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Researchers pin down enzyme role in muscle 'aging'

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Researchers at the University of Birmingham have identified the role of an enzyme in muscle wasting, and associated age-related problems. They believe that inhibiting it could hold the key to developing ways of preventing, or reversing, the adverse effects.

The research, published in the *Journal of Clinical Endocrinology & Metabolism*, is a significant step in understanding the role played by the enzyme '11β-HSD1' in the degenerative effects of ageing - including sarcopenia (age related muscle wasting).

The expression of 11β-HSD1, responsible for activating the steroid hormone cortisol, was increased in the muscles of older females.

134 healthy volunteers, aged between 20-80, underwent physical and biochemical tests at a clinical research facility, including body composition analysis by DEXA, jump plate mechanography, grip strength analysis, baseline biochemical profiling, urine collection, and vastus lateralis muscle biopsy.

The findings show that expression of 11β-HSD1 in skeletal muscles is increased 2.72-fold in women aged over 60 years of age, compared to those aged between 20 and 40. In male participants, no difference was seen.

High levels of the enzyme aligned with increased levels of cortisol, reduced grip strength, insulin resistance and a poorer body composition

profile.

Dr Zaki Hassan-Smith, from the University of Birmingham, said, "As yet, we don't know why it appears to only occur in women, it is obviously an interesting area for further research. We are planning to look at whether hormones such as estrogens could be involved."

With many countries seeing emerging healthcare problems associated with an ageing population, the research team wanted to investigate novel ways of increasing the healthy life span - the years in which people can maintain active lifestyles without the debilitating impact of muscle wasting.

The research team were able to draw on expertise from both the University of Birmingham and Queen Elizabeth Hospitals Birmingham, and apply their knowledge of Cushing's Syndrome to a new problem.

Dr Hassan-Smith explained, "Looking at this particular enzyme seemed like an intriguing way forward. We knew how it works in relation to Cushing's Syndrome, which is characterised by similar symptoms, and thought it would be worthwhile applying what we knew to the ageing population."

Cushing's Syndrome is a rare disease caused by high cortisol levels, and those who suffer from the syndrome see marked changes in their body composition. The effects can be devastating for patients who can develop features such as muscle wasting and weakness, weight gain, thinning of the bones, diabetes, high blood pressure and heart disease.

At present there is no accepted pharmacological treatment for sarcopenia but pharmaceutical companies are developing and testing inhibitors of 11β-HSD1 with a focus on treatments for such conditions as diabetes.

The team is excited about taking the results of their study forward into future research, with one eye on adapting the inhibitors already in development to combat muscle ageing.

Dr Hassan Smith added, "The next stage is a 'proof of concept' study to look at the effects of these inhibitive pharmaceuticals on muscle function, before opening it up into a clinical trial. It's an as yet unexplored area that could yield beneficial results for a problem that is becoming more prevalent as our lifespans increase."

Provided by University of Birmingham