

## 論 文 要 旨

Antagonism for NPY signaling reverses cognitive behavior defects  
induced by activity-based anorexia in mice

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Patients with AN often express psychological symptoms such as body image distortion, cognitive biases, abnormal facial recognition, and deficits in working memory. However, the molecular mechanisms underlying the impairment of cognitive behaviors in AN remain unknown.

In the present study, we measured cognitive behavior using novel object recognition (NOR) tasks and mRNA expressions in hypothalamic neuropeptides in female C57BL/6J mice with activity-based anorexia (ABA). Additionally, we evaluated the effects of antagonists with intracerebroventricular (icv) administration on the impairment of cognitive behavior in NOR tasks.

Our results showed that NOR indices were lowered, subsequently increasing mRNA levels of agouti-related peptide (AgRP) and neuropeptide Y (NPY), and c-Fos- and AgRP- or NPY-positive cells in the hypothalamic arcuate nucleus in ABA mice. We also observed that icv administration of anti-NPY antiserum (2  $\mu$ l), anti-AgRP antibody (0.1  $\mu$ g), and Y5 receptor antagonist CPG71683 (15 nmol) significantly reversed the decreased NOR indices.

Therefore, our results suggest that increased NPY and AgRP signaling in the brain might contribute to the impairment of cognitive behavior in AN.