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### Neuroscience 2000 Abstract

<b>Presentation Number:</b>	128.14
<b>Abstract Title:</b>	Differential functions of Rab3A in regulating excitatory and inhibitory transmission in hippocampal neurons.
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<b>Primary Theme and Topics</b>	C. Excitable Membranes and Synaptic Transmission - 30. Presynaptic mechanisms
<b>Secondary Theme and Topics</b>	D. Neurotransmitters, Modulators, Transporters, and Receptors - 42. Excitatory amino acids
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Rab3A is a small GTPase localized to synaptic vesicles. Studies of Rab3A knock-out (KO) mice showed changes in synaptic transmission, but the precise function of Rab3A remain controversial. We cultured CA1-CA3 hippocampal neurons from postnatal wild type (WT) and Rab3A KO mice. In contrast to previous reports, we found that the basal amplitude of evoked EPSCs was reduced in Rab3A KO compared to WT neurons ( $232 \pm 51$  pA,  $n=46$  vs.  $687 \pm 200$  pA,  $n=21$ ,  $p < 0.05$ ). However, the basal amplitude of IPSCs was not different in KO and WT neurons ( $685 \pm 86$  pA,  $n=89$  vs.  $785 \pm 131$  pA,  $n=38$ ,  $p > 0.4$ ). Similarly, effects of overexpression of Rab3A by transfection were also selective for excitatory but not inhibitory transmission: in WT neurons, EPSC amplitude was significantly reduced ( $79 \pm 36$  pA,  $n=7$ ,  $p < 0.007$ ), whereas IPSC amplitude was not affected ( $574 \pm 194$  pA,  $n=10$ ,  $p > 0.3$ ). Transfection with a Rab3A mutant deficient in GTP hydrolysis (Rab3aQ81L) produced qualitatively similar results. We next examined adaptation of excitatory and inhibitory transmission during trains of 25 stimuli. For both EPSCs and IPSCs, the ratio of steady-state and basal amplitudes was smaller in KO than in WT neurons. In both instances, transfection of KO neurons with Rab3AWT restored the ratio to WT levels, while transfection with Rab3AQ81L overcompensated for the effect of the KO. Our results suggest that Rab3A acts selectively in regulating basal excitatory transmission as opposed to inhibitory transmission, but exerts a similar influence on vesicle mobilization in both cases.

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