

発達脳におけるシナプス除去と機能成熟に関与するシグナル伝達系

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Research Project

All ▼

Project/Area Number

12053226

Research Category

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Allocation Type

Single-year Grants

Review Section

Biological Sciences

Research Institution

Kanazawa University

Principal Investigator

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Project Period (FY)

2000 – 2004

Project Status

Completed (Fiscal Year 2004)

Budget Amount *help

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Fiscal Year 2004: ¥11,600,000 (Direct Cost: ¥11,600,000)

Fiscal Year 2003: ¥11,900,000 (Direct Cost: ¥11,900,000)

Fiscal Year 2002: ¥11,700,000 (Direct Cost: ¥11,700,000)

Fiscal Year 2001: ¥12,800,000 (Direct Cost: ¥12,800,000)

Fiscal Year 2000: ¥12,200,000 (Direct Cost: ¥12,200,000)

Keywords

Research Abstract

本研究では、発達期小脳でみられる登上線維シナプス除去と機能成熟の分子機構を解明することを目標とし、種々の自然発生ミュータントマウスおよび遺伝子改変マウスの解析を行ってきた。本年度は、高閾値型のP/Qタイプカルシウムチャンネルを形成する $\alpha 1A$ サブユニットのノックアウトマウス($\alpha 1A^{-/-}$)と、抑制性伝達物質のGABA合成酵素GAD67のノックアウトマウスと野生型マウスとのヘテロマウス(GAD67 $+/ -$)を調べた。生後3~4週目の $\alpha 1A^{-/-}$ では、80%以上のプルキンエ細胞が複数の登上線維による多重支配を受けていることが電気生理学的及び形態学的解析の結果明らかになった。生後1日目からの発達の様子を電気生理学的に詳細に解析した結果、 $\alpha 1A^{-/-}$ では、生後10日までの過剰な登上線維シナプス除去(前期シナプス除去過程)が著しく障害されていることが判明した。一方、生後10日から16日の間の除去(後期シナプス除去過程)は正常におこった。これから、P/Qタイプカルシウムチャンネルを介するプルキンエ細胞へのカルシウム流入が、前期シナプス除去過程に必須であり、後期シナプス除去過程には別の機構が関与することが示唆された。GAD67 $+/ -$ では、成熟しても多重登上線維支配を受けるプルキンエ細胞の割合が野生型マウスに比べて明らかに高いという予備的結果を得た。このGAD67 $+/ -$ の生後1日目からの発達を電気生理学的および形態学的に詳細に解析するとともに、もうひとつのGABA合成酵素であるGAD65のノックアウトマウスを調べ、登上線維シナプス除去と機能成熟に対する抑制性シナプス入力役割を明らかにするのが今後の課題である。

Report (5 results)

- 2004 Annual Research Report
- 2003 Annual Research Report
- 2002 Annual Research Report
- 2001 Annual Research Report
- 2000 Annual Research Report

Research Products (67 results)

All	2005	2004	Other
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All	Journal Article (10 results)	Publications (57 results)
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- [Journal Article] Phospholipase C β serves as a coincidence detector through its Ca²⁺ dependency for triggering endocannabinoid signal. **2005** ▾
- [Journal Article] GABAergic activation of an inwardly rectifying K⁺ current in mouse cerebellar Purkinje cells. **2005** ▾
- [Journal Article] Two distinct classes of muscarinic action on hippocampal inhibitory synapses : M₂-mediated direct suppression and M₁/M₃-mediated indirect suppression through endocannabinoid signaling. **2004** ▾
- [Journal Article] Distinct roles of G α_q and G α_{11} for Purkinje cell signaling and motor behavior. **2004** ▾
- [Journal Article] Altered agonist sensitivity and desensitization of neuronal mGluR1 responses in knock-in mice by a single amino acid substitution at the PKC phosphorylation site. **2004** ▾
- [Journal Article] Ca²⁺ activity at GABA_B receptors constitutively promotes metabotropic glutamate signaling in the absence of GABA. **2004** ▾
- [Journal Article] A novel action of stargazin as an enhancer of AMPA receptor activity. **2004** ▾

- [Journal Article] Signaling complex formation of phospholipase C β 4 with mGluR1a and IP3 receptor at the perisynapse and endoplasmic reticulum in the mouse brain. 2004
- [Journal Article] Retrograde modulation of synaptic transmission mediated by endogenous cannabinoids. 2004
- [Journal Article] Calcium-dependence of native metabotropic glutamate receptor signaling in central neurons. 2004
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