

# Mode of action and physiological significance of endogenous cannabinoids as a retrograde messenger at central synapses

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## 2004 年度 研究成果報告書概要

## シナプスにおける逆行性伝達物質としての内因性カンナビノイドの作用機構と生理的意義

研究課題

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研究代表者	狩野 方伸 金沢大学, 医学系研究科, 教授 (40185963)
研究分担者	少作 隆子 (OHNO Takako) 金沢大学, 医学系研究科, 助教授 (60179025) 田端 俊英 金沢大学, 医学系研究科, 助手 (80303270)
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キーワード	逆行性シグナル / カンナビノイド / シナプス伝達 / 小脳 / 海馬 / カルシウム / CB1受容体 / Gq結合型受容体
研究概要	<p>マリファナの活性成分であるΔ9-テトラヒドロカンナビノールは、中枢神経系に広く分布するCB1カンナビノイド受容体を介して作用を発現する。CB1受容体に対する内因性のリガンド(内因性カンナビノイド、以下eCBと略す)の候補として、アナンタミドと2-アラキドノイルグリセロールがある。CB1は中枢ニューロンのシナプス前線維に局在し、その活性化によって伝達物質放出の減少が起こる。しかし、本研究開始時点で、eCBがどのような刺激によって生成され、どのような生理機能を果たすかという最も重要な点についてはほとんど明らかにできていなかった。本研究では、eCBのシナプス伝達における役割を主として電気生理学的手法を用いて調べ、以下の結果を得た。</p> <p>海馬神経細胞および小脳プルキンエ細胞において、シナプス後細胞の脱分極と細胞内Ca<sup>2+</sup>濃度上昇によりeCBが放出され、逆行性に抑制性および興奮性シナプス終末のCB1受容体に作用して伝達物質放出の一過性減少が起こることを明らかにした。また、グループI代謝型グルタミン酸受容体や、M<sub>1</sub>及びM<sub>3</sub>ムスカリニックアセチルコリン受容体などのGq結合型受容体の活性化によってeCB放出が起こり、逆行性にCB1受容体に作用して伝達物質放出の一過性減少が起こることを発見した。さらに、海馬培養細胞において、単独ではeCB放出を起こさない程度の弱いM<sub>1</sub>/M<sub>3</sub>受容体の活性化と弱い脱分極を同時に与えると、eCBが効率よく産生された。これは、海馬神経細胞に存在するフォスフォリパーゼCB1(PLCB1)の酵素活性が、M<sub>1</sub>/M<sub>3</sub>受容体の活性化と細胞内Ca<sup>2+</sup>の両方に依存することが原因である。したがって、PLCB1はコリナージック入力(シナプス前活動)と細胞内Ca<sup>2+</sup>濃度上昇(シナプス後神経活動)の同期性検出分子として機能することが明らかになった。</p>

## 研究成果 (70件)

	すべて	2005	2004	2003	2002	2001
	すべて	雑誌論文	図書			
[雑誌論文] Phospholipase CB serves as a coincidence detector through its Ca <sup>2+</sup> dependency for triggering endocannabinoid signal.					2005	▼
[雑誌論文] GABAergic activation of an inwardly rectifying K <sup>+</sup> current in mouse cerebellar Purkinje cells.					2005	▼
[雑誌論文] Phospholipase Cα serves as a coincidence detector through its Ca <sup>2+</sup> dependency for triggering endocannabinoid signal.					2005	▼
[雑誌論文] GABAergic activation of an inwardly rectifying K <sup>+</sup> current in mouse cerebellar Purkinje cells.					2005	▼
[雑誌論文] ORP150/HSP12A regulates Purkinje cell survival : A role for ER stress in cerebellar development.					2004	▼
[雑誌論文] P/Q-type Ca <sup>2+</sup> channel α1A regulates synaptic competition on developing cerebellar Purkinje cells.					2004	▼
[雑誌論文] Two distinct classes of muscarinic action on hippocampal inhibitory synapses : M <sub>2</sub> -mediated direct suppression and M <sub>1</sub> /M <sub>3</sub> -mediated indirect suppression through endocannabinoid signaling.					2004	▼
[雑誌論文] Distinct roles of Ga <sub>q</sub> and Ga <sub>11</sub> for Purkinje cell signaling and motor behavior.					2004	▼
[雑誌論文] 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	▼
[雑誌論文] Ca <sup>2+</sup> activity at GABA <sub>B</sub> receptors constitutively promotes metabotropic glutamate signaling in the absence of GABA.					2004	▼
[雑誌論文] A novel action of stargazin as an enhancer of AMPA receptor activity.					2004	▼
[雑誌論文] Signaling complex formation of phospholipase Cβ4 with mGluR1α and IP3 receptor at the perisynapse and endoplasmic reticulum in the mouse brain.					2004	▼
[雑誌論文] Retrograde modulation of synaptic transmission mediated by endogenous cannabinoids.					2004	▼
[雑誌論文] Calcium-dependence of native metabotropic glutamate receptor signaling in central neurons.					2004	▼

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[雜誌論文] Distinct roles of G $\alpha_q$ and G $\alpha_{11}$ for Purkinje cell signaling and motor behavior.	2004	▼
[雜誌論文] 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	▼
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[雜誌論文] Signaling complex formation of phospholipase C $\delta$ 4 with mGluR1a and IP <sub>3</sub> receptor at the perisynapse and endoplasmic reticulum in the mouse brain.	2004	▼
[雜誌論文] Retrograde modulation of synaptic transmission mediated by endogenous cannabinoids.	2004	▼
[雜誌論文] Calcium-dependence of native metabotropic glutamate receptor signaling in central neurons.	2004	▼
[雜誌論文] Effects of insulin-like growth factor I on climbing fiber synapse elimination during cerebellar development.	2003	▼
[雜誌論文] Insulin-like growth factor-I as a promoting factor for cerebellar Purkinje cell development.	2003	▼
[雜誌論文] Functional differentiation of multiple climbing fiber inputs during synapse elimination in the developing cerebellum.	2003	▼
[雜誌論文] Postsynaptic M <sub>1</sub> and M <sub>3</sub> receptors are responsible for the muscarinic enhancement of retrograde endocannabinoid signaling in the hippocampus.	2003	▼
[雜誌論文] Impaired motor coordination in mice lacking neural recognition molecule NB-3 of the contactin/F3 subgroup.	2003	▼
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[雜誌論文] Heterogeneous intrinsic firing properties of vertebrate retinal ganglion cells.	2002	▼
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[雜誌論文] Cooperative endocannabinoid production by neuronal depolarization and group I metabotropic glutamate receptor activation.	2002	▼
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[雜誌論文] Presynaptic cannabinoid sensitivity is a major determinant of depolarization-induced retrograde suppression at hippocampal synapses.	2002	▼
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[雜誌論文] mGluR1 in cerebellar Purkinje cells is required for normal association of temporally contiguous stimuli in classical conditioning.	2002	▼
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