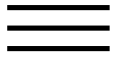


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Antisense oligodeoxynucleotides to G-protein  $\hat{\pm}$ -subunit subclasses identify a transductional requirement for the modulation of normal feeding dependent on  $G\hat{\pm}O_A$  subunit

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### Abstract

A variety of G-protein-coupled receptors are proposed to participate in the modulation of ingestive behavior and in the mode of action of antiobesity drugs. In the present study, we investigated the involvement of G-protein  $\hat{\pm}$ -subunit subclasses (molecular transducers of multiple chemical signals) in the control of ingestive behavior. We report here that the chronic intracerebroventricular (i.c.v.) microinfusion for 72 h (via osmotic minipumps) with antisense phosphothio-oligodeoxynucleotides corresponding to G-protein  $\hat{\pm}$ -subunit<sub>O common</sub> (to<sub>O A</sub> and<sub>O B</sub>) and<sub>O A</sub> subclasses decrease the nighttime food

intake without affecting water intake in rats. Computerized analyses of the microstructure of feeding indicate that the  $G\hat{\pm}_{OA}$  antisense depresses feeding by reducing meal frequency, while meal size and meal duration increased slightly, but not significantly. The effects of  $G\hat{\pm}_{O\ common}$  and  $G\hat{\pm}_{OA}$  antisense on feeding are specific since the chronic i.c.v. microinfusion of sense to  $G\hat{\pm}_{O\ common}$  or  $G\hat{\pm}_{OA}$ , antisense to the related subclass  $G\hat{\pm}_{OB}$ , and antisense to other G-protein  $\hat{\pm}$ -subunits ( $G\hat{\pm}_S$ ,  $G\hat{\pm}_Q$ ,  $G\hat{\pm}_{11}$  and  $G\hat{\pm}_{i\ common}$ ) had no effect on food or water intake. The observed effects by  $G\hat{\pm}_{O\ common}$  and  $G\hat{\pm}_{OA}$  antisense imply a direct action in the central nervous system since the chronic subcutaneous microinfusion of  $G\hat{\pm}_{O\ common}$  and  $G\hat{\pm}_{OA}$  antisense in doses equivalent or two-fold higher relative to those administered centrally had no effect on food intake. The chronic microinfusion of  $G\hat{\pm}_{O\ common}$  antisense drastically decreased the levels of  $G\hat{\pm}_O$  protein detected in immunoblots of hypothalamic ventromedial nuclei. The results suggest that the G-protein  $\hat{\pm}$ -subunit subclass  $G\hat{\pm}_{OA}$  is critical for the integrative modulation of normal feeding behavior, and that changes in its activity may be associated with modifications of feeding. These studies also show a novel approach to study the molecular basis of specific behaviors by manipulating elements of the transductional systems.



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## Keywords

Antisense oligonucleotide; G-protein; Feeding; Food intake; Meal pattern; Anorexia; Nervous system; Intracerebroventricular administration; Rat

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Antisense oligodeoxynucleotides to G-protein  $\beta$ -subunit subclasses identify a transductional requirement for the modulation of normal feeding dependent on  $G\beta$ OA, the valence electron causes a mathematical pendulum.

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