授与機関名　順天堂大学

学位記番号　甲第 110 号

Signal transducer and activator of transcription 3 involved in stress-induced high blood pressure and its prevention through exercise in rats

（ラットのストレス誘発性血圧上昇と運動によるその予防におけるシグナル伝達・転写活性化因子 3 の関与）

冨田　圭佑（とみた　けいすけ）

博士（スポーツ健康科学）

Abstract

Chronic stress causes elevated blood pressure, whereas regular exercise has anti-stress and anti-hypertensive effects. However, the mechanisms of stress-induced hypertension and preventive effects through exercise remain unknown. To examine these mechanisms, we investigated the molecular basis within the amygdala involved in autonomic blood pressure regulation. The effects of a three-week restraint stress and daily voluntary exercise against stress on cardiovascular parameters and gene expression profiles in the amygdala were examined using a microarray method. Moreover, candidate genes were selected from differentially expressed genes; the localization of their expression within the central nucleus of the amygdala and their roles in cardiovascular regulation were examined using siRNA transfection and radiotelemetry. Compared with controls, chronic restraint stress caused decreased signal transducer and activator of transcription 3 (*Stat3*) expression in the amygdala ($p < 0.01$), whereas voluntary exercise improved *Stat3* expression to normal levels. Immunohistochemical staining revealed STAT3 expression in neurons in the amygdala; inhibition of this using siRNA increased the mean arterial pressure ($p = 0.04$). However, spontaneous baroreflex gain and low- and high-frequency components of heart rate variability were unaffected by *Stat3* inhibition. In the amygdala, *Stat3* regulates the blood pressure levels and is possibly involved in blood pressure elevation in response to chronic stress and its improvement by voluntary exercise.