Rewiring the damaged obese hypothalamus with polyunsaturated fats

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The apoptotic loss of hypothalamic neurons involved in the control of feeding and energy expenditure is believed to play an important role in the development and perpetuation of obesity. Studies have shown that similar to the subventricular zone of the lateral ventricles and the subgranular zone of the dentate gyrus, the hypothalamus presents constitutive and stimulated neurogenesis, suggesting that obesity-associated hypothalamic dysfunction could be repaired. Here, we explore the hypothesis that ω-3 polyunsaturated fatty acids (PUFAs) induce hypothalamic neurogenesis. Both in the diet and injected directly into the hypothalamus, PUFAs are capable of increasing hypothalamic neurogenesis to levels similar or superior to the effect of BDNF. Most of the neurogenic activity induced by PUFAs results in increased numbers of POMC but not NPY neurons and is accompanied by increased expression of BDNF and GPR40. The inhibition of GPR40 is capable of reducing the neurogenic effect of docosahexaenoic acid while the inhibition of BDNF results in the reduction of global cell proliferation in the hypothalamus. Thus, PUFAs emerge as a potential dietary approach to correct obesity-associated hypothalamic neuronal loss.