

## Time restricted feeding attenuates metabolic dysregulation and demonstrates legacy effect in high fat diet rat model

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The global rise in obesity, particularly in developing countries, has become a critical public health concern due to its strong association with diabetes, hypertension, cardiovascular diseases, and certain cancers. The limited long-term efficacy of current nutritional and pharmaceutical therapies underscores the need for durable, efficient approaches that address underlying circadian disturbances and metabolic disorders. Core circadian genes like *Per1* and *Bmal1*, which control daily cycles of fat absorption, storage, and the metabolism of glucose, lipids, and cholesterol, are disrupted in obesity. A promising lifestyle modification that synchronises food intake with circadian rhythms and may enhance metabolic outcomes is time-restricted feeding (TRF). This study sought to understand how TRF affects metabolic profiles and gene expression in obese Wistar rats at the physiological and molecular levels. Fifteen rats were split into two groups: an experimental group (n=9) that was rendered obese by a high-fat diet (HFD; *ad libitum*) for two months, and a control group (n=6) that was fed a chow diet for six months. Six of the obese rats were converted to TRF (12-hour fasting from 8:00 pm to 8:00 am, followed by 12-hour HFD access) for three months, while three were put down for baseline evaluations. The findings revealed that, in comparison to controls, HFD-fed rats had significantly higher blood glucose and body weight ( $P=0.0263$ ,  $P=0.0089$ ), lower levels of melatonin and insulin ( $P=0.006$ ), lower HDL, and higher levels of total cholesterol (TC), triglycerides (TG), and LDL. The TRF intervention increased insulin, melatonin, TC, and HDL while decreasing body weight, blood glucose, TG, and LDL. Significantly, TRF exhibited circadian modulation by modulating the expression of *Per1* and *Bmal1*, and its metabolic benefits continued even after the return to *ad libitum* feeding. These results imply that TRF is a workable, non-pharmacological method of reducing metabolic and circadian disruptions associated with obesity, deserving of more research as a human preventive and treatment approach.

**Keywords:** *Bmal1*, *Per1*, High fat diet, TRF, Life style modification