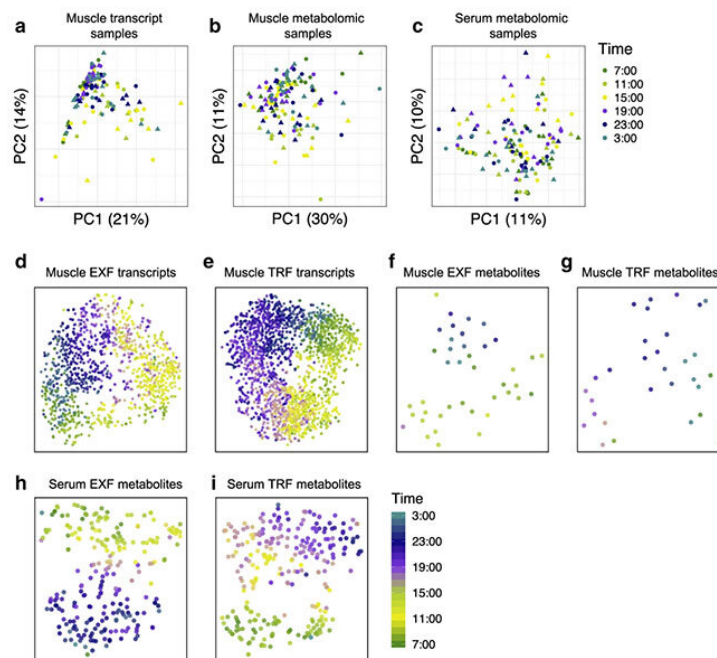


Time-restricted feeding improves health without altering the body's core clock

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Principal component analysis (PCA) of samples based on skeletal muscle genes (a), skeletal muscle metabolites (b), and serum metabolites (c), with color indicating sampling time. Circle indicates extended feeding (EXF), and triangle indicates time-restricted feeding (TRF). t-SNE clustering of periodic transcripts in skeletal muscle after EXF (d), and TRF (e). Periodic metabolites in skeletal muscle after EXF (f), and TRF (g), and serum metabolites after EXF (h), and TRF (i). n = 11 participants.

When it comes to metabolic health, it's not just what you eat, it's when

you eat it. Studies have shown that one effective means of losing weight and tackling obesity is to reduce the number of hours in the day that you eat. Time-restricted feeding—otherwise known as intermittent fasting—has also been shown to improve health even before weight loss kicks in.

The biological explanation for the phenomenon remains poorly understood. So scientists from the University of Copenhagen, the Australian Catholic University and Karolinska Institutet investigated the body's early adaptations to time-restricted feeding. Their study identified a number of key changes in the genetic activity of muscles, as well as the content of [muscle](#) fats and proteins, which could explain the positive impact of time-restricted feeding.

Novel insights on short-term time-restricted feeding

The study is the first time scientists have examined the oscillations of metabolites in skeletal muscle and in blood, as well as gene expression in skeletal muscle after time-restricted feeding. By focusing on the short-term and early effects of time-restricted feeding, the goal was to disentangle the signals that govern health from those associated with weight loss.

"We observe that the rhythm of skeletal muscle core clock genes is unchanged by time-restricted feeding, suggesting that any differences are driven more by diet, rather than inherent rhythms," says Postdoc Leonidas Lundell, from the Novo Nordisk Foundation Center for Basic Metabolic Research (CBMR) at the University of Copenhagen.

"We also see that the metabolite profile of [skeletal muscle](#) switches from being predominantly lipid based, to amino acid based, after time-restricted feeding. This coincides with changes in rhythmicity of amino acid transporters, indicating that part of the amino acid profile could be

due to absorption from the blood."

Research Fellow Evelyn Parr from the Mary MacKillop Institute for Health Research at the Australian Catholic University, adds "Our research is an important step towards understanding how time-restricted eating can improve [metabolic health](#), while bridging the gap between animal models and human intervention studies. It was important to capture these early metabolic responses before assessing what changes might occur after a longer period following a time-restricted feeding pattern."

Eating behavior does not impact the body's core clock

In the study, 11 men with overweight/obesity were assigned one of two eating protocols for a period of five days, either unrestricted feeding, or eight-hours of time restricted feeding. On the fifth day, samples were taken every four hours for a full day. After a 10-day break, they repeated the experiment following the other eating protocol.

After each intervention, the team of scientists studied the gene expression in muscles, as well as the profile of metabolites—molecules that are formed through metabolic processes—in the blood and muscles.

They discovered that time-restricted feeding changed the rhythmic concentration of metabolites in blood and muscle. Time-restricted feeding also influenced the rhythmic expression of genes expressed by muscle, particularly those responsible for helping the transport of [amino acids](#), the building blocks of proteins.

Critically, the study showed that time-restricted feeding did not alter the muscle's core clock—the cell's inbuilt metronome that regulates its daily cycle of activity. This suggests that the altered rhythmicity of metabolite and [gene expression](#) caused by time-restricted feeding could be

responsible for the positive health impact.

"Our findings open new avenues for scientists who are interested in understanding the causal relationship between time-restricted feeding and improved metabolic health. These insights could help develop new therapies to improve the lives of people who live with obesity," says Professor Juleen Zierath from Karolinska Institutet and CBMR at the University of Copenhagen.

More information: Leonidas S. Lundell et al, Time-restricted feeding alters lipid and amino acid metabolite rhythmicity without perturbing clock gene expression, *Nature Communications* (2020). [DOI: 10.1038/s41467-020-18412-w](https://doi.org/10.1038/s41467-020-18412-w)

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