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New insight of obesity-driven NAFLD: Dysregulated "crosstalk" between multi-organ and the liver?

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Obesity plays a crucial role in the development of non-alcoholic fatty liver disease (NAFLD). However, the underlying mechanism for the pathogenesis of obesity-driven NAFLD remains largely obscure. Although the "multiple hit" theory provides a more accurate explanation of NAFLD pathogenesis, it still cannot fully explain precisely how obesity causes NAFLD. The liver is the key integrator of the body's energy needs, receiving input from multiple metabolically active organs. Thus, recent studies have advocated the "multiple crosstalk" hypothesis, highlighting that obesity-related hepatic steatosis may be the result of dysregulated "crosstalk" among multiple extra-hepatic organs and the liver in obesity. A wide variety of circulating endocrine hormones work together to orchestrate this "crosstalk". Of note, with deepening understanding of the endocrine system, the perception of hormones has gradually risen from the narrow sense (i.e. traditional hormones) to the broad sense of hormones as organokines and exosomes. In this review, we focus on the perspective of classic endocrine hormones (traditional hormones), organic endocrine hormones (organokines), and molecular endocrine hormones (exosomes), summarizing systematically how the three types of hormones mediate the dialogue between extra-hepatic organs and liver in the pathogenesis of obesity-related NAFLD.