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论著

# LRRN3对大鼠小脑出生后发育的调控

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摘要：

目的：探讨神经系统富亮氨酸重复蛋白3（neuronal leucine rich repeat 3, LRRN3）蛋白对大鼠小脑出生后发育的影响及可能机制。方法：新生大鼠随机分为实验组和对照组，各组分别设3个不同时间点亚组。采用行为学实验、HE染色和免疫组织化学等方法观察抗体注射对大鼠小脑发育的影响。结果：实验组动物平衡能力较对照组差，相同时间点两组动物静态平衡时间（balance latency, BL）差异具有统计学意义（P＜0.05）；HE染色显示2组动物从第7天到第21天皮质逐渐增厚，结构出现动态改变；囊泡膜谷氨酸转运体1（vesicular glutamate transporter 1, VGluT1）在对照组和实验组大鼠出生后第7天、第14天和第21天的小脑中均有表达，从出生后第7天到第21天VGluT1阳性分子层随发育进行而不断增厚；对照组和实验组VGluT1阳性分子层厚度在出生后第7天差异无统计学意义（P>0.05）；在出生后第14天和第21天，对照组明显厚于实验组，差异具有统计学意义（P＜0.01）。结论：LRRN3蛋白对小脑出生后发育过程有重要作用，腹腔注射抗LRRN3抗体能降低小脑VGluT1的表达，减少分子层突触形成，降低分子层厚度，从而抑制小脑皮层的生长和功能性神经回路的形成。

关键词： 神经系统富亮氨酸重复蛋白3 小脑发育 静态平衡时间 囊泡膜谷氨酸转运体1

## Role of LRRN3 in the cerebellum postnatal development in rats

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Abstract:

ObjectiveTo explore the effect and possible mechanism of LRRN3 in the cerebellum postnatal development in rats. MethodsNew born rats were randomly divided into an experimental group and a control group, and each group included 3 sub-groups of different time points. Behavioral experiment, hematoxylin-eosin （HE） staining and immunohistochemistry were used to evaluate the effects of anti-LRRN3 injection on the cerebellum development in new born rats. ResultsCompared with the control, the balance ability in the experiment group was weak, and there was significant difference in the static balance between the 2 groups (P＜0.05). HE staining showed that molecular layer (ML) grew thicker from the 7th day to the 21st day after birth，and the structure changed dynamically. Vesicular glutamate transporter 1 （VGluT1） expression was positive in the cerebellum of all groups, and the positive ML grew thicker from the 7th day to the 21st day after birth. Compared with the control, there was no obvious difference between the 2 groups on the 7th day after birth （P＞0.05）, while on the 14th day and the 21st day, there was significant difference （P＜0.01）.ConclusionLRRN3 plays an important role in cerebellum postnatal deve-lopment. Anti-LRRN3 antibody injection may down-regulate the expression of VGluT1, reduce the synapse formation in the molecular layer,decrease the thickness of ML and inhibit the growth of cerebellum cortex and the functional neural circuit formation.

Keywords: neuronal leucine rich repeat 3 cerebellum development balance latency vesicular glutamate transporter 1

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参考文献：

［1］Yang J, Wang Y J, Cai Y, et al. Preparation of rabbit anti-rat LRRN3 polyclonal antibody and study of its expression［J］.Neural Regen Res,2010,5(13):1030-1034.
［2］Tsigilis N，Zachopoulou E，Mavridis T，et a1．Evaluation of the specificity of selected dynamic balance tests［J］.Percept Mot Skills,2001,92(3 Pt 1):827-833.
［3］Lichtman J W,Colman H.Synapse elimination and indelible memory［J］.Neuron, 2000,25(2):269-278.
［4］Crepel F,Delhaye-Bouchaud N,Dupont J L.Fate of the multiple innervation of cerebellar Purkinje cells by climbing fibers in immature control, X-irradiated and hypothyroid rats［J］.Brain Res,1981,227(1):59-71.
［5］Garacia-Ladona F J, de Barry J, Girard C,et al. Ectopic granule cell layer in mouse cerebellum after methyl-azoxy-methanol(NAM) treatment［J］.Exp Brain Res,1991,86(1):90-96.

［6］Sotelo C. Cellular and genetic regulation of the development of the cerebellar system［J］.Prog Neurobiol,2004,72(5):295-339.
［7］Fonnum F, Lock E A. Cerebellum as a target for toxic substances［J］.Toxicol Lett, 2000,112-113:9-16.
［8］Mattson M P.Cellular signaling mechanism common to the development and the degeneration of neuroarchitecture［J］.Mech Ageing Dev,1989,50(2):103-157.
［9］Dzubay J A, Otis T S.Climbing fiber activation ofmetabotrobic glutamate receptors on cerebellar Purkinje neurons［J］.Neuron,2002,36(6):1159-1167.
［10］Lujan R,Roberts J D,Shigemoto R,et al.Differential plasma membrane distribution of metabotropic glutamate receptors mGluR1α mGluR2 and mGluR5, relative to neurotransmitter release sites［J］.J Chem Neuroanat,1997,13(4):219-241.
［11］Ozawa S,Kamiya H,Tsuzuki K,et al.Glutamate receptors in the mammalian central nervous system［J］.Prog Neurobiol,1998,54(5):581-618.
［12］Pisu M B,Guioli S,Conforti E,et al.Signal molecules and receptors in the differential development of cerebellumlobules. Acute effects of cisplatin on nitric oxide and glutamate system in Purkinje cell population［J］.Dev Brain Res,2003,145(2):229-240.
［13］Pisu M B,Roda E,Avella D,et al.Developmental plasticity of rat cerebellar cortex after cisplatin injury:inhibitory synapses and differentiating Purkinje neurons［J］.Neuroscience,2004,129(3):655-664.
［14］Fremeau R T J,Voglmaier S,Seal R P,et al.VGluTs define subsets of excitatory neurons and suggest novel roles for glutamate［J］.Trends Neurosci,2004,27(2):98-103.
［15］Herzog E,Bellenchi G C,Gras C,et al.The existence of a second vesicular glutamate transporter specifies subpopulations of glutamatergic neurons［J］.J Neurosci,2001,21(22):RC181.
［16］Hioki H,Fujiyama F,Taki K,et al.Differential distribution of vesicular glutamate transporters in the rat cerebellar cortex［J］. Neuroscience,2003,117(1):1-6.
［17］Miyazaki T,Fukaya M,Shimizu H,et al.Subtype switching of vesicular glutamate transporters at parallel fibre-Purkinje cell synapses in developing mouse cerebellum［J］.Eur J Neurosci,2003,17(12):2563-2572.
［18］Avella D,Pisu M B,Roda E.Reorganization of the rat cerebellar cortex during postnatal development following cisplatin treatment［J］.Exp Neurol, 2006,201(1):131-143.

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