

(様式1)

公益社団法人日本栄養・食糧学会 研究業績

<学 会 賞>

1. 候補者

研究題目:(和)	食物摂取認知とアミノ酸恒常性維持に関わる脳機能の研究		
(英)	Research on the brain mechanisms of recognition for food intake and maintenance of amino acid homeostasis in rats		
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学 位:	農学(東京大学) 医学(名古屋大学)	最終学歴:	東京大学農学部畜産獣医学科
専門分野	①栄養生理学、②栄養生化学、③分子栄養学、④公衆栄養学、⑤臨床・病態栄養学、⑥食生態学、⑦調理科学、⑧食品化学・食品分析学、⑨食品機能学、⑩食品工学、⑪食品加工・流通・貯蔵学、⑫食品衛生・安全学、⑬生理学、⑭生化学、⑮分子生物学、⑯臨床医学(内科系)、⑰臨床医学(外科系) ⑱その他:脳科学、行動科学		
履 歴	ペンシルベニア大学 Monell chemical senses center(1977-79)訪問研究員、鳥居食情報調節プロジェクト((ERATO, 化学技術振興機構(JST))総括責任者(1990-96)、味の素(株)名誉理事		
会員番号:	0091027989	入会年度:	1984

## 2. 研究業績要旨(1,000字以内)

哺乳類では血中アミノ酸の各濃度は共通で、摂取蛋白質のアミノ酸組成により生じる変動を抑制する仕組みにより一日中ほぼ一定である。特定の必須アミノ酸欠乏ではそれを含む食物の選択摂取を高めて充足するが、困難な場合、生命活動の維持を優先し体蛋白質を分解して補充する。アミノ酸恒常性は、生命活動に必要な蛋白質、核酸、エネルギーなどを産生する上での前提である。

リジン欠乏をモデルした研究結果から欠乏の認知と適応での仕組みは、視床下部外側野を中心に摂食や嗜好性に関わる中枢にリジンに対する感受性が高まり、並行して脳内や血中のリジンの情報、リジン摂取後の消化器の迷走神経応答およびその入力野の延髄孤束核で生じるリジンに鋭敏に応答する可塑性が生じ、その担い手はアクチビンAであった。リジン欠乏ラットはリジンの定量的摂取を学習し、恒常性の回復により食欲の正常化とグルタミン酸嗜好性を示したが、リジン欠乏時に示した食塩嗜好性は低下した。この記憶は長期保持され、他のアミノ酸欠乏にも速やかに適応できた。リジン欠乏ラットのリジン摂取後の脳の応答性を機能型MRI(4.7T)で見ると、食欲や栄養素摂取、記憶と学習に関わる中枢が応答した。加えてリジン特有の手がかり音、味や匂い等の情報と連合して外側野ニューロンは応答する様な高次の可塑性も示した。又、ラットは蛋白質栄養状態が良好ならグルタミン酸を嗜好し、失調時は食塩とグリシンを嗜好するが、リジンに限らず他の必須アミノ酸欠乏状態でも同様である。グルタミン酸のうま味刺激は蛋白質摂取のマーカーの他に、胃の迷走神経求心性線維ではグルタミン酸のみ応答し、糖や食塩、他のアミノ酸には応答を示さないことから、食物摂取の認知とその後の消化吸收、代謝を調節していると考えられる。従ってグルタミン酸が含まれないアミノ酸食摂取ラットは全身状態が悪化し、脂肪蓄積や窒素平衡の悪化を生じた。加えてグルタミン酸のラット胃内投与後の機能型MRIによる脳の応答から、記憶学習と食事性産熱とに関係する中枢の活動を介してアミノ酸を含めた生体恒常性を維持しつつ、過食にともなう肥満を抑え、おいしく食べて健康づくりに貢献していると考えられる。

## 3. 報文等リスト

(1) この研究に直接関連するもの(10 編以内)

1. Turugizawa T, Uematsu A, Uneyama H, Torii K.:Reversible brain response to an intragastric load of l-lysine depletion in conscious rats. *Brit. J. Nutr.* 107, 1-7, 2012
2. Uematsu A, Tsurugizawa T, Uneyama H. and Torii K.:Brain-gut communication via vagus nerve modulated conditioned flavor preference. *Eur. J. Neurosci.* 1-8, 2010
3. Tsurugizawa T, Uematsu A, Nakamura E, Hasumura M, Hirota M, Uneyama H and Torii K.:Mechanisms of neural response to gastrointestinal nutritive stimuli:the gut-brain axis. *Gastroenterology* , 137(1)262-273, 2009
4. Uneyama H, Niijima A, San Gabriel A, Torii K.:Luminal amino acid sensing in the rat gastric mucosa. *Am. j. physiol. gastrointe. Liver Physiol*, 291:G1163-G1170, 2006
5. Smriga M, and Torii K.:L-Lysine acts like a partial serotonin receptor 4 antagonist and inhibits serotonin-mediated intestinal pathologies and anxiety in rats. *Proc Natl Acad Sci. USA* 100(26), 15370-5, 2003
6. 鳥居邦夫,「食事アミノ酸と脳機能」脳と栄養—行動の分子基盤を求めて—(齊藤昌之、鳥居邦夫、青山頼孝責任編集、日本栄養・食糧学会監修) PP23-61, 建帛社, 2003\*
7. Torii K. and Niijima A.:Effect of lysinse on afferent activity of the hepatic branch of the vagus nerve in the normal L-lysine deficient rats. *Physiol Behav*, 72(5), 2001
8. Smriga M, Murakami H, Mori M. and Torii K.:Effect of L-lysine deficient diet on the hypothalamic interstitial norepinephrine and diet-induced thermogenesis in rats in vivo. *Bio Factors*, 12(1-4), 137-42, 2000
9. Hawkins RL, Murata T, Inoue M, Mori M. and Torii K.:Activin antiserum infused into the lateral hypothalamic area affects operant behavior of rats fed lysine-deficient diet. *Proc. soc exp Biol Med.* 219(2), 149-53, 1998
10. 鳥居邦夫, ラットにおける蛋白質栄養とアミノ酸および食塩嗜好性に関する研究、*日本栄養・食糧学会誌*, 40(1)1-16, 1987\*

(2) その他の論文(編数制限なし)

1. Iwatsuki K, and Torii K. :Peripheral chemosensing system for tastants and nutrients. *Curr Opin Endocrinol Diabetes Obes*, 19, 19-25, 2012
2. Torii K., Uematsu A, and Tsurugizawa T. :Brain response to the luminal nutrient stimulation. *Chemosensory Perception* , 5, 110-116, 2012
3. Son Ho A, Hori E, Hong P, Nguyen T, Urakawa S, Kondoh T, Torii K., Ono T, and Nishijo H. Hippocampal neuronal responses during signaled licking of gustatory stimuli in different contexts, *Hippocampus* 21: 502-519, 2011
4. Tsurugizawa T, Uematsu A, Uneyama H, and Torii K. :Different Bold Responses to intragastric load of L-glutamate and inosine monophosphate in conscious rats. *Chem. Senses*, 36, 169-176, 2011
5. Uematsu A, Tsurugizawa T, Iwatsuki K, Uneyama H, Torii K. :Evaluation of the 'liking' and 'wanting' properties of umami compound in rats, *Physiol Behav* Jan 13, 2011
6. Kondoh T, Ueta Y, Torii K. :Pre-treatment of adrenomedullin suppresses cerebral edema caused by transient focal cerebral ischemia in rats detected by magnetic resonance imaging, *Brain Research Bulletin* 84, 69-74, 2011
7. Kitamura A, Uneyama H, Torii K., and Niijima A. :Role played by afferent signals from olfactory, gustatory and gastrointestinal sensors in regulation of autonomic nerve activity. *Biol Pharm Bull.* 33(11),

- 1778-82, 2010
8. Iwatsuki K, Ichikawa R, Uneyama H, Torii K, Shibata A and Nomura M, :Generation and Characterization of T1R2-LacZ Knock-in mouse, *Biochem Biophys Res Commun.* Nov 19, 402(3),95-9. 2010
  9. Kitamura, Uneyama H, Torii K, and Niijima A, :Effects of intragastric infusion of inosine monophosphate and L-glutamate on the vagal gastric afferent activity, and their reflex in the rat, *J Physiol Sci.* Jan;61(1), 65-71, 2011
  10. Nakamura E, Hasumura M, San Gabriel A, Uneyama H, and Torii K, :New frontiers in gut nutrient sensor research luminal glutamate-sensing cells in rat gastric mucosa, *J Pharmacol Science* 112, 13-18, 2010
  11. Uneyama H, Niijima A, Kitamura A, and Torii K, :Existence of NO-triggered vagal afferent activation in the rat gastric mucosa, *Life Sciences* 85,782-787, 2009
  12. San Gabriel A, Maekawa T. Uneyama H, and Torii K, :Metabotropic glutamate receptor type 1 in taste tissue. :*Am J Clin Nutr* 90 (3) 743S-746S, 2009
  13. Kondoh T, Mallick HN, and Torii K. :Physiological significance of glutamate signaling in the gut-brain communication. *Biosci. Microflora* 28 (4) 109-118, 2009
  14. Tsurugizawa T. Uematsu A. Nakamura E. Hasumura M. Hirota M. Uneyama H. and Torii K. :Mechanisms of neural response to gastrointestinal nutritive stimuli, the gut-brain axis, *Gastroenterology* 137(1) 262-273, 2009
  15. San Gabriel A. Uneyama H. Maekawa T. and Torii K. :The calcium-sensing receptor in taste tissue. *BBRC* 378, 414-418, 2009
  16. Shibata R. Kameishi M. Kondoh T. and Torii K. :Bilateral dopaminergic lesions in the ventral tegmental area of rats influence sucrose intake, but not umami and amino acid intake. *Physiol Behav* 96, 667-674, 2009
  17. Uematsu A. Tsurugizawa T. Kondoh T. and Torii K. :Conditioned flavor preference learning by intragastric administration of L-glutamate in rats, *Neuroscience Letters* 451, 190-193, 2009
  18. Kondoh T. Torii K. :MSG intake suppresses weight gain, fat deposition, and plasma leptin levels in male Sprague-Dawley rats. *Physiol Behav* 95, 135-144, 2008
  19. Tsurugizawa T. Kondoh T. Torii K. :Forebrain activation induced by postoral nutritive substances in rat. *NeuroReport* 19 (11), 1111-1115, 2008
  20. San Gabriel A. Maekawa T. Uneyama H. Yosie S and Torii K. :mGluR1 in the fundic glands of rat stomach. *FEBS Letters*, 581(1119-1123), 2007
  21. Smriga M. and Torii K. :Prolonged treatment with L-lysine and L-arginine reduces stress-induced anxiety in an elevated plus maze. *Nutr Neurosci*, 6(2), 125-8, 2003.
  22. Uneyama H. Niijima A. Tanaka T. and Torii K. :Receptor subtype specific activation of the rat gastric vagal afferent fibers to serotonin. *Life Sci*, 72(4-5), 415-23, 2002.
  23. Smriga M. Kameishi M. Uneyama H. and Torii K. :Dietary L-lysine deficiency increases stress-induced anxiety and fecal excretion in rats, *J of Ntri* 132(12), 3744-6, 2002.
  24. Tabuchi E. Yokawa, T. MallickH. Inubushi, T. Kondoh, T. Ono T. and Torii K. :Spatio-temporal dynamics of brain activated regions during drinking behavior in rats. *Brain Res*, 951(4), 270-9, 2002.
  25. Smriga M. and Torii T. :Preferable monosodium glutamate and sodium chloride solutions do not affect diurnal norepinephrine release in the rat lateral hypothalamus. *Nutr Neurosci*, vol.3, 367-72, 2000.
  26. Smriga M. Murakami H. Mori M. and Torii K. :Use of thermal photography to explore the age-dependent effect of monosodium glutamate, NaCl and glucose on brown adipose

- tissue thermogenesis. *Physiol Behav*, 71(3-4), 403-7, 2000.
27. Smriga M. and Torii K.:Release of hypothalamic norepinephrine during MSG intake in rats fed normal and nonprotein diet. *Physiol Behav*, 70(3-4), 413-5, 2000.
  28. Smriga M. Mori M. and Torii K. :Circadian release of hypothalamic norephrine in rats in vivo is depressed during early l-lysine deficiency. *J Nutr*, 130(6), 1641-3, 2000.
  29. Fujimura H. Ohsawa K. Funaba M. Murata T. Takahashi M. Abe M. and Torii K. ; Immunological localization and ontogenetic development of inhibin  $\alpha$  subunit in rat brain. *J Neuroendocrinol*, 11(3), 157-63, 1999.
  30. Hagino H. Tabuchi E. Kurachi M. Satoh O, Sun Y. Kondoh T. Ono T. and Torii K. :Effects of D<sub>2</sub> dopamine receptor agonist and antagonist on brain activity in the rat assessed by functional magnetic resonance imaging. *Brain Res*, 813(2), 367-73, 1998.
  31. Ikegaya Y. Saito H. Torii K. and Nishiyama N. :Activin selectively abolishes hippocampal long-term potentiation induced by weak titanic stimulation in vivo. *J J Pharmacol*, 75(1), 87-9, 1997.
  32. Miura Y. Murayama H. Tsuzuki S. Sugimoto E. and Torii K. :Long-term consumption of an amino acid diet reduces the pancreatic enzyme secretion response to a trypsin inhibitor in rats. *J Nutr*, 127(7), 1377-81, 1997.
  33. Iwahori Y. Saito H. Torii K. and Nishiyama N. :Activin exerts a neurotrophic effect on cultured hippocampal neurons. *Brain Res*, 760(1-2), 52-8, 1997.
  34. Murata T. Takizawa T. Funaba, M. Fujimura H. Murat E. Takahashi M. and Torii K. :Quantitative RT-PCR for inhibin/activin subunits: measurement of rat hypothalamic and ovarian inhibin/activin subunit mRNAs during the estrous cycle. *Endocr J*, 44(1), 35-42, 1997.
  35. Funaba M. Murata T. Fujimura H. Murata E. Abe M. and Torii K. :Immunolocalization of type I or type II activin receptors in the rat brain. *J Neuroendocrinol*, 9(2), 105-11, 1997.
  36. Funaba M. Murata T. Murata E. Ogawa K. Abe M. Takahashi M. and Torii K. :Suppressed bone induction by follistatin in spontaneously hypercholesterolemic rat bone. *Life Sci*, 61(6), 653-8, 1997.
  37. Okiyama A. Torii K. and Tordoff M.G. :Increased NaCl preference of rats fed low-protein diet. *Am J Physiol - Regulatory, Integrative and Comparative Physiology*, 270(6), 1189-96, 1996.
  38. Funaba M. Murata T. Fujimura H. Murata E. Abe M. Takahashi M. and Torii K. :Unique recognition of activin and lnhinin by polyclonal antibodies to inhibin subunits. *J Biochem*, 119(5), 1996.
  39. Torii K. Yokawa T. Tabuchi E. Hawkins R L. Mori M. Kondoh T. and Ono T. :Recognition of deficient nutrient intake in the brain of rat with l-lysine deficiency monitored by functional magnetic resonance imaging, electrophysiologically and behaviorally. *Amino Acids*, vol.10, 1996.
  40. Tabuchi E. Uwano T. Kondoh T. Ono T. and Torii K. :Contribution of chorda tympani and glossopharyngeal nerves to taste preferences of rat for amino acids and NaCl. *Brain Res*, 739(1-2), 139-55, 1996.
  41. Yokawa T. Tabuchi E. Takezawa M. Ono T. and Torii K. :Recognition and neural plasticity responding to deficient nutrient intake scanned by a functional MRI in the brain of rats with l-lysine deficiency. *Obes Res*, 3(supplement 5), 685-8, 1995.
  42. Hawkins RL. Inoue M. Mori M. and Torii K. :Effect of inhibin, follistatin, or activin infusion into the lateral hypothalamus on operant behavior of rats fed lysine deficient diet. *Brain Res*, 704(1), 1-9, 1995.
  43. Inoue M. Funaba M. Hawkins RL. Mori M. and Torii K. :Effect of continuous infusion of lysine via different routes and hepatic vagotomy on dietary choice in rats.

- Physiol Behav, 58(2), 379-85, 1995.
44. Hawkins RL. Richard L. Inoue M. Mori M. and Torii K. :Lysine deficient Diet and lysine replacement affect food directed operant behavior. Physiol Behav, 56(5), 1061-8, 1994.
  45. Ninomiya Y. Kajiura H. Natito Y. Mochizuki K. Katsukawa H. and Torii K. : Glossopharyngeal denervation alters responses to nutrients and toxic substances. Physiol Behav, 56(6), 1179-84, 1994.
  46. Torii K. Hanai K. Oosawa K. Funaba M. Okiyama A. Mori M. Murata T. and Takahashi M. :Activin A: serum levels and immunohistochemical brain localization in rats give diets deficient in l-lysine or protein. Physiol Behav, 54(3), 459-66, 1993.
  47. Torii K. and Cagan RH. :Biochemical studies of taste sensation. IX. Enhancement of l-[<sup>3</sup>H]glutamate binding to bovine taste papillae by 5' -rebonucleotides. Biochem Biophys Acta, 627(3), 313-23, 1980.

(3) 過去 5 年間の本学会での活動状況

1992 年～2011 年 8 月 評議委員  
2011 年 9 月～現在 代議員  
2006 年、2007 年度 監事

(4) 特記事項

11. 日本栄養・食糧学会奨励賞 1985 年 タンパク栄養とアミノ酸および食塩嗜好性に関する基礎研究
12. 日本味と匂い学会 2009 年学会賞 うま味の味覚、内臓感覚としての生体での役割解明
13. 文部科学大臣賞 2010 年 科学技術賞(開発部門)  
生体でのグルタミン酸シグナリングの有用性に基づく食品開発