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Relationship between calcium dynamics and release probability in single axon terminals

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Action potential (AP)-evoked local Ca2+ transients regulate the release of neurotransmitters from synaptic vesicles docked at presynaptic active zones (AZ). The probability of release (Pr) displays large variability across synapses that are also very diverse based on their morphological appearance. However, the relationship between the functional and structural features is largely unknown. Here we addressed whether Pr and AP evoked local [Ca2+] transients show any correlation with the ultrastructure of identified hippocampal glutamatergic axon terminals by combining two-photon Ca2+ imaging with correlated electron microscopic 3D reconstruction of the imaged structures. Optical quantal analysis revealed that the Pr of individual CA3 pyramidal cell local axon terminals varies between 0 and 0.5. Measurements of the morphological parameters demonstrated a strong correlation between the Pr and the AZ area. AP-evoked volume-averaged [Ca2+] transients measured in single boutons displayed a large, up to 3-fold variability across boutons (coefficient of variation=0.3). The peak amplitude of the [Ca2+] transients did not correlate with the bouton volume, but the total amount of fluxed Ca2+ showed a tight correlation with the AZ area. As freeze-fracture replica-labeling demonstrated the exclusive location of Cav2.1 subunits in the AZ, we propose that the number of Ca2+ channels is proportional to the AZ area and instructive in setting the Pr of the terminal.