EFFECTS OF PHYSICAL EXERCISE ON THE PI3K/AKT/mTOR SIGNALING PATHWAY IN SKELETAL MUSCLE OF POSTMENOPAUSAL WOMEN
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The ability of skeletal muscle to respond to loading is maintained as we get older, but even physically active persons gradually lose muscle mass and strength (sarcopenia). So far the best remedy against sarcopenia is physical activity, which utilizes the responsiveness of muscle tissue to extracellular signals such as mechanical load, hormones, growth factors and cytokines. However, the molecular mechanisms which could be used to prevent sarcopenia are largely unknown. Recent evidence suggests that the PI3K/AKT/mTOR pathway participates in the regulation of muscle growth. The pathway is activated by IGF-1 or insulin, which in turn respond to exercise. Once the signaling cascade is turned on, the phosphorylation steps follow each other leading to hypertrophy.

Our purpose was to study the effects of power exercise on the PI3K/AKT/mTOR pathway in skeletal muscle of 50-60-year-old postmenopausal women. The participants were randomly assigned into exercise (Ex, n=8) and control (Co, n=9) groups. The exercises participated in a 1-year progressive physical training program that included supervised circuit training session twice a week and a series of exercises at home four days per week. The control subjects were advised not to change their daily routines or level of physical activity. Needle biopsy samples from the vastus lateralis muscle were obtained at baseline and after the intervention. Biopsies were used to detect gene expressions with genome wide BeadChip arrays (Illumina), from which we report here the results concerning the PI3K/AKT/mTOR signaling pathway.

The PI3K/AKT/mTOR pathway is initially activated by binding of IGF-1 to the IGF receptor or by binding of insulin to the insulin receptor. The expression of IGF-1 decreased in both study groups where as the expressions of IGF-1 and insulin receptors increased in the Ex group and decreased in the Co group. These changes were, however, not significantly different between groups. The expressions of insulin (p=0.025), p85, which is a component of PI3K complex (p=0.027), PDK1 (p=0.032) and AKT (p=0.051) were increased in the Ex group compared to the Co group, where they decreased. Also the downstream component of AKT, FOXO3 (p=0.013), was significantly upregulated in the Ex group compared to the Co group. Because liganded androgen and estrogen receptors may have an influence on the magnitude of the PI3K/AKT/mTOR signaling, we also examined if their expressions were affected by exercise. In group comparisons a significant difference was observed in the behavior of the androgen receptor (p=0.026), but not in the estrogen receptors.

In conclusion, progressive power training was found to effect the expression of several components of the PI3K/AKT/mTOR pathway as well as the expression of the androgen receptor. The observed mRNA level changes in the gene expressions presumably lead on to higher signal-