Obesity: How inflammation influences appetite

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Credit: AI-generated image (disclaimer)

Sustained low-grade inflammation and an above-average appetite are commonly found in obese individuals. Therefore, it seems counterintuitive that the acute inflammation associated with many illnesses normally suppresses appetite. A team led by Weiping Han of the Singapore Bioimaging Consortium at A*STAR has used mice to

elucidate the molecular mechanisms that explain the different effects of chronic and acute inflammation on appetite. The study also helps to explain why obesity compromises appetite-suppression mechanisms.

The team's insights center around the different effects of acute inflammation and chronic obesity-related inflammation on the transcription of a gene expressed in neurons of the hypothalamus of the brain. A neurohormone called leptin controls transcription of the pro-opiomelanocortin (Pomc) gene, which suppresses appetite. Leptin is normally produced by fat cells at levels that ensure food intake matches energy expenditure. However, obese individuals often become insensitive to leptin, leading to a larger-than-normal appetite.

Previous studies by other groups and Han showed that in well-fed animals of normal body weight, leptin inhibited appetite by causing a protein called STAT3 to migrate to the nucleus of POMC neurons. The nuclear STAT3 suppressed appetite by sustaining normal levels of the Pomc gene's transcription.

In their recent study, again in well-fed animals of normal body weight, Han and co-workers found that acute inflammation—such as that caused by a viral infection—suppressed this translocation of STAT3, but more than compensated for the slight reduction in Pomc transcription by causing a protein called RELA to migrate to the nucleus. The nuclear RELA elevated the rate of Pomc transcription to above the normal level. This is consistent with the loss of appetite associated with most illnesses.

The researchers also found that in obese mice, methylation—a DNA modification that usually silences gene expression—prevented the nuclear RELA from binding to the Pomc promoter. RELA also blocked STAT3 from entering the nucleus.

"We believe that the lower than normal rates of Pomc transcription

caused by the combination of both of these effects accounts—at least, in part—for why obese individuals have a larger-than-normal appetite despite chronic inflammation," explains Han. He also notes that the role of RELA in sequestering STAT3 from Pomc promoter sequences provides a much-needed explanation of how chronic inflammation contributes to leptin resistance.

"We're hopeful that these insights into how different causes of inflammation interfere with leptin signaling might help to identify more effective and safer drugs to curb the appetite of obese individuals or better still, prevent leptin resistance," says Han.

More information: Shi, X. et al. Nuclear factor κB (NF-κB) suppresses food intake and energy expenditure in mice by directly activating the Pomc promoter. *Diabetologia* 56, 925–936 (2013). link.springer.com/article/10.1 … 07/s00125-013-2831-2

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