

# Studies on the elucidation of central functions of taurine to regulate body temperature, food intake and stress response in neonatal chicks

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論 文 名	Studies on the elucidation of central functions of taurine to regulate body temperature, food intake and stress response in neonatal chicks (ニワトリヒナの体温、摂食およびストレス応答を制御するタウリンの中枢機能の解明に関する研究)
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### 論 文 審 査 の 結 果 の 要 旨

Environmental stressors in poultry such as heat stress, social isolation stress, cold stress, etc. negatively affect poultry performance, health and welfare. Amino acids are getting attention nowadays as a novel approach to mitigate stress responses in poultry. In this study, novel roles and functional mechanisms of taurine have been investigated to mitigate stress response in neonatal chicks.

First, the thermoregulatory role of taurine was examined through intracerebroventricular (ICV) injection of taurine in neonatal chicks. ICV taurine was found to induce dose-dependent hypothermia and reduced food intake in neonatal chicks under control thermoneutral temperature (CT). Further, it was found that taurine-induced hypothermia was attenuated by co-injection of picrotoxin (inhibitor of  $\gamma$ -aminobutyric acid A (GABA<sub>A</sub>) receptor), which indicates that taurine mediates hypothermia via GABA<sub>A</sub> receptor. Central taurine further changed plasma metabolites under high ambient temperature (HT), suggesting that brain taurine may regulate peripheral metabolism under HT.

Second, the thermoregulatory behaviors following ICV taurine administration were investigated in heat-exposed chicks under fasting condition and the involvement of mitochondrial thermogenic genes in the process was examined. Central taurine afforded thermotolerance under 35°C at 30 min after central injection. In addition, the thermotolerance effect of taurine appeared until the studied period of 15 min under 40°C with rapid initiation of heat dissipation behaviors: panting and wing dropping, compared with control birds. Central taurine upregulated avian uncoupling protein and avian peroxisome proliferator-activated receptor  $\gamma$  coactivator-1 $\alpha$  under CT and HT. However, avian adenine nucleotide translocase and carnitine palmitoyltransferase-I in chicks were downregulated under CT and HT. These results elucidated a novel role of taurine to afford thermotolerance, which could influence mitochondrial thermogenic gene expressions.

Third, the behavioral responses of brain taurine have been clarified along with the thermoregulatory role. Central taurine attenuated hyperthermia and stress behaviors in chicks induced by social isolation stress and corticotropin-releasing factor through inducing sedative and hypnotic effects. The mechanism was likely to involve the repartitioning of amino acids to different metabolic pathways. In particular, brain leucine, isoleucine, cysteine, glutamate and glycine might have been mobilized to cope with acute stressors in response to central taurine.

Forth, the roles of brain amino acid and monoamine metabolisms in taurine-induced hypothermia and anorexia were investigated. It was found that central taurine increased diencephalic tryptophan (the precursor of serotonin (5-HT)), 5-HT and its metabolite 5-hydroxyindoleacetic acid concentrations. Moreover, central taurine decreased the diencephalic concentration of tyrosine (the precursor of L-DOPA, which converts to dopamine and norepinephrine (NE)). However, the NE concentration in the brainstem and its metabolite 3-methoxy-4-hydroxyphenylglycol in both the brainstem and diencephalon were increased after 30 min following central injection of taurine. It was further found that fusaric acid (dopamine hydroxylase inhibitor) completely and para-chlorophenylalanine (tryptophan hydroxylase inhibitor) partially attenuated taurine-induced hypothermia. These results indicate that NE and 5-HT mediate taurine-induced hypothermia, but 5-HT alone may be linked with taurine-induced anorexia.

In summary, this thesis provided a novel nutritional factor, taurine to alleviate heat stress and isolation-stress response in chicks. Furthermore, the central regulatory mechanisms of taurine provided a better understanding about thermoregulation, appetite regulation and stress response, which has far-reaching implications in a multitude of species and biological contexts. Therefore, this research deserves a degree, Doctor of Philosophy (Agricultural Science).