

一方、D-Leu であっても、至適濃度を外れた場合には添加効果を発揮しなかった。また、D-Leu 以外の D-アミノ酸には添加効果は観察されなかったことから、D-Leu はプリオン化抑制活性において特異性を有していることが明らかになった。さらに、本濃度における D-Leu は細胞毒性を有さないことも明らかにした。

以上の結果から、本研究による D-Leu のプリオン化抑制効果の発見は、新たなプリオン治療薬の可能性を示すものである。

P2-31.

Selective vulnerability and dispersion of dentate granule cells and their progenitors in pilocarpine-induced status epilepticus rat model

(大学院博士課程4年組織・神経解剖学分野)

○上森 健至

(大学 組織・神経解剖学分野)

戸田 景子、石 龍徳

Pilocarpine-induced status epilepticus model in rats has been commonly used to study the mechanisms of human temporal epilepsy. The epileptic seizures not only cause abnormal cellular organization in the dentate gyrus, but also increase neurogenesis of dentate granule cells. Here we examined the structural changes including neurogenesis in seizures-induced rats.

In rats displayed seizure activity, selective loss of Prox1 expression was observed only in the suprapyramidal blade of dentate granule cell layer. The changes were remarkable at the middle of septo-temporal axis in hippocampus. Furthermore, a few PSA+/Prox1+ cells appear to migrate from the subgranular zone to the molecular layer. These results suggest that the granule cell layer has distinct subdivisions along the septo-temporal axis, and in infra- and suprapyramidal blades in terms of the vulnerability to epileptic seizures and seizure-induced neurogenesis.

P2-32.

Apollon is upregulated by Humanin

(大学：薬理学分野)

○橋本 祐一、竹下 裕二、外山 由夏

松岡 正明

(大学：麻酔科学分野)

竹下 裕二、内野 博之

Humanin (HN), a short bioactive peptide consists of 24 amino acids, inhibits a variety of cell deaths. HN-mediated inhibition of neuronal cell death, caused by an Alzheimer's disease (AD)-linked mutant gene occurs via binding of HN to its heterotrimeric HN receptor (htHNR), which results in the activation of the Janus-associated kinases (JAKs) and signal transducer and activator and transcription 3 (STAT3) signaling pathway. A previous study demonstrated that the HN-induced activation of the htHNR/JAK2/STAT3 signaling pathway leads to increased expression of SH3 domain-binding protein 5 (SH3BP5), which is an essential effector of HN's anti-cell death activity in some cultured neuronal cells. However, it remains unknown whether SH3BP5 is the sole effector of the HN signaling pathway via htHNR/JAKs/STAT3. Here we show that the HN signaling pathway via htHNR/JAKs/STAT3 increased the expression levels of mRNA and protein of Apollon, an unusual member of the inhibitors of apoptosis proteins, and that overexpression of Apollon inhibits neuronal death, caused by a London-type familial AD-linked mutant (V642I) of amyloid β precursor protein. Overall, the results indicate that expression of Apollon is upregulated by HN and Apollon could be an effector of HN in a context-dependent manner.

P2-33.

Temporal progression of hypothalamic patterning by BMP

(BMPによる視床下部のパターン形成進行)

(大学：組織・神経解剖学分野)

○大山 恭司、石 龍徳

Hypothalamus plays a key role in homeostasis, yet it is