largest number of participants in any competitive and organized team sport, certainly has the most significant impact with regard to all sports injuries (see Chapter 2). Similar to soccer in the Netherlands, in New Zealand rugby is by far the biggest contributor to sports injuries[10], as 'Australian Rules Football' is in Australia[7].

In 2002, Chalmers wrote[9]: "*From a 'public health' perspective we might be interested in the most common injuries, the most severe, the most debilitating, or the most costly*". Our method of selection of target groups for injury prevention is a combination of some of the public health arguments he mentioned, but with an emphasis on the necessity of medical treatment. Less emphasis is put on the relative risk of an injury (e.g. incidence rates). Any perspective, whether that from policymakers in public health, from physicians in public health, from national sports organizations, or from individual sports participants, will inevitably lead to some specific preferences in the target list of sports for injury prevention. Such a list is also likely to vary if the sources of data change, for instance, from a general survey to a registration system of emergency room (ER) treatments in hospitals. The Dutch Factsheet on sports injuries[11] defines severity of injuries by the number of ER treatments and all estimated costs due to treatment at the ER or hospitalization. With severity as a significant argument to put specific sports on a target list, mountain biking and cycling were both placed on the Consumer Safety Institute target list for injury prevention in the Netherlands. However, the estimated costs used to calculate these severity statistics covered 'only' 40% of the total costs associated with sports injuries[11]. This, of course, limits the validity of the used severity arguments. Based on the IPAN data, the participants selected from the nine Dutch sports in specific age and gender cohorts, were responsible for 66% of all sports injuries, as well as for more than 2/3 of the estimated direct and indirect costs associated with sports injuries. This illustrates why an IPAN 'public health' approach is more justifiable for development of central government policies on sports injury prevention than any system with a restricted coverage of sports injuries.

Male soccer players as target group

In the Netherlands, outdoor soccer makes the largest contribution to all sports injuries (28%, see Chapter 2, Table 2.3). With males under 35 years of age (juniors and seniors) as a target group for sports injury prevention in general, a further refinement to specific target groups for injury prevention in outdoor soccer was presented in Chapter 3. Male junior and, in particular senior, soccer players active in the highest age-specific amateur competition levels were defined as the most important target groups (see Chapter 3).

RISK FACTORS AND PREVENTION

IPAN and risk factor

The IPAN survey collects data on multiple injury-related topics, but it is not designed to evaluate risk factors. Without any information about the prevalence of risk factors among non-injured players, the impact of risk factors cannot be quantified. An extensive review by

Bahr and Krosshaug[5] on risk factors in general stresses the role of three major components in the occurrence of injuries: intrinsic risk factors, extrinsic risk factors, and injury mechanisms (inciting events). Some injury mechanisms, such as physical contact (56% of the injuries) and reinjuries (19% of the injuries) were discussed in Chapter 3, but particularly in cases of reinjury the IPAN survey does not provide sufficient details for further analysis. In Chapter 3, age, gender and skill level (the latter judged from the time spent on training and matches per week) were used as intrinsic risk factors. Other intrinsic risk factors (such as anatomy, psychological factors or previous injuries) were unknown and could not be used. The IPAN survey also registered some external factors, such as the use of protective equipment. Unfortunately, data on protective equipment were available in only 25% of the uninjured players, and the validity and reliability of these data must be treated with caution.

Risk factors in soccer injuries

Prospective studies on risk factors in soccer have reported on the issue of reinjuries[2,3,17]. From a preventive perspective, the history of a current injury can be considered as an internal risk factor[5]. The link between history and a current injury is often sought in terms of an incomplete rehabilitation. Controlled rehabilitation has been subject to studies for injury prevention in general. According to Hägglund et al.[21], the reinjury risk in soccer players could be reduced by 66% after a controlled rehabilitation program. Their program, implemented by coaches, showed the largest preventive effect within the first week of the return to play. However, the intervention group was confronted with an increased number of ‘new injuries’, and the seasonal incidence rate of injuries in this group did not differ from the control group. The authors provided an explanation for the relatively high overall incidence rate in the intervention group. They suggested an increased awareness by coaches of both injuries and complaints, which presumably resulted in a relatively large total number of new sports injuries in the intervention group compared to the control group. However, the impact of the relatively poor compliance (68%) to the program remains unknown. Moreover, there may be other explanations for the identical overall injury rates and the number of injuries in both groups.

First, an incomplete recovery itself cannot be the cause of a reinjury. Residual pain, articular limitations, and specifically swelling can be associated with incomplete rehabilitation. However, the occurrence of a (re)injury at least requires an initiating factor or inciting event[5]. The intervention does not influence the inciting events. For example, with a previous ankle inversion, without adequate rehabilitation an uneven surface may enhance the risk of a new inversion trauma. But when properly healed, such an impact may lead to a different injury, e.g. a knee distortion. In other words, with a similar number of inciting events in the control and intervention group, the intervention only causes a redistribution from old to other new injuries with the same players.

Second, after sustaining an initial injury, players from the intervention group will stay out of match play for a longer period than those in the control group. This increases the likelihood in the intervention group that matches are played by players other than those who have been previously uninjured. Automatically, if the substitute player sustains an injury, it is also increasingly likely that their injuries will not be a reinjury. Both alternative explanations may have caused the shift from reinjuries to non-reinjuries (or new injuries) in the experimental group. More research is needed to evaluate the practical importance of controlled rehabilitation programs.

Location-specific prophylactic programs in soccer

Several prevention programs in soccer addressed the most frequently affected body locations, being the knee, ankle and hamstrings. Prevention of ankle and knee distortions has been achieved with specific programs focusing on stability training or neuromuscular control training ([8,18,33,35]). Kraemer and Knobloch[27] reported positive effects of a balance-training program in the prevention of hamstring injuries and tendinopathy in elite female soccer players. Similarly, the prevention of hamstring injuries using eccentric strength exercises was successful in male elite Icelandic and Norwegian soccer players[4].

However, the reported results of a general prophylactic program in soccer that combines these specific types of exercises into one program (e.g., F-MARC bricks, a forerunner of “The 11”) are not yet convincing. Some moderate results of this program were observed in male youth soccer players[25], but neither a reduction in the overall injury risk nor any specific reduction in ankle and knee distortions could be observed in young female soccer players[44].

Compliance and prevention

An injury prevention program called “The 11” suffered from a relatively poor compliance (52% at team level[44]). A revised version of “The 11” (The 11+, a comprehensive warm-up program) in young female Norwegian soccer players showed an improved compliance (77% at team level) and a reduced injury risk. The improved compliance was explained by the increased variety of exercises in the program[43]. Interestingly, an ongoing controlled trial conducted by our department with the original version of “The 11” (i.e., without an increased variety of exercises) resulted in similar first-year team compliance scores (75%; unpublished data) in male Dutch amateur soccer players with a high skill level. The question then arises, whether the variety of the content of the program influences compliance considerably.

Of course, gender difference as well as an age difference between participants may also play a role in compliance. But more possibilities exist. In the Norwegian trial, compliance was highly correlated with total training and match exposure time[43]. Exposure time was three times higher in the high compliance teams than in the low compliance teams. Because the total exposure time increases with the skill level, these results suggested that high compliance teams actually played at higher levels than low compliance teams. An average intervention effect of the program was shown earlier[42]. Their take-home message - i.e. that soccer players with a relatively high compliance to the program would suffer from fewer injuries - may be flawed by an alternative explanation, namely that this type of program works in soccer at higher skill levels but not at lower levels.

Apparently, we should be aware that in prophylactic methods there is no ‘one size fits all’ strategy: certain methods may work in one cohort but not in another. The effectiveness of such a method may in fact be different in identical, or almost identical cohorts (e.g. same level, same age, same sports) from different countries. This may be associated with different internal and external risk factors influencing the occurrence of injuries. This underlines the importance of testing prophylactic programs before implementation is on the agenda. With limited resources available, this also explains why the central topic in Chapters 2 and 3 is important: to first define target groups for injury prevention.

Nevertheless, a systematic lack of compliance may kill any preventive program. According to Soligard et al.[43], 57% of the football coaches had never conducted any injury preventive training sessions before the start of that specific intervention study. Furthermore, 75% of the coaches participating in the Norwegian study were only inclined to apply an injury prevention training session because others told them to do so. If a similar attitude would be found among Dutch soccer coaches, the introduction of strategies to prevent injuries as an integral part of the educational program of coaches could be effective. However, it also implies that implementation of prevention programs should be optimized [see Finch[19]: TRIPP stage 5 or Van Tiggelen et al.[54]: step 6].

SPORTS INJURY SURVEYS: PITFALLS AND LIMITATIONS

No method to define the injury prevention target list with cohorts of sports participants will be flawless. This is well illustrated by the fact that the IPAN “public health” perspective did not include basketball on the list. Despite the fact that in the Netherlands basketball has the second highest incidence rate (32.0 injuries per 10,000 hours, see Chapter 2, Table 2.3), it failed to appear as a top-3 injury sport within the investigated age and gender cohorts (see Chapter 2, Table 2.4). Overall, 25% of the basketball injuries occurred during physical education at school. Moreover, with an estimated 75% of all basketball players getting injured, male junior basketball players are responsible for more than half of all basketball-related injuries. Based on these data, we recommend that basketball players, and specifically male junior players, should be included in the target list for injury prevention.

Another pitfall may be the fact that sports participants aged over 55 years are completely omitted from the target list. With increasing numbers of Dutch elderly participating in sports (from 374,000 55+ participants in 1986/1987 to 1,190,000 in 2002/2003 [38,39]) injuries will become an increasing problem in this cohort. The rising number of elderly participating in sports is not only a Dutch trend. Ueblacker et al.[47] reported a comparable trend among the elderly in Germany, and there is no specific reason to believe that this trend will be different in other West European countries. In addition, as cardiac risks are known to occur more often among the elderly[13,29,46], an increasing number of sudden cardiac deaths in this population may be expected, unless sufficient medical attention is paid to this group of sports participants. Inevitably, such ‘medical attention’ requires a study on the sports-related cardiovascular risk factors in the specific elderly population.

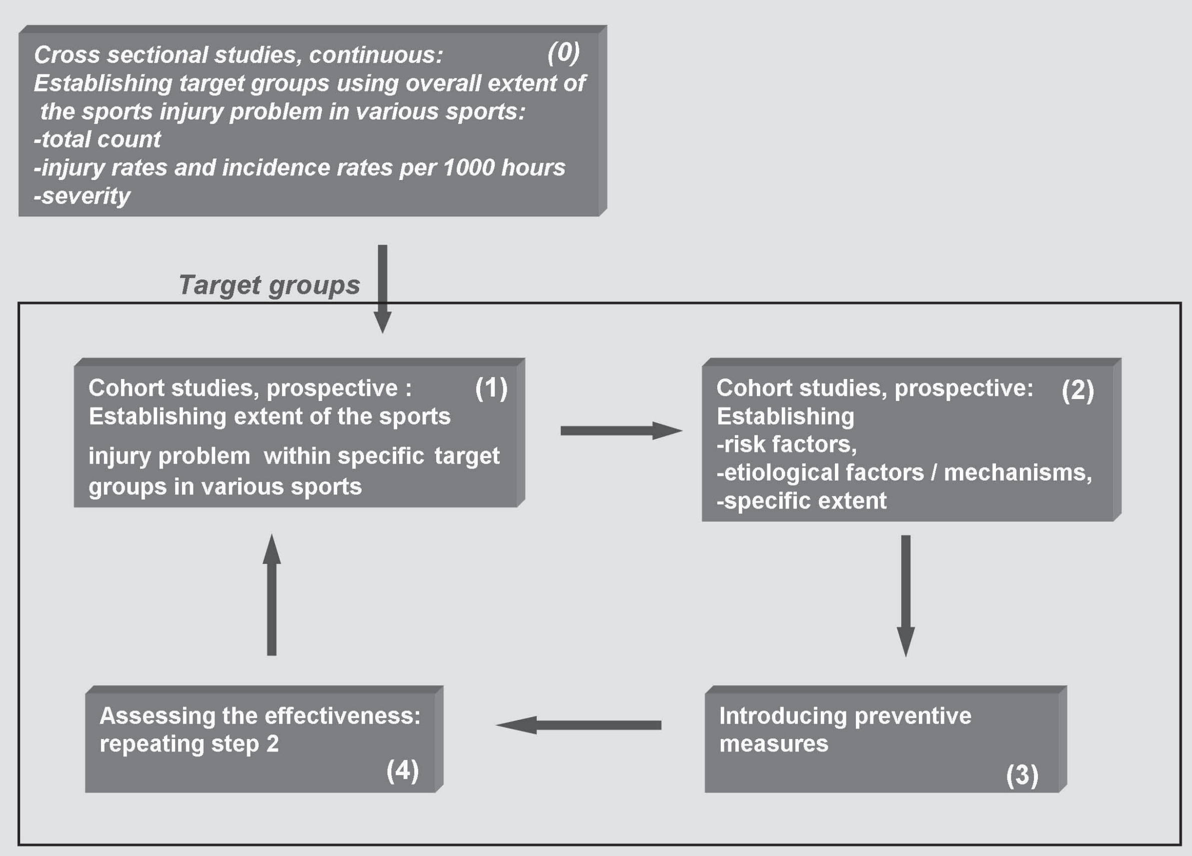

Figure 9.1 A modification (in italics) of the original prevention sequence model by van Mechelen et al.[53]

Therefore, retrospective registration systems, such as the IPAN surveys, are limited in testing the effectiveness of preventive programs in sports, as well as the monitoring of overuse injuries. In these cases, prospective studies are required. When testing the effectiveness of preventive programs, specific cohorts and a (randomized) controlled intervention are preferred[53].

One of the most powerful arguments against retrospective methods is derived from the effect of recall periods on data acquisition. Recall bias is known to influence the validity and reliability of the data. Even severe injuries needing medical treatment may be forgotten[24], although it is reported that a short recall period (i.e. four weeks) may provide surprisingly consistent laymen's diagnoses compared to those provided by medical professionals[51]. Junge and Dvorak[24] more or less concluded that retrospective methods are inferior to prospective methods, and a consensus statement on injury definitions and data collection procedures described that (soccer) injuries should be registered using a prospective design[20].

However, the results in Chapters 2 and 3 showed that the retrospective IPAN survey does offer good prospects for specifying different cohorts suitable for sports injury prevention programs. In conjunction with other registration systems, such as LIS (see Chapter 4), these registration systems may be considered as primary instruments in the preparation of the start of the original prevention sequence (steps 1-4, see Figure 9.1).

MULTIVARIATE APPROACH IN OVERTRAINING RESEARCH

Studies on overreaching and overtraining, particularly those directed at finding diagnostic parameters, have always used parameters based on some model assumptions of a stress-induced adaptation process. Initially, most of the focus was on the stress responses of the hypothalamic-pituitary-adrenal (HPA) and hypothalamic-pituitary-gonadal (HPG) axes. However, every single outcome parameter associated with these axes (serum levels of ACTH, cortisol, epinephrine, testosterone, etc.) failed to distinguish independently the overreached or overtrained athlete from controls. Although methodological issues, such as the use of different definitions for overreaching or overtraining, played their role in this lack of success, the mostly small-scaled studies were confronted with none or only small between-group differences that failed to reach significance because of large intrinsic variations. This lack of success partially explains why other explanatory models were introduced (e.g., glycogen-depletion hypothesis, glutamine-related immune response hypothesis, serotonin-related central fatigue hypothesis, etc). More parameters were tested (often in an univariate manner), but according to the latest large reviews[1,22,30] we still lack a diagnostic parameter that helps us solve the problem.

As a result, the current state of the art in this research domain forces us to stay with a *per exclusionem* diagnostic procedure[49] with retrospectively obtained information about the duration of the complaints, to decide whether an athlete is either (non-functionally) overreached (NFO) or overtrained (OTS). Especially when focussing on prevention, this is hardly satisfying for an athlete, or for the coach or the (sports) physician.

In Chapters 6, 7 and 8 we focused on the interrelationship between various parameters that could differentiate between healthy athletes and athletes who were (non-functionally) overreached (NFO). Chapter 6 showed that a multivariate three-factorial model explained 84% of the total variance in all selected performance-related parameters. The model provides a functional interpretation of the regulative characteristics of the oxygen transport capacity, the anabolic activity, and the catabolic activity. If these systems are functioning differently in overreached/overtrained athletes and controls, the errors of the model will be able to classify athletes with or without a lasting performance decrement. We then showed that the errors of the model indeed predicted a performance decrement. This provides evidence that a multivariate approach delivers parameters with potentially diagnostic qualities. In the study of Chapter 7, a more simplified multivariate method was used because the limited number of athletes did not allow us to test many HPA-axis associated outcome parameters at once. Under resting conditions, the combination of mood scores (POMS) and a blunted free cortisol response relative to serum ACTH levels illustrated two different profiles: one typical for NFO athletes and one for controls. This study design would have allowed us to test some potential predictors of NFO by means of a logistic regression procedure. We refrained from publishing such results because of the limited number of participants. Nevertheless, one analysis with just two endocrine parameters (resting levels of serum ACTH and salivary cortisol) was sufficient to classify correctly all but one athlete in each group. One psychological subscale (anger) and one hormone level after the first maximal exercise (serum cortisol) resulted in a similar prediction. Although statistical robustness demands more data, these results did show the potential of a multi-dimensional decision tree to diagnose the NFO athletes. In Chapter 8 we showed that under resting conditions, differences exist in neural network communication in cortical brain areas between NFO and control athletes. In addition, we observed that F3-F4 coherence values in the theta frequency band were positively correlated with salivary cortisol levels in NFO athletes, while in controls the alpha F3-F4 coherence values were inversely related to salivary cortisol levels. Again, both results suggest different processes in NFO athletes compared to controls.

Blunted response of salivary cortisol: a diagnostic tool in NFO?

The blunted salivary cortisol response as described in Chapter 7, has also been examined by other investigators. Steinacker et al.[45] used results from different studies[6,28,41,48,56] to graphically represent the blunting mechanism as a gradual change in circulating ACTH and cortisol from the compensated to a decompensated phase (see Figure 9.2). Our NFO athletes will be located in the lighter shaded rectangle, while control athletes with are found in the compensation phase on the left side of the graph.

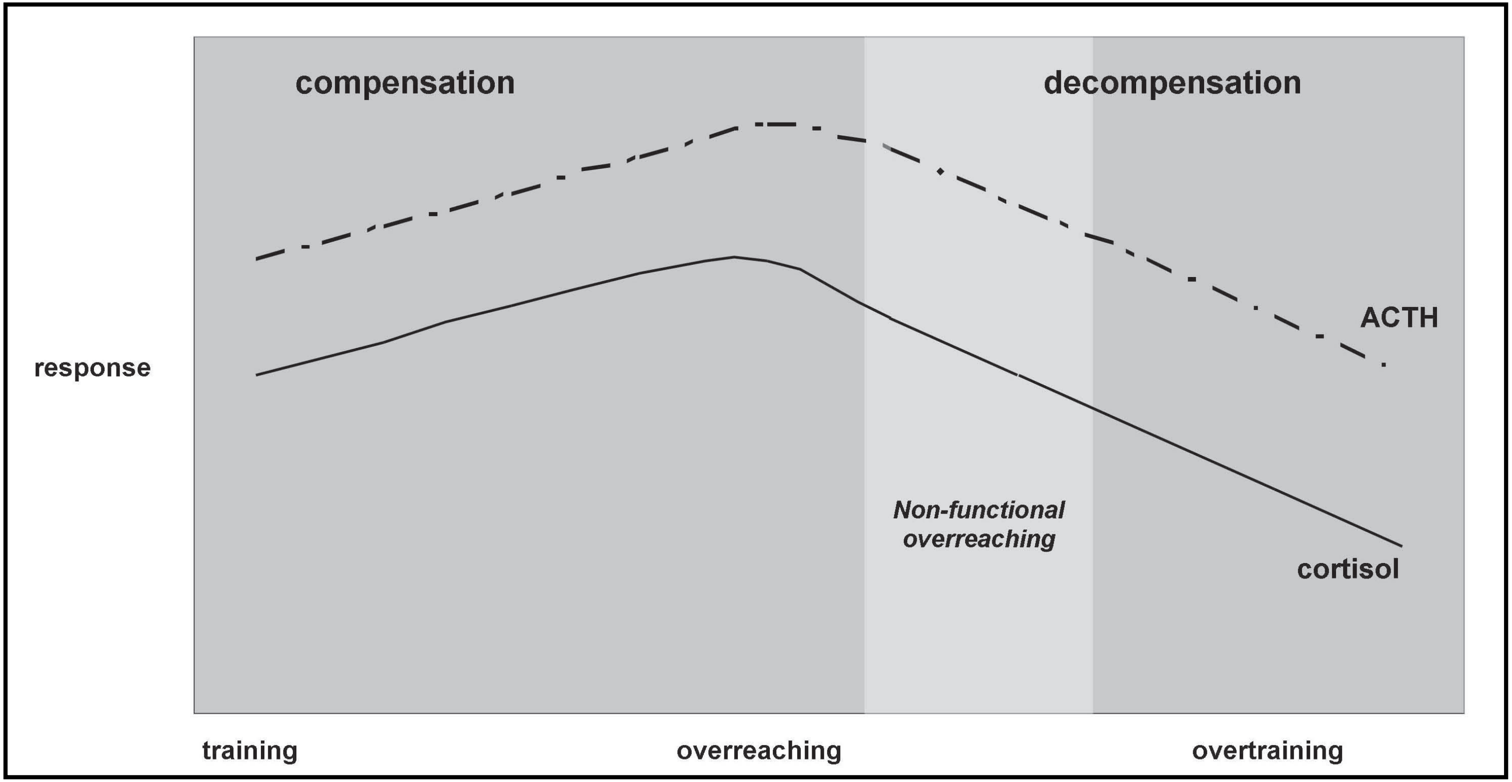

Figure 9.2 The gradual change in HPA-axis response in the compensated (after physical stress) and decompensated stage (under resting conditions) in athletes as a result of intensified training, overreaching and overtraining(redrawn after Steinacker et al.[45]).

Most of the studies explained a blunted cortisol response by a reduced receptor sensitivity to ACTH[26], which may be considered a simple adaptation process to prevent the adrenal cortex from overshooting the levels of circulating plasma cortisol. However, it is important to note that most of these studies referred to a blunted response during physical exercise, whereas we observed the blunting at rest. Wittert et al.[56] suggested that ultramarathon athletes reacted with a reduced adrenal sensitivity to ACTH because at rest they showed relatively high circulating ACTH levels with normal cortisol levels. Unfortunately, this cannot be compared with the results of our study, because in the study of Wittert et al.[56] no NFO or overtrained athletes participated and the controls consisted of recreational sports participants. Snyder et al.[41] reported a reduced resting plasma cortisol level in the majority (75%) of highly trained endurance athletes after 15 days of 'overtraining'. Unpublished results from our study in Chapter 7 showed that cortisol responses to maximal exercise were similar in controls and NFO athletes, while ACTH responses were more obvious in controls. Therefore, the resting pattern and the response to maximal exercise on the HPA-axis could indicate a specific phase of decompensation in NFO athletes. The blunted cortisol response at rest, combined with a reduced ACTH response after exercise despite a cortisol response comparable to that in controls, may enable adequate cortisol responses under too much physical (or mental) stress. Because we did not measure corticotropin-releasing hormone (CRH), we do not know if this is associated with (exercise-related) reduced hypothalamic activity levels. It should also be noted, that this hormonal pattern is highly significant when tested with the data from both type of athletes (mixed design: soccer players and runners) or from soccer players only, as well as in a mixed design with data weighted to counter the unequal distribution of runners and soccer players in the NFO athletes and controls.

In summary, differences in methodology influenced the comparison of our data with results from other studies, but the blunted response of cortisol is not an unfamiliar phenomenon. This response at rest, as well as the blunted ACTH response to exercise, might be the basis of a new diagnostic tool of NFO. However, more data are needed in order to develop a robust decision tree for diagnostic purposes. Additional studies are necessary to test whether this adaptation pattern may be extended to, for example, high endurance and high resistance exercise trained athletes.

THE LINK BETWEEN OVERUSE INJURIES AND OVERTRAINING SYNDROME

In 2000, Dvorak et al.[16] reported about general injury risk factors in male amateur soccer. In the extensive list of factors, they mentioned two psychosocial risk factors: stressful life events and changing clubs. From a total set of 17 risk factors, experiencing stressful life events was the second most significant. These psychosocial risk factors are also linked with the development of NFO and OTS[1,22,30,45]. In Chapter 1 (page 9) we already suggested a link between the process that causes overuse injuries and the overtraining process. To discuss this possible link, first the concepts of overuse injuries and the overtraining syndrome will be presented.

There is no generally accepted definition of an overuse injury in sports. Overuse injuries are often described as tissue damage resulting from repetitive stress (such as shear, tension, compression, impingement, vibration, and contraction) and trauma to the tissues of the body (muscles, tendons, bones and joints), when there is not enough time for proper healing of that tissue. Sometimes these injuries are called cumulative trauma, repetitive stress injuries or chronic injuries. The trauma cannot be major, because this would interfere with one of the most important aspects of the overuse injury: the repetitiveness. This process has been used in figure 1.1 (right side) to illustrate how an overuse injury may occur. It should be noted that the timeframe in this figure has been limited to days only for illustrational purposes. Overuse injuries may also result from a more gradual process lasting for many weeks or several months.

The process of overtraining, including that of non-functional overreaching, may be described as a concept in sports that concentrates on the imbalance between total stress and recovery. The process involves a general maladaptation of body and mind that induces a reduced performance and various physiological and psychological symptoms.

Compared with the description of overuse injuries, in which physical stress is the dominant factor, the description of overtraining includes both physical and psychological stress, thereby emphasizing the multi-causal etiology. Also, the concept of overtraining shifts ‘the damage’ from local tissue (i.e. loss of function) to changes in the functioning of systems that support recovery (e.g. metabolic system or immune system) and systems that activate body and mind (e.g. the autonomic nervous system). Consequently, it could be suggested that the process leading to overuse injuries is a subset of all the processes that lead to the overtraining syndrome. However, because of the excessive physical workload in elite athletes, a large contribution of local overuse may be expected in the overtraining process.

Changes in the activation and recovery systems in the overtraining process are described as increasingly adaptive with the ongoing overloading[22,30]. For instance, the glycogen depletion hypothesis describes a growing shortage of glycogen in muscles as processes start to fail that normally support the build-up of glycogen. Similarly, in the explanation of the ‘the Unexplained Underperformance Syndrome” (a synonym of the Overtraining Syndrome) by Robson[37] the acute effect of excessive Interleukin-6 release (IL-6) from heavy exercise causing ‘IL-6 sickness’ evolved into a phenomena called time-dependent sensitisation (TDS). TDS is considered a progressive and persistent amplification of behavioural, endocrine and immunological responses to repeated, intermittent stimuli over time. TDS then can be associated with changes in the activity of neuroendocrine systems, such as in the production of stress hormones. TDS is also used to explain the symptoms of depression in OTS. Thus, an increasing TDS can be considered as a hallmark of the ongoing process of inadequate recovery, although from a defensive perspective of health it can also be considered as very adequate.

The accumulation of micro traumas (AMT, Chapter 1, figure 1.1), which results from inadequate recovery, may be represented by the summation of the load over time in all local overuse processes under the condition that tissue capacity drops. In Figure 1.1 (Chapter 1) on the right side, AMT in a single local overuse process can be estimated using the area under the load curve after day 2, and more progressively, after day 6 until day 8.

In Figure 9.3, the influence of AMT on the quality of the recovery processes and activation is depicted. The left axis of Figure 9.3 represents the quality of the recovery systems: the quality drops once AMT exceeds a certain level. This, of course, accelerates the negative effects of a persistent load on the total recovery (which includes not only quality but also duration of recovery). The physiological response then enforces a reduced activity level (right axis of Figure 9.3) to induce homeostasis.

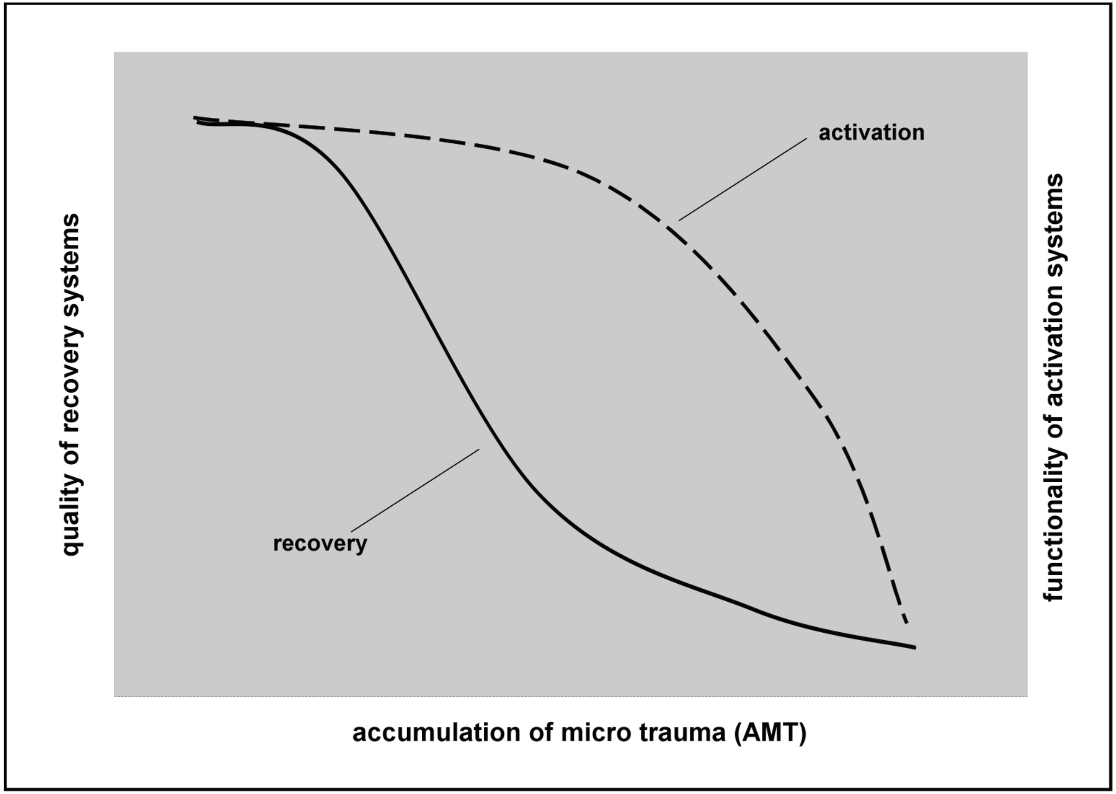

Figure 9.3 Accumulation of macro traumas (AMT), and subsequent responses of recovery systems (left axis: solid line) and activating systems (right axis: dotted line).

Figure 9.3 also integrates the two types of overtraining, often described as the sympathetic (Basedowic) and parasympathetic (Addisonic) modes of overtraining[23]. In the top left part of the graph, a strong reduction in recovery capacity is not timely countered with a significantly reduced physical activation. As a result, the athlete is still eager, but suffers from a quick onset of fatigue and a reduced performance causing a rapid further reduction of the recovery capacity. In the bottom right part of the graph athletes are increasingly forced to reduce activity (lower functioning of activating systems), aimed at countering the reduced recovery capacity. This profile fits a parasympathetically overtrained athlete, with for example lethargic characteristics and a reduced capacity to peak.
Given the suggested theoretical link between the processes of the overuse injury and the overtraining syndrome, it may be postulated that the prevention of overuse injuries is also one of the essentials in the prevention of the overtraining syndrome.

A MONITORING SYSTEM IN OVERTRAINING: READY FOR IMPLEMENTATION?

As prevention of OTS was the primary goal of the second part of this thesis, we aimed to develop a monitoring system that would recognize a phase prior to overtraining that would enable coaches and trainers to timely act and intervene.
In our prospective study (see Chapters 7 and 9), we used the model by Meeusen et al.[30] to introduce a time frame of NFO. Embedded in a monitoring system with standardized performance tests, we used a minimum period of one month of reduced performance, without causes other than physical (and mental) overload, to recognize NFO.
First, we tried to answer the question whether this specific duration and the minimum amount of decrease in performance could be measured at all. In Chapters 7 and 9, we described the procedures and results of these performance measurements, indicating that the use of a monitoring system within the setting of these sports is realistic and practical.
Second, the question needed to be answered whether the data from this monitor could be used to distinguish NFO athletes from controls in such a way that the differences would fit the expected process of maladaptation. Apart from the univariate differences (e.g. in resting plasma cortisol levels), multivariate analyses provided promising diagnostic strategies for NFO. However, up to now the dataset is too small to introduce straightforward decision schemes with clinical parameters. Thus, from a scientific viewpoint, more data are needed before a definite answer to the second question can be provided.

While the scientific approach to answering the second question is driven by what we *do not know* or understand, the practical approach to this question is driven more by the opposite: what *do we know*. We developed a method to detect an unexpected long-term performance decrement without the need of a laboratory test. According to a theoretical framework originating from a consensus on prevention, diagnosis and treatment of OTS[30], such a performance decrement is currently the most important signal for NFO in athletes.

Combined with an easy-to-use administration of mood profiles, the entire setting of such a monitor could function completely outside a sports medical clinic (see Figure 9.4).

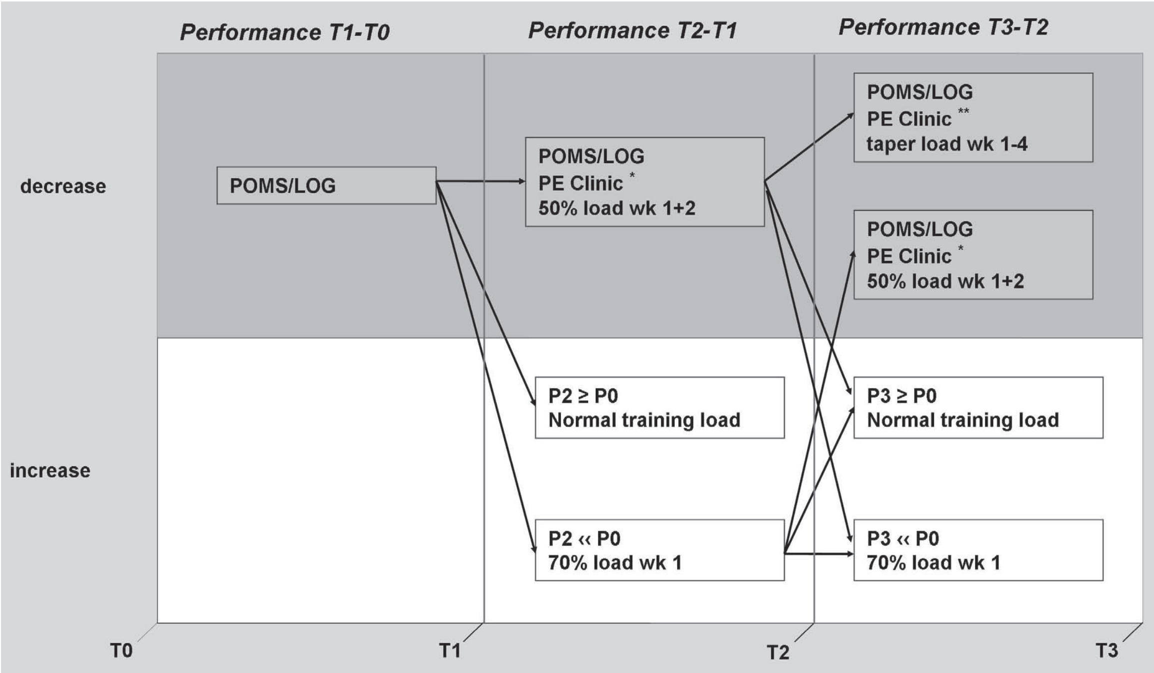

Figure 9.4 Work flow of the overtraining monitor using monthly performance assessment.

- *POMS/LOG: changes in mood (POMS Depression, Anger) and rate of perceived exertion and recovery (Logbook using Borg scale)*
- *P0=performance at T0, P1=performance at T1, P2=performance at T2, P3=performance at T3*
- *PE Clinic : Per Exclusionem Diagnosis protocol (see e.g. Uusitalo, 2001)*

  ** if a positive result on PE is found, treatment including load is altered accordingly*

  *** only if previous PE was positive*

Classifying an athlete as suffering from NFO after a minimum of one-month performance decrement (e.g. performance decrease at T1 compared to T0) is then realistic, provided that the performance is measured with a field test sensitive to the specific physical demands in various sports. Moreover, such an approach does not carry a large risk of misjudging the health status of the athlete.
After all, if the performance measurement is valid, such a reduction in performance is usually undesirable whatever the cause may be. Thus, from this viewpoint the monitor is ready to be introduced, although selectively ready for male soccer players, and perhaps, male mid-distance runners. Serious thought should be given to whether this monitor is ready for use in team sports, such as field hockey and rugby. From a physiological viewpoint, these sports are very similar to soccer and may benefit from this monitoring approach as well.
A valid monitor also enables us to work on the “finishing touch” of the clinical parameters to diagnose NFO. The knowledge emerging from that research may also be applicable elsewhere. Theoretically, a better understanding of the HPA-axis adaptation in NFO could be useful in treatment strategies in other fatigue-related syndromes. Furthermore, the concept of reduced performance in athletes and adaptive processes as a result of physical overload may also be applicable to patients in hospitals with reduced physical capacity. Thus, a valid monitor may also help to improve programs intended to train and rehabilitate patients.

DOES BRAIN COMMUNICATION FIT INTO PREVENTION OF OVERTRAINING?

The theoretical framework of neural efficiency predicts positive effects of sports and physical exercise on the brain among athletes[14,15,52,55]. EEG measurements provide information about the activity of neurons in the brain, and it has been demonstrated that the brain of an athlete communicates differently from the brain of a non-athlete (unpublished data: Chapter 8). Whether these differences are induced by athletic training, sport activities, selection effects, or genetic differences, separately or in combination, has not yet been elucidated. However, a study by Schneider et al.[40] showed instant effects of exercise on mood that interacted with brain activity measured by EEG. As an example, the alpha power (7.5-10 Hz) increased after exercise and was associated with an improved perceived physical state. Therefore, there are convincing indications that physical exercise changes brain activity.
One can expect that ‘too much’ physical exercise (as described in Chapter 8), may also elicit changes in brain activity. EEG coherence was used as a marker for changed information transfer between cortical areas. This approach is a challenging new field in the research of overreaching/overtraining, but our current knowledge is insufficient to make this information a part of a diagnostic instrument. We first need to better understand the changes of inter- and intra-hemispheric brain communication in association with excessive exercise, i.e., whether these changes are related to transitions in regional blood flow (fMRI technology), or to alterations in neurotransmitters and their receptors (PET-scan technology). Additionally, studies on activity in specific parts of the brain (e.g. activity in the motor cortex) may help to explain why an overtrained athlete is often characterized by a lack of concentration, a reduced motor control, or a psychomotor slowness, as suggested by Rietjens et al.[36] and Nederhof et al [34].

IMPLICATIONS AND RECOMMENDATIONS FOR POLICY, RESEARCH AND PUBLIC HEALTH IN SPORTS

Table 9.1 presents a list of implications and recommendations concerning the prevention of sports injuries related to the overtraining syndrome. Although an attempt has been made to divide the content into three main areas (public health, research, policy), implications and recommendations do not always have such a clear boundary. The content shown in Table 9.1 is an interpretation of a point of view, as discussed in the following two sections.

Registration and prevention of acute injuries and overuse injuries

The 'public health' approach in the analysis of the extent and severity of sports injuries in the Netherlands, as introduced in this thesis, has provided a compact set of ten sports, specified by age and by gender, that may be considered as a target list for injury prevention. Future studies that aim to produce new target lists should be supported by additional data from other sources in our medical health system and by prospective instruments that help us estimate the extent and severity of overuse injuries. Although data on sports injuries treated at the emergency room are available, there is insufficient or infrequent data to validate estimates on medical treatment by the general practitioner [50], and the physical therapist and medical specialist in the hospital. Given that most of the costs associated with sports injuries are not from medical treatment but from work absence, there is good reason to initiate a registration system that provides information on work absence due to sports injuries.

Subsequently, this information needs to be translated into action. If a consensus exists about the target list with the restriction of both funding and time, a proper analysis of existing knowledge concerning steps 1-3 of the injury prevention sequence more or less defines the workload for scientists and field organizations in the coming years. There is of course a great need for this entire process to be well structured, well-guided and appropriately evaluated. Without this, are simply reporting numbers.

Prevention of the overtraining syndrome

We proposed a method to prevent the overtraining syndrome (OTS) by means of the early recognition of the non-functionally overreached state (NFO) of the athlete. The validity and reliability of this method, which is put to work in the field and not in the clinic, needs to be explored in more sports than in soccer and in track and field. More knowledge is required to help define a short and simple, though variable, log including mood assessments, to help increase compliance and validity of a monitoring instrument for exposed athletes. Performance testing is essential with this method. Therefore, more standardized testing procedures in different sports need to be developed and evaluated.

The method of monitoring proved to reveal differences between NFO athletes and controls, provided that these differences were analyzed using a multivariate approach. Whether these differences will eventually produce diagnostic parameters is still debatable. More data on such parameters are necessary, and more parameters are necessary as well, before a diagnostic protocol can be defined. Such a protocol will convert the diagnosis of NFO (and most likely the diagnosis of OTS) into something more than just a retrospective evaluation of the duration of complaints that could not be explained otherwise.

The process of overtraining as it stands now is a multi-causal health phenomenon, mainly described in athletes. This means that input is needed from various medical disciplines such as neurology, endocrinology, exercise physiology, cardiology, immunology, aswell as psychology and epidemiology. This probably also accounts for other syndromes such as chronic fatigue, burnout, post-traumatic stress, or even fibromyalgia. It might be advisable to bring the knowledge of all these fatigue-related syndromes together to strengthen the quality of research and, consequently, of public health.

Epilogue

To ultimately improve the prevention of damage in sports, a considerable commitment is required (see Table 9.1). Although injuries and even overtraining are known to damage elite, amateur and recreational athletes, we are still beginning to learn how to deal with it. However, if sports can attract so many participants, if it can prevent diseases related to an inactive lifestyle, if it can result in a huge industry (ranging from construction to entertainment), if it even stops the government from working during the finals of important sports events, then there has to be a mutual goal and a way to make it work.

Table 9.1 Implications and recommendations concerning the prevention of sports injuries and the overtraining syndrome.

<table>
<tr><th></th><th>POLICY</th><th>RESEARCH</th><th>PUBLIC HEALTH</th></tr>
<tr><td rowspan="6">Sports injuries</td><td rowspan="3">Injury prevention targeted at :
-outdoor soccer (males high-level, amateur 18-34 yrs and 4-17 yrs, females (4-17 yrs)
-indoor soccer (males 18-34 yrs)
-tennis (males/females 35-54 yrs)
-volleyball (females 18-54 yrs),
-field hockey (males 18-34 yrs, females 4-17 yrs)
-running/jogging (males/females 35-54 yrs)
-gymnastics (males/females (4-17 yrs),
-skiing/snowboarding (males 4-17 yrs, females 18-34 yrs)
-equestrian sports (females 18-34 yrs)
-basketball (males 4-17yrs)</td><td>Medical costs at <u>all</u> treatment locations and work absence should be implemented as a part of the severity index of sports injuries.</td><td rowspan="3"></td></tr>
<tr><td>Implementation of the “Sporters Dossiers” in prospective studies, e.g. in the study on overuse injuries.</td></tr>
<tr><td>Risk factors in female soccer, particularly anterior cruciate ligament injuries.</td></tr>
<tr><td>Improve, disseminate and implement knowledge on working preventive strategies [12].</td><td colspan="2">Study the options of injury prevention in the 10 target sports:Tailor- made prevention programs</td></tr>
<tr><td colspan="2">Initiate intermittent registration of sports injuries at all relevant medical treatment locations to validate IPAN data.</td><td></td></tr>
<tr><td>IPAN modification should be limited, well prepared by means of pretesting, and well described.</td><td colspan="2">Monitor sports-related health impairment in the population aged 55+ years.</td></tr>
<tr><td rowspan="6">Overtraining syndrome</td><td rowspan="6">Propagate the overtraining monitor (Fig. 9.4).</td><td>Validate adrenocorticotropic hormone–cortisol profile in NFO in different sports (e.g. endurance and resistance exercise sports).</td><td rowspan="2"></td></tr>
<tr><td>Pathophysiology of adrenocorticotropic hormone–cortisol profile, e.g. sensitivity of receptors on adrenal cortex and pituitary gland.</td></tr>
<tr><td colspan="2">Prospective studies on hormones: single maximal exercise test.</td></tr>
<tr><td>Retrospective or cross-sectional studies/clinical evaluation of hormones: double max exercise test.</td><td rowspan="3">Implementation of performance testing and the load monitor to evaluate the rehabilitation of NFO or OTS patients in a clinical setting.</td></tr>
<tr><td>Simplify and validate the monitor of load (inc. rate of perceived exertion and recovery) and mood to design an instrument with a variable content but with a constant predictive value.</td></tr>
<tr><td>Changes in neural communication in NFO athletes: blood flow (fMRI), neurotransmitters PET or [carbonyl-11C]WAY-100635) and stress hormone receptors (immunocytochemical methods).</td></tr>
</table>

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Summary

Samenvatting

SUMMARY

The damage emerging from sports emphasizes the importance of adequate primary and secondary prevention as well as proper treatment. The general research domain on primary and secondary prevention and the treatment of sports injuries is too extensive to be covered in a single thesis. Therefore, the focus in this thesis is on a selective number of aspects of primary and secundary prevention.

Chapter 1 distinguishes two specific concepts of the damage in sports: local damage and systemic damage. Local damage refers to acute and overuse injuries, while systemic damage is related to the process of overtraining. This process leads to non-functional overreaching (NFO), or ultimately, the overtraining syndrome (OTS). The local and systemic types of damage are linked with each other as time dependent effects of an imbalance between physical and mental load and the capacity to cope with this load.

The first part of the thesis (**Chapters 2-4**) addresses the hypothesis that epidemiological sports injury data from surveys can be used to define specific populations most eligible for sports injury prevention.

In the second part of this thesis it is assumed that an intervention in the process of overtraining in its early stages will prevent the development of OTS. Therefore, in **Chapters 5-8** we tested the hypothesis if we can timely recognize the onset of the overtraining process by identifying athletes who are non-functional overreached (NFO).

In **Chapter 2 and 3**, the 2000-2005 analyses of data from a nationwide telephone survey called IPAN (Injuries and Physical Activity Netherlands) are presented. IPAN covers all sports participants aged four years and older. In **Chapter 2**, the focus is on finding age and gender specific target groups for injury prevention among approximately 8 million sports participants in the Netherlands.

Several epidemiological statistics were used to select the target groups: the volume of injuries, the incidence per 1000 hours, and the proportion of medically treated injuries. Age and gender specific target groups could be selected from nine sports: outdoor and indoor soccer, tennis, volleyball, field hockey, running/jogging, gymnastics, skiing/snowboarding and equestrian sports. The target groups were responsible for 66% of all sports injuries, as well as for 66% of the indirect and 70% of the direct costs of sports injuries.

The largest contribution to the total burden of sports injuries was found in male outdoor soccer players under 55 years of age, and particularly, in those under 35 years. The latter group was subject to further analyses in **Chapter 3**. The male soccer population under 35 years of age consisted of 800.000 playing members of the Royal Netherlands Football Association, acting in various age categories and at different skill levels. Therefore, it was necessary to refine target groups for injury prevention. Junior players were distinguished from senior players (seniors:18 years and older). Three different exposure time-related skill levels (0-3 hours, 4-5 hours and 5+ hours) were used for further specification of the proportion of injured soccer players. Despite highly similar injury characteristics, the proportion of injured players generally was highest among the seniors. With increasing skill levels, the proportion of injured players increased as well.

We conclude that senior soccer players, spending more than three hours per week on games and training sessions, are the most eligible target group for injury prevention in outdoor soccer.
Generally, the results from **Chapter 2 and 3** confirm that the IPAN-survey is capable of selecting target groups for sports injury prevention. Limitations of IPAN, such as the relatively small number of injuries for in-depth analysis and the laymen's diagnosis, are discussed and suggestions are made to handle them properly.

With the general aim of the Dutch government to establish a safe and healthy life style with sports activities, sports injuries have been drawing the attention since the late 70's of the previous century. **Chapter 4** describes the timeline along which the various Dutch sports injury registration systems have been developed. It specifically evaluates the development of IPAN as a nation wide survey with a large variety of topics related to sports injuries. It shows how IPAN content varies with changes in the Dutch government policy, the vulnerability of IPAN data to these changes, as well as the limitations of the IPAN-system. We concluded that registration instruments within the medical care system (e.g. in the emergency room, at the general practitioner, physical therapist, and in the hospital clinic) were elementary to achieve a complete and valid description of the sports injury problem over time. However, only the registration of sports injuries treated in the emergency room had been been a consistent factor over the years. Other registrations were lacking, incomplete or producing data infrequently.
Furthermore, there was no strategy to optimize methods and definitions to make data compatible at each level of registration. A new structure of registration systems is suggested, umbrella shaped, with a nation wide survey such as IPAN being supported by several (care specific) registration systems using compatible methods, concepts and definitions.

Chapter 5 introduces the theoretical framework of non-functional overreaching (NFO) as an integral part of the overtraining process. This process may cause athletes to suffer from a variety of symptoms of the overtraining syndrome (OTS). It is not uncommon that some never fully recover from this syndrome, forcing them to end their career as an athlete. Firstly, the model behind the concept of NFO and OTS is discussed. Secondly, some studies of NFO are evaluated. This evaluation revealed that the principles of NFO are still 'under construction', and no single parameter or a combination of parameters is known to recognize NFO. The latter conlusion introduces the topics for **Chapters 6, 7 and 8.**

In **Chapter 6,** data from athletes visiting our sports medical department between 1990 and 2000 were used to test if a multivariate model could distinguish athletes with symptoms possibly related to the overtraining process from asymptomatic athletes. The symptoms, particularly a loss of performance capacity, were derived from a small questionnaire referring to the weeks before visiting our sports medical department. The multivariate model described the interaction between the various hematological, endocrine and metabolic parameters, in predominantly ‘healthy controls’. A poor fit of the model to the real data was then used to predict athletes with and without symptoms. Compared to univariate models, we found that a multivariate approach was much more robust in predicting symptoms such as a loss of performance capacity. A poor performance capacity was predicted in cases with a model-misfit in sex hormone-binding protein (SHBG) and hematocrit (Ht). Together with hemoglobin (Hb, the only univariately relevant parameter), the model can be used to explain 55% of the variance in performance capacity. Although our multivariate approach supports the assumption that regulatory systems related to oxygen transport and the anabolic and catabolic activity may be sensitive to NFO or OTS-related symptoms, the cross sectionally obtained data does not allow us to exclude other explanations of the results. Furthermore, performance capacity relies on the subjective interpretation of performances. Therefore, prospective studies and objective data of performance capacity are necessary to verify whether this approach may contribute to the early detection of NFO.

In **Chapter 7,** tools to recognize NFO were evaluated. A minimum one-month performance decrease was used in sports specific field tests to differentiate between young elite athletes possibly suffering from NFO (N=8) and their (controls (N=7). The psychological profile of the group with a performance decrease showed an increase anger and depression. This is consistent with the expected mood profiles of NFO-athletes. Endocrine profiles were also different between both groups. The profiles sugged that NFO could be characterized by an ACTH-insensitivity at the adrenal level that leads to reduced circulating cortisol levels at rest. We concluded that the endocrine and the psychological profiles in athletes with a long term performance decrease supported the theoretical concept of NFO as introduced in **Chapter 5** within the OTS-model. However, more athletes from different sports need to be tested before these findings can be become a generalized concept in a strategy to prevent of OTS.

Chapter 8 introduces specific changes in brain activity as a possible marker of NFO. Recent studies suggest that well-trained healthy athletes show a specific adaptation to the exercise-induced high levels of the central neurotransmitter serotonin. Athletes who suffer from NFO or OTS did not show this kind of adaptation. The study in **Chapter 8** addressed the question whether brain activity in NFO-athletes may also be different from athletes without NFO. Saliva derived free levels of the stress hormone cortisol were related to brain activity in the same group of NFO-athletes and controls as described in **Chapter 6**. The connectivity between various parts of the cortex, as measured with electroencephalogram (EEG) coherences, was used as a marker of functional activity of the brain network. The results showed that left frontal (F3)-right parietal (P4) interhemispheric connectivity in the θ frequency band was significantly lower in NFO athletes compared to controls. Moreover, correlations of the left frontal (F3)-right frontal (F4) interhemispheric connectivity (in θ and α frequency bands) with FC were significantly different in NFO-athletes and controls. The results from **Chapter 6 and Chapter 8** support the practical use of field tests to trace a possible development of NFO in elite athletes. The results show that mood, neuro-endocrine activity and brain activity together may play a complex but important role in the diagnoses of NFO and OTS. However, similar to the results in **Chapter 6**, these results need to be verified in larger samples, and extended with the inclusion of athletes from different types of sports.

In **Chapter 9,** the epidemiological relevance of the results presented in the **Chapters 2-4** on sports injuries is discussed, amongst others in relation to the four steps of the prevention sequence model. The results from the studies on the early detection of NFO in the **Chapters 5-8** are evaluated and translated into a theoretical model that describes the process of overtraining as a function of activation and recovery. Furthermore, a guideline for sports specific performance tests is introduced to monitor closely the onset of NFO. Overall, some important methodological issues are brought forward, and recommendations are made for policy and research.

SAMENVATTING

De schade die ontstaat door sportbeoefening benadrukt het belang van primaire en secundaire preventie, evenals het belang van adequate behandeling. Het complete onderzoeksdomein van de primaire en secundaire preventie en de behandeling van sportblessures is te omvangrijk om in één proefschrift gevat te worden. Daarom wordt in dit proefschrift de nadruk gelegd op een beperkt aantal aspecten van primaire en secundaire preventie.

Hoofdstuk 1 onderscheidt twee specifieke concepten van schade in de sport: locale schade en systemische schade. Locale schade verwijst naar acute blessures en overbelastingsblessures, terwijl systemische schade gekoppeld is aan het proces van overtraining. Dit proces veroorzaakt niet-functionele overbelasting (NFO), of uiteindelijk het overtrainingssyndroom (OTS). De locale en systemische schade zijn met elkaar verbonden als tijdsafhankelijke effecten van een disbalans tussen fysieke en mentale belasting en het vermogen om met deze belasting om te gaan.
Het eerste deel van het proefschrift **(Hoofdstukken 2-4)** toetst de hypothese dat epidemiologische data van sportblessures uit landelijke registratiesystemen gebruikt kunnen worden voor het vaststellen van specifieke doelpopulaties voor blessurepreventie.
In het tweede deel van het proefschrift wordt aangenomen dat de ontwikkeling van OTS voorkomen wordt met een ingreep in het begin van het proces van overtraining. Daarom gaat in de **Hoofdstukken 5-8** de aandacht vooral uit naar vroege herkenning van het proces dat kan leiden tot OTS door NFO bij sporters te identificeren.

In **Hoofdstuk 2 en 3** worden de resultaten uit de landelijke OBiN 2000-2005 enquête gepresenteerd. OBiN (Ongevallen en Bewegen in Nederland) registreert gegevens van sporters vanaf 4 jaar. In **Hoofdstuk 2** ligt het accent op het vinden van leeftijd- en geslachtspecifieke doelgroepen voor blessurepreventie onder de ongeveer 8 miljoen sportende Nederlanders.
Een combinatie van epidemiologische statistieken werd gebruikt voor het selecteren van doelgroepen: het totale volume aan sportblessures, de incidentie per 1000 uren sport en het percentage blessures dat medisch wordt behandeld. Leeftijd- en geslachtspecifieke groepen werden gekozen uit negen sporttakken: veld- en zaalvoetbal, tennis, volleybal, veldhockey, hardlopen/trimmen/joggen, turnen, skiën en snowboarden, en paardensport. Deze groepen waren verantwoordelijk voor 66% van alle blessures, maar ook voor 66% van alle indirecte en 70% van alle directe kosten door sportblessures.
Het grootste deel van de fysieke schade door sportblessures werd veroorzaakt door mannelijke veldvoetballers onder de 55 jaar, en in het bijzonder, onder de 35 jaar. Deze laatste groep staat centraal in **Hoofdstuk 3**. De populatie mannelijke veldvoetballers onder 35 jaar telde destijds ongeveer 800.000 actieve leden van de KNVB, verdeeld over diverse leeftijdscategorieën en verschillende spelniveaus. Daarom was het noodzakelijk nauwkeuriger vast te stellen wat precies de doelgroepen voor blessurepreventie in het veldvoetbal zijn.

Junioren zijn onderscheiden van senioren (18 jaar en ouder). Drie verschillende, aan expositietijd gekoppelde niveaus (0-3 uur, 4-5 uur en 5+ uur) werden gebruikt voor een andere specificatie van het percentage geblesseerde spelers. Ondanks de overeenkomsten in het blessurebeeld was in het algemeen het percentage geblesseerden het hoogst bij de senioren. De kans op een blessure nam toe met toename van het niveau waarop werd gespeeld. We concluderen daarom dat senioren die meer dan drie uur per week actief zijn de belangrijkste doelgroep vormen voor blessurepreventie in het veldvoetbal.
In algemene zin onderschrijven de resultaten van de **Hoofdstukken 2 en 3** dat OBiN geschikt is voor het selecteren van doelgroepen voor de preventie van sportblessures. Beperkingen van OBiN, zoals het relatief kleine aantal blessures voor diepte-analyse en de lekendiagnoses, zijn ter discussie gesteld en suggesties zijn voorgelegd om deze beperkingen aan te pakken.

Met het doel van de Nederlandse overheid om een veilige en gezonde leefstijl met sport te realiseren, trekken de sportblessures sinds de eind 70'er jaren van de vorige eeuw de aandacht. In **Hoofdstuk 4** beschrijven we daarom de diverse Nederlandse registratiesystemen van sportblessures en hun ontwikkeling over de tijd.
In het bijzonder evalueerden we de ontwikkeling van OBiN als landelijk registratiesysteem met een breed palet van onderwerpen over sportblessures. Aan bod kwamen de gewijzigde inhoud van OBiN naar aanleiding van veranderingen in overheidsbeleid, de gevoeligheid van de data voor deze wijzigingen, alsmede de beperkingen van het OBiN-systeem. Geconstateerd werd dat registratiesystemen binnen de medische wereld (bijvoorbeeld SEH, huisarts, fysiotherapeut of polikliniek) van groot belang waren (en zijn) voor een complete en valide beschrijving van de ontwikkeling van het sportblessureprobleem. Echter, in de loop der jaren leverde alleen de registratie van sportblessures op SEH's hieraan een constante bijdrage. Andere registraties ontbraken of produceerden mondjesmaat cijfers. Bovendien, ontbrak een strategie voor het optimaliseren van methoden en definities, zodat de verkregen data op elk niveau van registratie compatibel werd. Een organisatie van registratiesystemen in een parapluvorm wordt voorgesteld, waarbij een algemeen landelijke registratie als OBiN aangevuld en ondersteund wordt door meerdere systemen (binnen de relevante medische domeinen) met behulp van op elkaar aansluitende methoden, begrippen en definities.

Hoofdstuk 5 introduceert het theoretische kader van het begrip niet-functionele overbelasting (NFO) als integraal element van het overtrainingsproces. Dit overtrainingsproces kan de aanleiding zijn voor een reeks van symptomen die gerelateerd zijn aan het overtrainingssyndroom (OTS). Soms herstelt de sporter niet volledig van dit syndroom en luidt dit het einde van een sportcarrière in. Allereerst is het model achter het concept van NFO en OTS besproken. Als tweede zijn enkele studies van NFO geëvalueerd. Deze evaluatie laat zien dat de principes achter NFO nog 'in ontwikkeling' zijn, en dat er geen losse parameter of combinatie van parameters bekend is waarmee NFO kan worden herkend. Dit laatste vormt de aanleiding voor de onderwerpen in de **Hoofdstukken 6, 7 en 8.**

In **Hoofdstuk 6** gebruiken we gegevens van sporters die tussen 1990 en 2000 onze sportmedische afdeling bezochten. De gegevens zijn ingezet om een multivariaat model te testen voor het onderscheiden van sporters met en zonder aan het overtrainingsproces gerelateerde symptomen.
De symptomen, hoofdzakelijk een verminderd vermogen tot presteren, werden afgeleid van een kleine enquête die verwees naar de weken voorafgaande aan het bezoek aan de afdeling. Het multivariate model gaf de interactie weer tussen hematologische, endocriene en metabole parameters van voornamelijk ‘gezonde’ controle personen. Grote afwijkingen van het model ten opzichte van de oorspronkelijke data werden gebruikt om te voorspellen welke sporters wel en welke geen symptomen hadden. Univariate modellen waren, in vergelijking tot de multivariate versies, veel beter in staat de symptomen te voorspellen. Slechte prestaties werden geconstateerd indien het model niet in staat was de correcte spiegels van het geslachtshormoonbindende eiwit (SHBG) en hematocriet (Ht) te voorspellen. Inclusief hemoglobine (Hb, de enige univariaat relevante parameter), kon het model 55% van de variantie in prestatievermogen voorspellen. De multivariate benadering bevestigt dat regulerende systemen van het zuurstoftransport, de anabole en catabole activatie samen kunnen hangen met NFO of OTS gerelateerde symptomen. Echter, de cross-sectionele kenmerken van de data staan ons niet toe alternatieve verklaringen uit te sluiten. Bovendien is het prestatievermogen gebaseerd op een subjectieve inschatting van prestaties. Daarom zijn er prospectieve studies met objectieve gegevens over prestaties nodig om na te gaan of deze benadering kan bijdragen aan de vroege detectie van NFO.

In **Hoofdstuk 7** worden verschillende instrumenten behandeld waarmee NFO kan worden vastgesteld. We hanteerden een prestatiedaling van ten minste één maand in sportspecifieke testen om jonge topsporters die mogelijk niet functioneel overbelast waren (N=8) te onderscheiden van de overige sporters (N=7). Het stemmingsprofiel van de groep met prestatiedaling kenmerkte zich door woede en depressieve gevoelens. Dit kwam overeen met de verwachte stemmingsprofielen van sporters met NFO. Ook de endocriene profielen van de twee groepen waren verschillend. Dit suggereert dat NFO gekenmerkt wordt door een ACTH-ongevoeligheid op de bijnierschors met een gedaalde cortisolspiegel in rust als gevolg. Geconcludeerd wordt dat de endocriene en psychologische profielen van sporters met een langdurige prestatiedaling het theoretische concept van NFO binnen het OTS-model ondersteunen, zoals geïntroduceerd in **Hoofdstuk 5**. Echter, eerst moeten meer sporters uit verschillende sporttakken getest worden alvorens dit concept als algemene benadering voor de preventie van OTS kan worden ingezet.

Hoofdstuk 8 stelt specifieke veranderingen in hersenactiviteit voor als mogelijke marker van NFO. Recent onderzoek toont aan dat goed getrainde sporters een specifieke aanpassing vertonen op de door inspanning verhoogde spiegels van de neurotransmitter serotonine.

Bij sporters met NFO of OTS zou deze aanpassing ontbreken. In **Hoofdstuk 8** wordt nagegaan of in een groep NFO-atleten en een controlegroep de hersenactiviteit verschillend is. Vrij cortisol (in dit hoofdstuk omschreven als speeksel cortisol) wordt gerelateerd aan hersenactiviteit van de sporters met en zonder NFO die reeds beschreven zijn in **Hoofdstuk 6**. De verbinding tussen verschillende delen van de cortex, gekwantificeerd met een coherentiemaat die is afgeleid van electroencephalogram (EEG), werd ingezet als maat voor de functionele activiteit van de hersenen. In vergelijking tot de controlegroep, was de links frontale (F3) - rechts parietale (P4) interhemisferische activiteit in θ frequentieband significant lager in de sporters met NFO. Bovendien was de correlatie tussen de links frontaal (F3)- rechts frontaal (F4) interhemisferische activiteit (in de θ en α frequentieband) met vrij cortisol in de sporters met NFO anders dan in de controlegroep. De resultaten van de **Hoofdstukken 6 en 8** onderschrijven daarmee het praktische nut van veldtesten bij het opsporen van de mogelijke ontwikkeling van NFO. De resultaten laten zien dat stemming, neuro-endocriene activatie en hersenactiviteit een belangrijke rol kunnen spelen in de diagnose van NFO en OTS. Net als bij de resultaten van **Hoofdstuk 6,** moeten deze bevindingen wel eerst geverifieerd worden in grotere steekproeven met een uitgebreidere inclusie van sporters uit andere sporttakken.

In **Hoofdstuk 9** wordt de epidemiologische relevantie van de resultaten uit de **Hoofdstukken 2-4** besproken, onder andere in het licht van de vier stappen van het preventiesequentie-model. De resultaten van de studies naar de vroege detectie van NFO uit de **Hoofdstukken 5-8** worden vertaald naar een theoretisch model, dat het proces van overtraining beschrijft aan de hand van activaterende en herstellende functies. Bovendien wordt een stappenplan voor sportspecifieke prestatietesten voorgesteld om de ontwikkeling van NFO te monitoren. In algemene zin worden methodologische kwesties aan de orde gesteld en zijn er aanbevelingen gedaan voor zowel beleid als onderzoek.

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Han Inklaar was sportarts bij de KNVB, ook met een zwak voor wetenschappelijk onderzoek. Hij had een dataset die zo complex en groot werd dat een simpele T-toets niet meer voldoende was om zijn wetenschappelijke nieuwsgierigheid te temmen. Het was enorm leuk om bij jou voor de tweede keer paranimf te zijn. De vele, vooral gedreven telefoongesprekken over het vak zal ik nooit meer vergeten. Han, dank voor vriendschap, je morele en inhoudelijke steun gedurende al die jaren.

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Curriculum Vitae
Publications

CURRICULUM VITAE

Sándor László Schmikli was born in Haarlem on April 19th 1961. He was raised in Tiel and in Amsterdam. In Amsterdam, he played his first games of soccer. From that moment on the game pretty much dominated his daily activities. He finished secondary school, first at the Reina Prinsen Geerligs in 1979 (HAVO), and then in 1981 at the Cartesius Lyceum (VWO). With the Military Service in between, he started his academic education with Geology and Geophysics in Utrecht in 1983. He switched to Social Sciences in Utrecht in January 1985, because he was more interested in Sports and Psychology. In 1989, he conducted a research project on overtraining with rowers at the Department of Medical Physiology and Sports Medicine in Utrecht. After having received his doctorandus degree in that same year, he continued to work for this Department on various projects in sports medicine. In 1995, together with Dr Eduard Bol and Dr Frank Backx, he wrote the book “Sportblessures nader uitgediept”. In the first years after the turn of the century, he survived a UMC Utrecht reorganization called ‘Durven Kiezen’. From 2003 onwards, he has been working as a staff member of a research group on Sports Medicine, integrated in the Department of Rehabilitation, Nursing Science and Sport of the Neuroscience Division at the UMC Utrecht. This work provided the onset of a PhD project. Currently, he lives in Ede with his wife Corine and his two daughters, Rosalie and Charlotte.

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