学位論文抄録

Mapping neuronal activity in the mouse brain by analyzing immediate early gene expression

（最初期遺伝子の発現解析を用いたマウス脳における神経活動マッピング）

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Abstract of Thesis

Background and Objective: A precise identification of activated neurons facilitates understanding brain functions in physiology and diseases. We aimed at establishing a set of in situ hybridization probes of immediate early genes (IEGs) for mapping brain activity in mice with high spatial resolution.

Methods: First, we performed in situ hybridization to analyze mRNA expression of IEGs in the mouse brain after odorant exposure. We used wild type mice and the cyclic nucleotide-gated channel subunit A2 (*Cnga2*)-null mice since CNGA2 is a key component of the olfactory signal transduction pathway in the main olfactory system.

Second, we performed unilateral optogenetic stimulation of the striatum in freely moving transgenic mice that expressed a channelrhodopsin-2 (ChR2) variant ChR2(C128S) in striatal medium spiny neurons (MSNs). To identify photoactivated neurons we then analyzed IEG expression patterns by in situ hybridization.

Results and Discussions: First, we observed rapid, robust and transient induction of as many as ten immediate early genes (IEGs) in the mouse olfactory bulb (OB) after odorant stimulation. In *Cnga2*-null mice, which are usually anosmic and sexually unresponsive, glomerular activation was insignificant as expected. However, a subtle induction of *c-fos* took place in a few mutants which exhibited sexual arousal. Interestingly, very strong glomerular activation was observed in mutants after exposure to a predator odor suggesting involvement of CNGA2-independent signaling pathways in the main olfactory system.

Second, we found that after in vivo unilateral photoactivation of the striatum induction of commonly used IEGs such as *c-fos*, *Arc* and *Egr1* was not apparent whereas *Npas4* was robustly induced in MSNs ipsilaterally.

Conclusion: Olfactory stimulation induced several IEGs in the mouse brain and the expression level corresponded well with the nature of the stimuli as well as interanimal behavioral differences. Using optogenetic manipulation we show that *Npas4* is a reliable marker of photoactivated MSNs. Together, our in situ hybridization probe set will be very useful to study brain activity at the cellular level in mice.