What can athletes learn from intensive stress research?

HEAVY EXERCISE MEANS ELEVATED CORTISOL LEVELS. **DR PETER KOEPPEL** SHARES FRESH DATA WITH US, SHOWING THAT NUCLEOTIDE SUPPLEMENTATION CAN HELP ATTENUATE CORTISOL LEVELS POST RESISTANCE TRAINING.

In order to increase fitness, improve the capacity of the body, and to change the strength and the size of muscles, intensive training is a regular routine for athletes. This change is only possible because of the adaptability of the body and the muscles. Adaptation to different conditions is an important ability of the body, which enables it to adapt to increasing performances. Physical training forces the body to adapt to the stress of physical effort (1). The stress needs to be high enough to force the body into this adaptation: if the stress is too low, no adaptation occurs, but on the other hand, too high a stress increases the risk of injuries or over-training. Therefore, each training session needs to be properly planned to avoid negative effects.

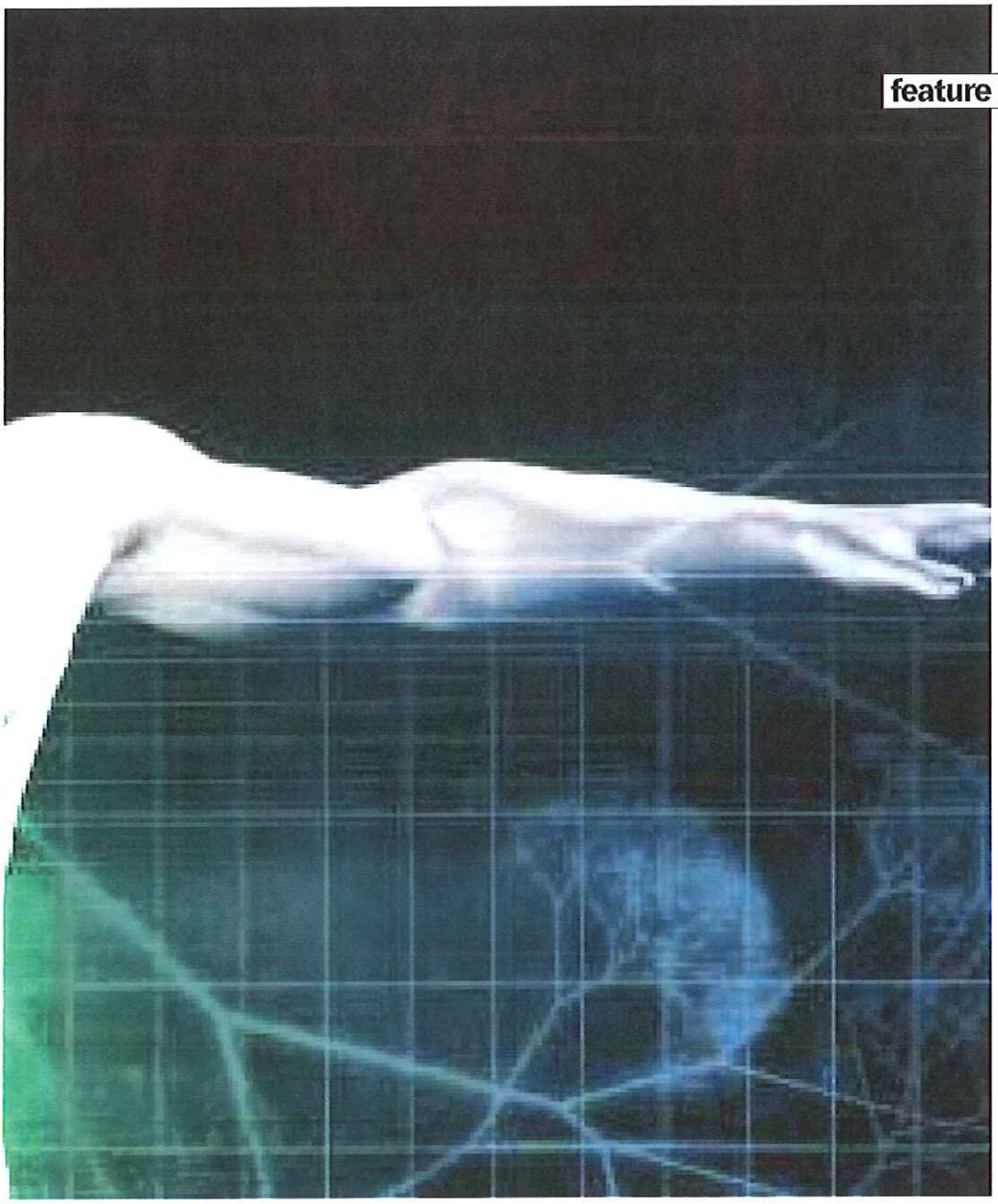
Training stress not only forces the body to adapt to physical forces, but can have negative effects on the body; e.g. an increased production of cortisol and consequently, suppression of the immune system. Studies have shown that moderate to high intensity exercise provokes an increased level of circulating cortisol (2).

Cortisol also increases blood sugar levels via gluconeogenesis and aids in the metabolism of fat, protein, and carbohydrates (3). Additionally, it decreases bone formation (3). Indirectly, cortisol plays an important role in liver and muscle glycogenolysis; the breaking down of glycogen to glucose-1-phosphate and glucose. Elevated levels of cortisol, if prolonged, can lead to proteolysis (breakdown of proteins) and muscle wasting (4).

The control of cortisol levels is of the greatest importance for athletes. Substances with the capacity to regulate the level of cortisol could enable athletes to train their body without impairment of the immune system and other organs in the body, and to increase performance in an efficient way.

Nucleotides and physiological benefits

Dietary nucleotides have been shown to improve the relationship between exercise, the immune system and host protection (5). The transport of energy in the body is fully dependent on the availability of



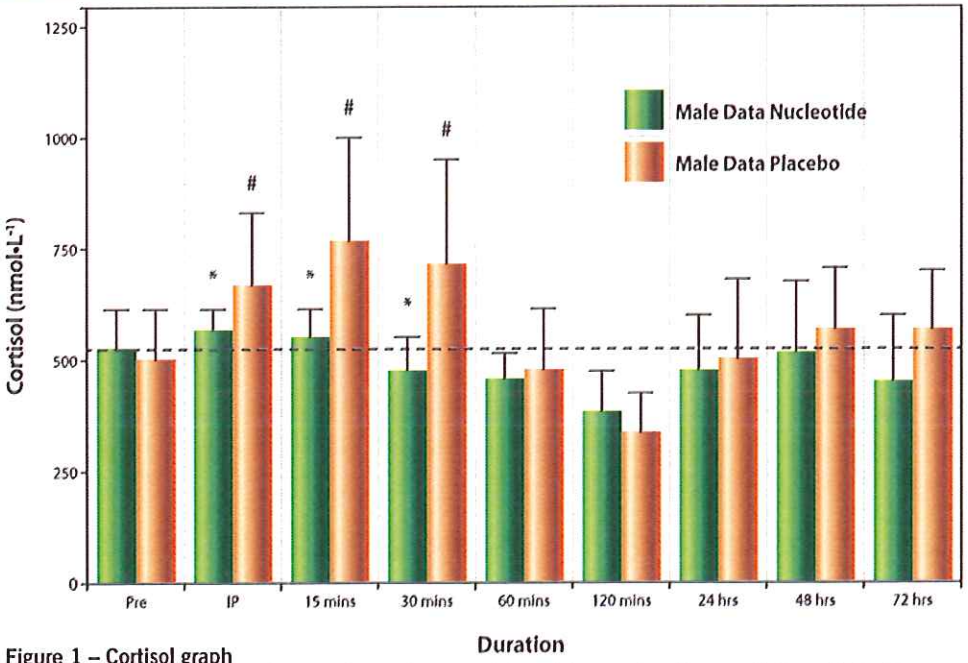


Figure 1 – Cortisol graph

Data are presented as means +/- SD. Nucleotide supplementation attenuated the cortisol response to resistance exercise in men. Post resistance exercise increases in cortisol concentrations were only observed in the placebo conditions.

* = Significantly different from corresponding placebo condition.

\# = Significantly different from corresponding PRE value.

Significance set at $p \leq 0.05$.

— level pre-exercise.

nucleotides in the form of ATP, GTP and UTP. Nucleotides also support oxygen supply in the body, leading to potentially diminished lactate levels in athletes. Critical too, is the digestion and the absorption of nutrients from the gut. Trials have shown that nucleotides improve the diversity of the gut flora, the gut health, and the length of the villi.

Nucleotides are involved in nearly all biological processes, including DNA and RNA synthesis, coenzyme synthesis, energy metabolism, cellular signalling and protein synthesis (6,7), and therefore also in tissue repair. The *de novo* production of nucleotides in some organs of the body is often insufficient to meet the needs of rapidly proliferating tissues and therefore only nucleotides from exogenous sources can fill this gap (8).

Therefore, supplementary nucleotides may be necessary to maintain immune function, tissue growth and cellular repair, all of which are affected by exercise (8).

Exercise significantly increases the demands on the immune system and can temporarily diminish immune cell function, mainly due to the increased levels of cortisol. Consequently, there has been a growing interest in the potential implications of nucleotide supplementation on exercise-induced immune responses. Trials done by McNaughton and colleagues have demonstrated that nucleotide supplementation can attenuate the immunosuppression that normally follows exercise (9,10). Following acute exercise bouts, serum and salivary immunoglobulin levels were higher with nucleotide supplementation, whereas cortisol levels were lower, hence explaining the reduced immunosuppression.

Other trials with athletes (11,12) showed enhanced natural killer cell (NKC) count and higher cytotoxicity after nucleotide supplementation. Nucleotides therefore have an influence on both humoral and innate immune reactions. It is known that the elevated immune activity supports the recovery from exercise (13).

In animal models, similar attenuated cortisol responses

to stressful stimuli have been observed by the supplementation of nucleotides (14). This has also been demonstrated in trials with racing horses (15), in which the cortisol levels in nucleotide supplemented animals were lower during the aerobic and anaerobic phases of the trial. During the same phases, higher oxygen uptake and increased expiration of CO_2 of treated horses could be measured, leading to lower lactate concentrations in the blood.

The previously mentioned studies (9,10,11,12) demonstrated the effects of nucleotide supplementation only immediately following acute exercise, but did not measure the effects of nucleotides during recovery in the days following. It is known that elevated cortisol levels over a prolonged period lead to an increase in protein degradation and a decrease in protein synthesis. It would therefore be interesting to follow the effects of nucleotides over a longer period.

A longer term nucleotide trial

In a new trial, the cortisol levels were analysed during a double blind, placebo controlled, cross over test after an acute bout of heavy resistance exercise (16).

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Ten male athletes underwent two supplementation and testing cycles, which were separated by a one-week washout period. The two treatment cycles consisted of a nucleotide* or placebo supplement, with the cycle order randomised and balanced. Each cycle began with a two week loading phase, in which subjects took the supplement while maintaining their normal exercise routines. Cortisol levels were measured before, immediately after the exercise, and at 15, 30, 60, 120 minutes, and 24, 48 and 72 hours post-exercise.

The results were quite striking. As shown in Figure 1 (on the previous page), the cortisol levels at 15 and 30 minutes post-exercise were significantly lower in the supplemented group compared to the placebo group. Whereas the cortisol levels in nucleotide supplemented athletes remained at the same level, a significant increase could be observed in the placebo group period up until 60 minutes post-exercise. This clearly confirms the earlier results of McNaughton and the racing horse trial in Belgium. It demonstrates that the supplementation of nucleotides is able to control or prevent an increase of cortisol after the high stress load of exercise training.

The most important outcome of the study was that nucleotide supplementation increased the peak force in the back squat isometric force test immediately after the exercise and at 24 hrs, 48 hrs and 72 hrs post-exercise. As shown in Figure 2 above, the isometric force in supplemented athletes did not change after acute heavy resistance exercise, whereas in not-supplemented athletes, the peak force was significantly reduced and they required 48 hours for full recovery. In the same trial, the creatine kinase (CK) values were also significantly lower in the treated group; it can therefore be postulated that the supplementation of nucleotides reduces exercise-induced muscle damage.

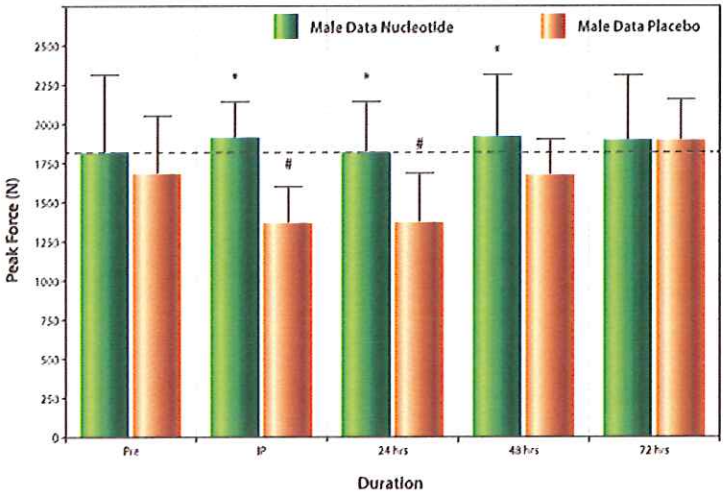

Figure 2 – Peak force graph

Data are presented as means +/- SD. Nucleotide supplementation attenuated the decrease in isometric force following the resistance exercise protocol in men. In nucleotide-supplemented men, no decrease in isometric force was observed.

* = Significantly different from corresponding placebo condition.

\# = Significantly different from corresponding PRE value.

Significance set at $p \leq 0.05$.

--- level pre-exercise.

"Nucleotide supplement facilitates a faster isometric force recovery during the first 48 hours"

Conclusions

It can be concluded that nucleotide supplementation lowers the stress response, reduces muscle damage and preserves force production capabilities after intensive resistance exercise, plus improves the recovery from strenuous exercise. All of these effects enable athletes to train hard with less negative side effects and to achieve speedier returns to training after strenuous competition. FSN

*Proprietary nucleotide (yeast extracts) supplement by ProBio AG, Augst, Switzerland.

About the author

Dr Peter Koeppel has a PhD in Biochemistry and Immunology. He was trained in Biochemistry with a special interest in clinical Immunology at the Institute of Virology at the University of Zürich. He then worked as a researcher in osteoarthritis and osteoporosis in a pharmaceutical company in Basel. Since 1989, he has been involved in producing special additives for human nutrition for ProBio Ltd, latterly becoming the managing director of this company in year 2000.

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