(Form 13)

Summary of Thesis Examination

Report No.	Diploma No. 624	Applicant	Natasya Trivena Rokot

Examination Committee Members				
	Chief Examiner	KUWAKI Tomoyuki	Degree	Doctor of Philosophy in Medical Science
	Examiner	OKUNO Hiroyuki	Examiner	HORIUCHI Masahisa
	Examiner	TAGAWA Yoshiaki	Examiner	SAGIYAMA Ken'ichiro

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

(神経ペプチドYのシグナル伝達系の拮抗は、活動性拒食症モデルマウスにおける認識機能低下を改善する)

Anorexia nervosa (AN) is a serious eating disorder that often occurs in adolescent women and has a higher comorbidity rate with psychiatric disorders and suicide attempts compared to other psychiatric disorders. Patients with AN often express psychological symptoms such as body image distortion, cognitive biases, abnormal facial recognition, and deficits in working memory. The molecular mechanisms underlying the impairment of cognitive behaviors in AN remain unknown. This study aimed to investigate the relationship between central neuropeptides associated with feeding behavior and the deficiency of cognition behaviors in a novel object recognition (NOR) task in ABA model mice.

Cognitive behavior was measured using the NOR task and the mRNA expressions in hypothalamic neuropeptides of female C57BL/6J mice with activity-based anorexia (ABA) was measured using RT-PCR. The effects of antagonists with intracerebroventricular (ICV) administration on the impairment of cognitive behavior in NOR tasks were evaluated. This research 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. ICV administration of anti-NPY antiserum (2 μl), anti-AgRP antibody (0.1 μg), and Y5 receptor antagonist CPG71683 (15 nmol) significantly reversed the decreased NOR indices. Therefore, this experiment suggests that increased NPY and AgRP signaling in the brain might contribute to the impairment of cognitive behavior in AN.

Hence, we confirm that this study is valuable as a degree thesis.