Doping with the anabolic steroid Stanozolol: experimental evaluation of the side effects in tendons

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Introduction
In competitive sports anabolic steroid hormones still seem to belong to the most frequently used drugs in doping, based on the positive tests published by the IOC accredited doping laboratories. Interestingly, among the anabolic steroid hormones detected by these laboratories the old compound Stanozolol is frequently found, although the drug was withdrawn from the market decades ago. The endocrine pharmacology of this compound clearly indicates that it may induce strong androgenic reactions. Since numerous individual reports claim that athletes who mostly take Stanozolol in suprapharmacological doses may suffer from tendon injuries it appeared expedient to design an animal experiment to investigate this phenomenon.

Methods
The proximal part of tendons of flexor digitorum longus muscles were taken from 6-8 week old female NMRI mice. To create a model of tendon loading mice were made to run a treadmill. The exercise was performed daily over periods up to 10 weeks. Each of 15 mice from exercised and unexercised mice received Stanozolol given by i.m injection in a dose of 3mg/kg body weight. The controls received sesame oil as placebo. Electron microscopy was done of proximal parts of the tendon near the muscle tendon junction and by morphometrical methods characteristic signs of collagen dysplasia in the tendons was calculated.

Results
In tendons which were both exercised and trained the greatest numerical density of collagen fibrils was achieved, but their volume fraction did not come up to the controls. This reduction is due to the accumulation of small fibrils with the consequence of dramatic changes in the distribution of collagen fibril diameters. The most striking result is the appearance of dysplastic collagen fibrils especially after long term treatment: Control tendons contain only up to 8% dysplastic collagen fibrils whereas trained and treated tendons display over 30% of dysplastic collagen fibrils.

Conclusion
Interestingly, there is no difference in volume fraction and numerical density of collagen fibrils in the tendons which were both exercised and given Stanozolol compared to those which were only exercised and received placebo. By far the most striking result is the appearance of dysplastic collagen fibrils after treatment with Stanozolol since biomechanical examinations of tendons with similar dysplastic collagen fibrils has provided evidence of a reduction in tensile strength. The overall ultrastructure of the tendons provide tentative evidence that Stanozolol may induce collagen abnormalities dependent on the duration of treatment: a direct effect of high doses of Stanozolol has, therefore, to be taken into account when considering clinical disorders of tendons and ligaments from high class athletes.

Fig. 1: High power electron microscopy of tendon collagen fibrils, note regular morphology
Fig. 2: Tendon collagen fibrils with characteristic signs of dysplastic changes