Dietary triglycerides act on mesolimbic structures to regulate the rewarding and motivational aspects of feeding

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Circulating triglycerides (TG) normally increase after a meal but are altered in pathophysiological conditions such as obesity. Although TG metabolism in the brain remains poorly understood, several brain structures express enzymes that process TG-enriched particles, including mesolimbic structures. For this reason, and because consumption of high fat diet alters dopamine signalling, we tested the hypothesis that TG might directly target mesolimbic reward circuits to control reward-seeking behaviors. We found that the delivery of small amounts of TG to the brain through the carotid artery rapidly reduced both spontaneous and amphetamine-induced locomotion, abolished preference for palatable food, and reduced the motivation to engage in food-seeking behavior. Conversely, targeted disruption of the TG-hydrolyzing enzyme lipoprotein lipase specifically in the nucleus accumbens increased palatable food preference and food seeking behavior. Finally, prolonged TG perfusion resulted in a return to normal palatable food preference despite continued locomotor suppression, suggesting that adaptive mechanisms occur. These findings reveal new mechanisms by which dietary fat may alter mesolimbic circuit function and reward seeking.