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Timing of NSAID treatment after muscle injury or training

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Injury of skeletal muscle, either severe accidental injury or microdamage as a result of exercise training, is an inevitable outcome of participation in sport, as is the inflammation that follows. Non-steroidal anti-inflammatory drugs (NSAIDs) are probably the most widely used anti-inflammatory treatment. However, many studies have failed to show a benefit of NSAID treatment on actual muscle healing, while some even suggested that it may prolong the recovery period, although it effectively reduces pain and swelling. These conclusions may have been reached due to the fact that NSAIDs treatment is often administered at the wrong time after injury.

In order to elucidate this issue, it is necessary to understand the time course of inflammatory events after injury, and the mechanism by which the immune system mediates inflammation.

What happens when?

Two major immune cell types are implicated in the inflammatory response to skeletal muscle injury. Neutrophils are recruited in the injured area first – usually within an hour, with cell numbers in the injured area peaking by 24 hours.[1]

Neutrophils have two main functions. Firstly, they are phagocytic, and clear the injury site of necrotic debris so that regeneration can take place. Unfortunately this necessary process often results in more damage, as healthy surrounding tissue may be damaged accidentally, e.g. by free radicals released during the phagocytic process and the neutrophil oxidative burst. Indeed, experimental neutrophil depletion prior to injury was shown to reduce muscle damage by almost 40% in both cardiac and skeletal muscle, suggesting that neutrophils may contribute to so-called 'secondary damage' after injury. Secondly, neutrophils magnify the inflammatory response by facilitating the release of various pro-inflammatory cytokines.[2,3] Although the latter causes pain and swelling, this is another vital step in the repair process, since these cytokines are key in facilitating recruitment of various growth factors and precursor cells to the injured muscle.

Neutrophil numbers may stay elevated for up to 5 days after injury, but start declining already after 24 hours. Concomitant to this decrease, an increase in macrophage numbers is seen.[3,4] Unlike neutrophils, different subpopulations of macrophages exist. It is commonly accepted that the subtype recruited earliest, $ED1^+$ cells, is phagocytic and plays a role in the removal of cellular debris. $ED2^+$ and $ED3^+$ macrophages, which appear later,[2] are not considered to have important phagocytic effects, but rather to facilitate beneficial effects in regenerating muscle via their secretion of various cytokines,[5,6] such as the limitation of apoptosis and enhanced angiogenesis and muscle growth in regenerating tissue.

From the above it is clear that the timing of anti-inflammatory treatment is crucial. When prescribing anti-inflammatory treatment to alleviate the swelling and pain associated with inflammation, it is vital to suppress the actions of specific cell types only, and to do so for an optimal duration, to prevent detrimental effects on muscle regeneration. Although the literature is used as a guideline when prescribing NSAIDs, confusion is created by the use of vague, generic terms such as 'early', 'late', 'acute' and 'chronic', which may be interpreted in terms of days in some disciplines, and in weeks or months in others. It is important to know that in the case of anti-inflammatory treatment, the optimal treatment regimen is of very short duration and should be measured in *days*.

NSAIDs: When to treat

Studies on muscle injury[1,3] and skin-wound healing[7,8] are in agreement that limiting the extent of inflammation in the short term, during the 'neutrophil phase' of inflammation, could limit the extent of damage, while retaining the benefit of decreased pain and swelling. On the other hand, depletion of macrophages (i.e. the later phase of inflammation) has long been known to have negative consequences on the healing process.[9,10] Research using small animal and *in vitro* models (e.g. cell culture) has shown that short-term NSAID treatment during the early repair phase (1 - 3 days) may result in a reduction of inflammatory symptoms (swelling and pain), while if taken for a longer period, even as little as 5 days, it may in fact have negative effects on the healing of the injured muscle and result in excessive fibrosis,[11] which has been linked to slow and incomplete recovery of muscle strength,[12,13] slower resolution of inflammation,[14] and recurrent muscle tears.[15]

The literature holds enough evidence that NSAIDs will effectively reduce pain and swelling without having a negative effect on muscle recovery if their use is limited to a maximum of 3 days after injury, while treatment for even 2 days longer has definite detrimental effects. In conclusion, the need for recovery time should be stressed, specifically to athletes using over-the-counter NSAIDs almost chronically to reduce post-exercise pain and swelling, since they are putting themselves at risk of long-term effects of suboptimal recovery.

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Talent identification in sport: Practices and issues

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Sport is no different to other domains such as science, music and the arts, where the attainment of excellence is the primary goal of many individuals.[1] Expert performance is acknowledged by spectators and sponsors alike, but achievement of excellence is no easy feat as the gap between success and failure in elite competition continues to narrow and the weight of national pride and expectation continues to increase.[2] Consequently, the study of expertise in sport, together with the identification and development of future elite performers, has become a popular focus area within the sport sciences.[1]

A basic definition of talent identification (TI) encompasses the recognition of a natural endowment or ability of superior quality. But, identifying a talented athlete within sport is multifaceted and complex. Talent in sport is identified by characteristics that are at least partially genetically determined, affected by numerous environmental conditions and currently difficult to determine accurately.[3]

The disparity between practice and theory involved in TI has become apparent and, while researchers are currently closing this gap, the advent of gene mapping and the subsequent potential for gene testing and therapy have added a new dimension to this endeavour.

Systematic approaches to TI

Systematic TI is no new phenomenon. Several countries, in particular the former 'Eastern block' countries, have applied systematic TI since the 1960s and early 1970s with astounding results during the Olympics of 1972, 1976 and 1980. These successes were ascribed to their thorough TI processes adopted in the late 1960s.[4]

Western countries also initiated systematic TI programmes, albeit with their own unique variation and mostly without the associated political ideology. Australia was the first Western country to implement such a programme, the Sport Search Programme, in 1994.[5] South Africa, in an endeavour to find solutions for the disproportionate representation of the South African population in representative teams, commissioned research in the early nineties to investigate solutions to the problem.[6] An adapted version of the Australian sport search programme was subsequently applied in the late nineties, and follow-up sport-specific programmes involving selected national sport federations were planned, but all these efforts lost momentum with continuous changes in the national governance of sport.

Other countries such as the UK also adopted the Australian concept of TI and embarked on a systematic and organised approach. However, these systematic approaches to TI, although very inclusive, proved to be very expensive and the returns did not seem to justify the costs, especially for team sports. Subsequently, more focused approaches that rely on multidisciplinary inputs have been initiated with evidence of more success.[3]

Gene mapping and therapy for sports doping

The elucidation of the complete human genome with approximately 30 000 different genes has led to new possibilities, not only for the diagnosis and prevention of a wide variety of diseases, but also for the purpose of TI. Close to 200 genes, or loci linked to or associated with human performance and health-related fitness, have already been identified.[7] Testing such genes, some propose, can be a legitimate aspect of TI and training programme development – a valid adjunct to current physiological, biochemical and psychological testing.[8] Gene technology companies are already supplying testing kits for the purpose of identifying selected genes (e.g. www.gtg.com.au).

In addition, the knowledge of gene mapping may be used for the design of new therapeutics, including gene therapy, based on DNA sequence information. Gene therapy may not only be applied for the treatment of serious diseases, but also for less life-threatening situations or injuries such as sports injuries.[9] In addition, athletes may be able to use gene therapy to improve their bodies for better performance. Many genes with the potential to enhance athletic performance are available. The most relevant of these for performance enhancement are erythropoietin (EPO), growth factors, myostatin and endorphins.[9]

Gene therapy also opens the door for gene doping, a practice disapproved by both the International Olympic Committee … and the World Anti-Doping Agency.

Risks of gene doping and ethics involved in the detection thereof

A number of risks are associated with gene doping, especially where gene transfer vectors are produced in non-controlled laboratories.[9] Furthermore, the detection of gene doping is currently very difficult and evokes many ethical concerns. [10]

Conclusion

While the need for TI practices and the drive for countries to prove dominance at major international competitions remain, researchers are interrogating the scientific justification for current and past practices and are calling for more focused research in this area. For a more comprehensive evaluation of current practices see the academic review commissioned by Sport Scotland.[4] These endeavours to find more appropriate methods of TI will continue as long as the drive for success in the international arena persists. Although gene testing and gene therapy/doping have the potential to dominate TI in the future, the myriad of ethical issues and health risks of disreputable therapy practices may delay its impact.

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