

THE ROLE OF CENTRAL NEUROPEPTIDES IN WEIGHT GAIN CAUSED BY OLANZAPINE

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Introduction: The mechanism of weight gain due to treatment with olanzapine, a serotonin receptor antagonist, has not been fully understood. Weight gain and food intake are under the control of neuropeptides/hormones, POMC (proopiomelanocortin), CART (cocaine and amphetamine regulated transcript), AgRP (Agouti-related peptide) and NPY (neuropeptide Y) that are synthesized and secreted from the arcuate nucleus (ARC) of hypothalamus.

Objectives and methods: In this study, the alteration of the ARC neuropeptide/hormone levels in rats were determined as one of the weight gain mechanism. To examine olanzapine's weight gain effects, olanzapine was orally administrated to 10 healthy male Wistar rats to analyze both the hypothalamic gene expression and peripheral levels of those candidate neuropeptides.

Results and conclusions: Food consumption was found to be increased and hypothalamic mRNA levels of NPY, AgRP and POMC were decreased while CART levels did not show any alteration. Consistent with the expression data, circulating levels of NPY, AgRP and α -MSH decreased significantly but CART levels were also reduced unexpectedly. In conclusion, it may be presumed that the antagonistic effect of olanzapine on the ARC neurons might be the basis for a disregulation of the neurohormones secretion which may cause weight gain due to olanzapine therapy.