

RIM-Binding Protein 2 positively regulates the abundance and release site coupling of presynaptic Ca²⁺ channels at a fast central synapse

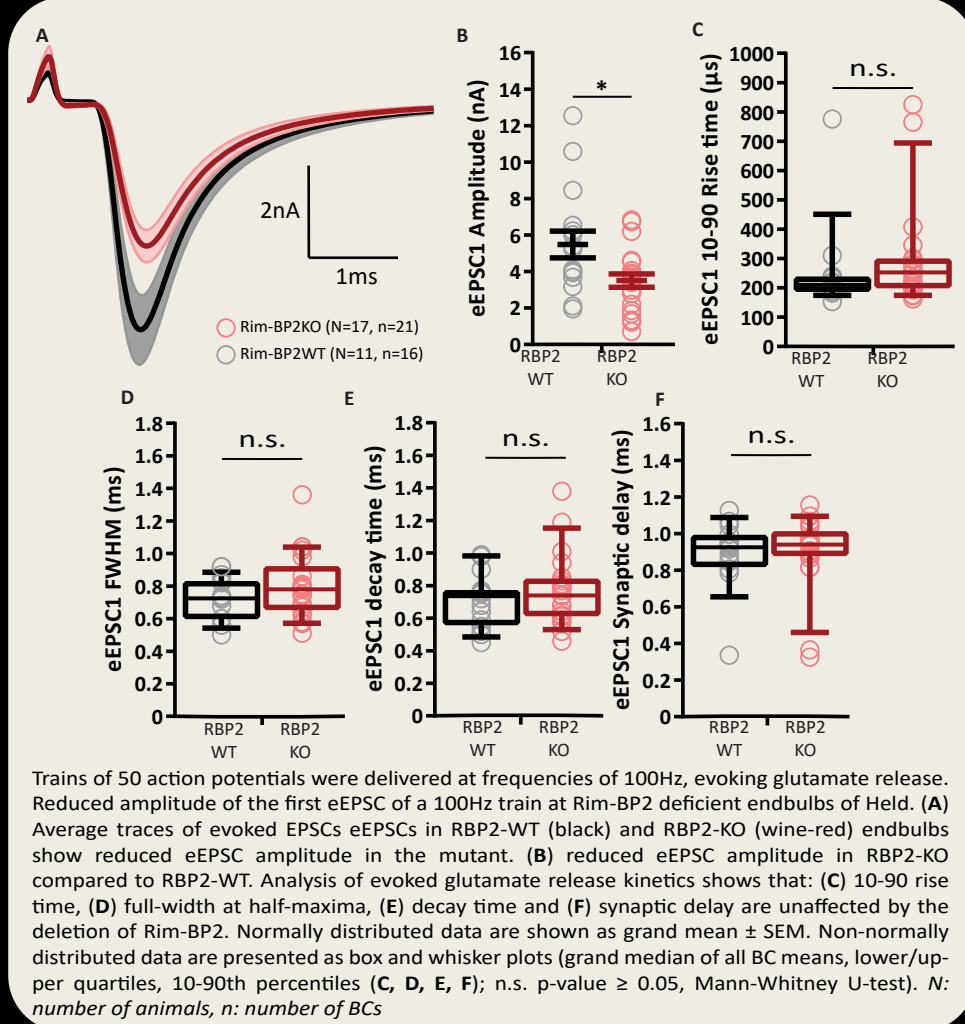
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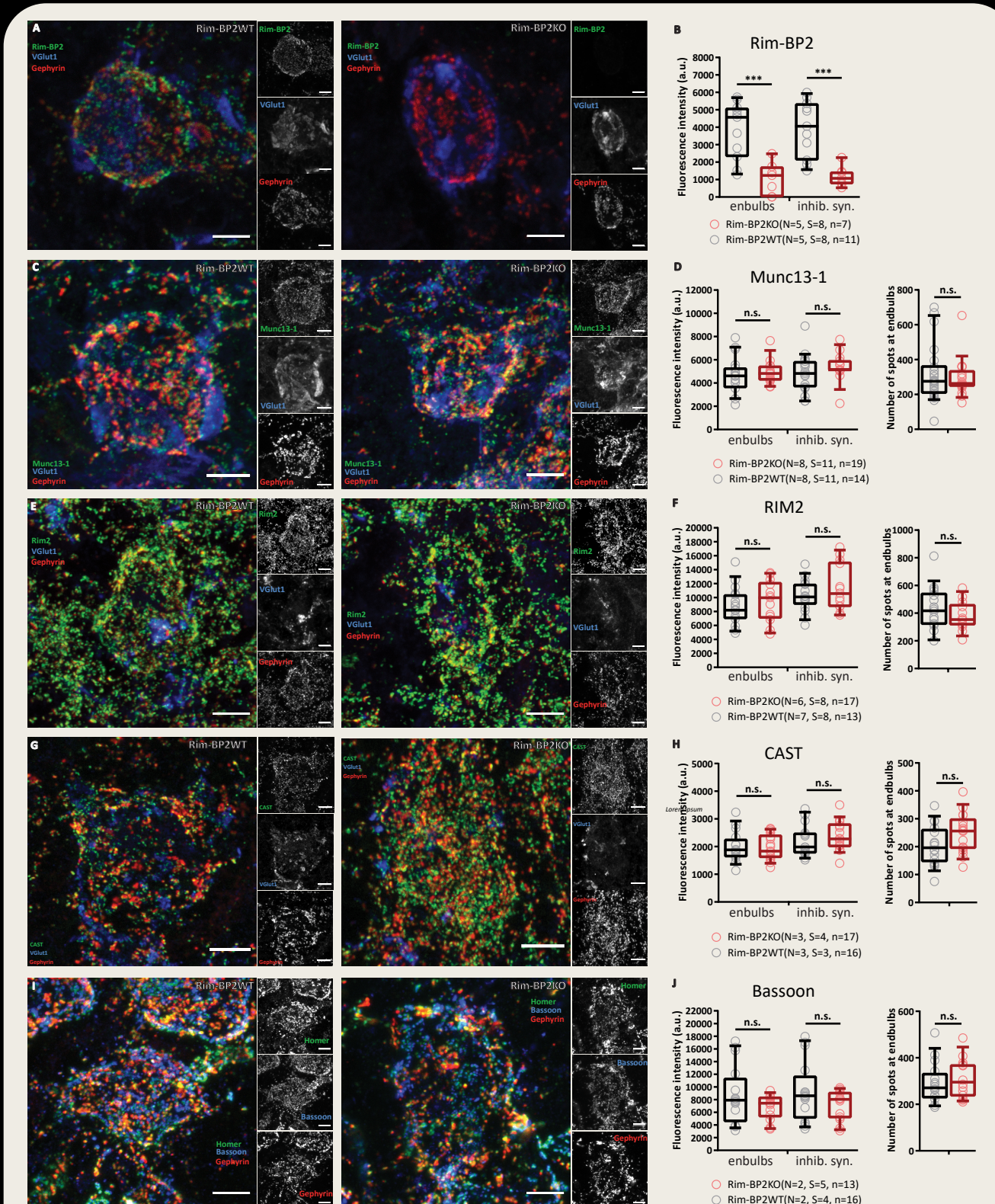
1. Abstract

RIM-Binding Protein 2 (RIM-BP2) is a multidomain protein of the presynaptic active zone (AZ). By binding to Rab-interacting protein (RIM), Bassoon and voltage-gated Ca²⁺ channels (Ca_v), it is considered to be central organizer of the topography of Ca_v and release sites of synaptic vesicles (SVs). Here, we investigated the role of RIM-BP2 at the endbulb of Held synapse, a fast relay of the auditory pathway with high release probability. Disruption of RIM-BP2 reduced the amplitude of evoked excitatory postsynaptic currents (EPSCs) and altered short-term plasticity due to reduced vesicular release probability. In addition, SV replenishment to the readily releasable SV pool was slowed. Augmenting Ca²⁺ influx by adding extracellular Ca²⁺ restored normal transmission. Presynaptic Ca_v channels were reduced and their topography altered. Moreover, there were fewer SVs in a distance of 2-20 nm to the AZ membrane. We conclude that RIM-BP2 positively regulates the clustering and SV coupling of Ca_v channels at the endbulb of Held

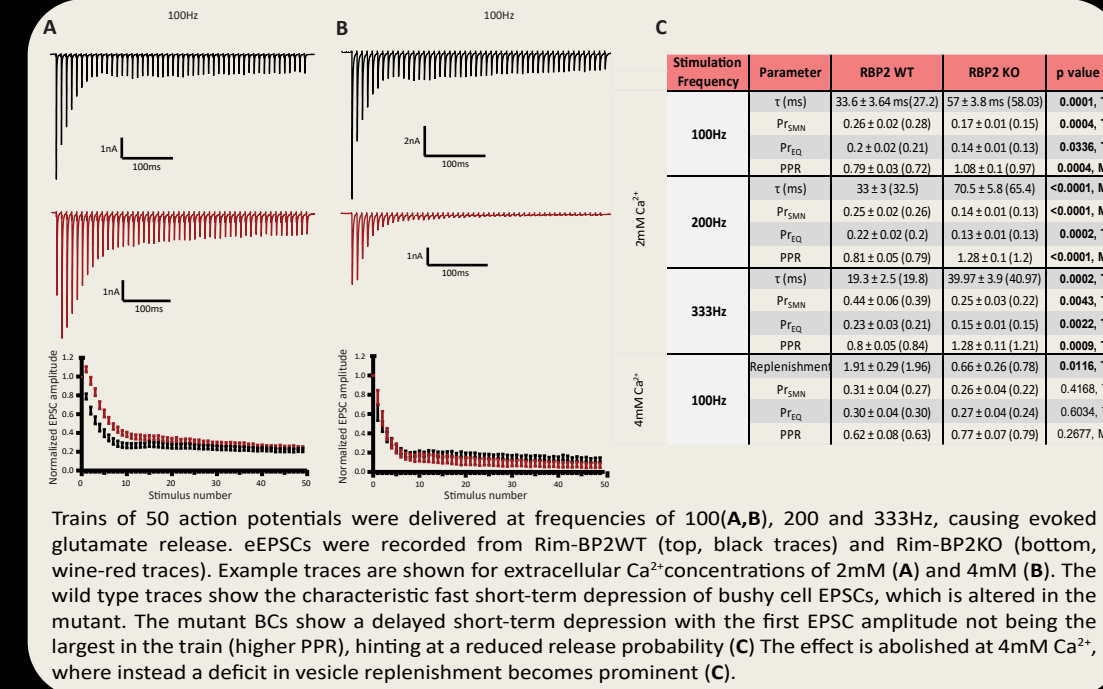
2. Smaller eEPSCs in the Rim-BP2^{-/-}



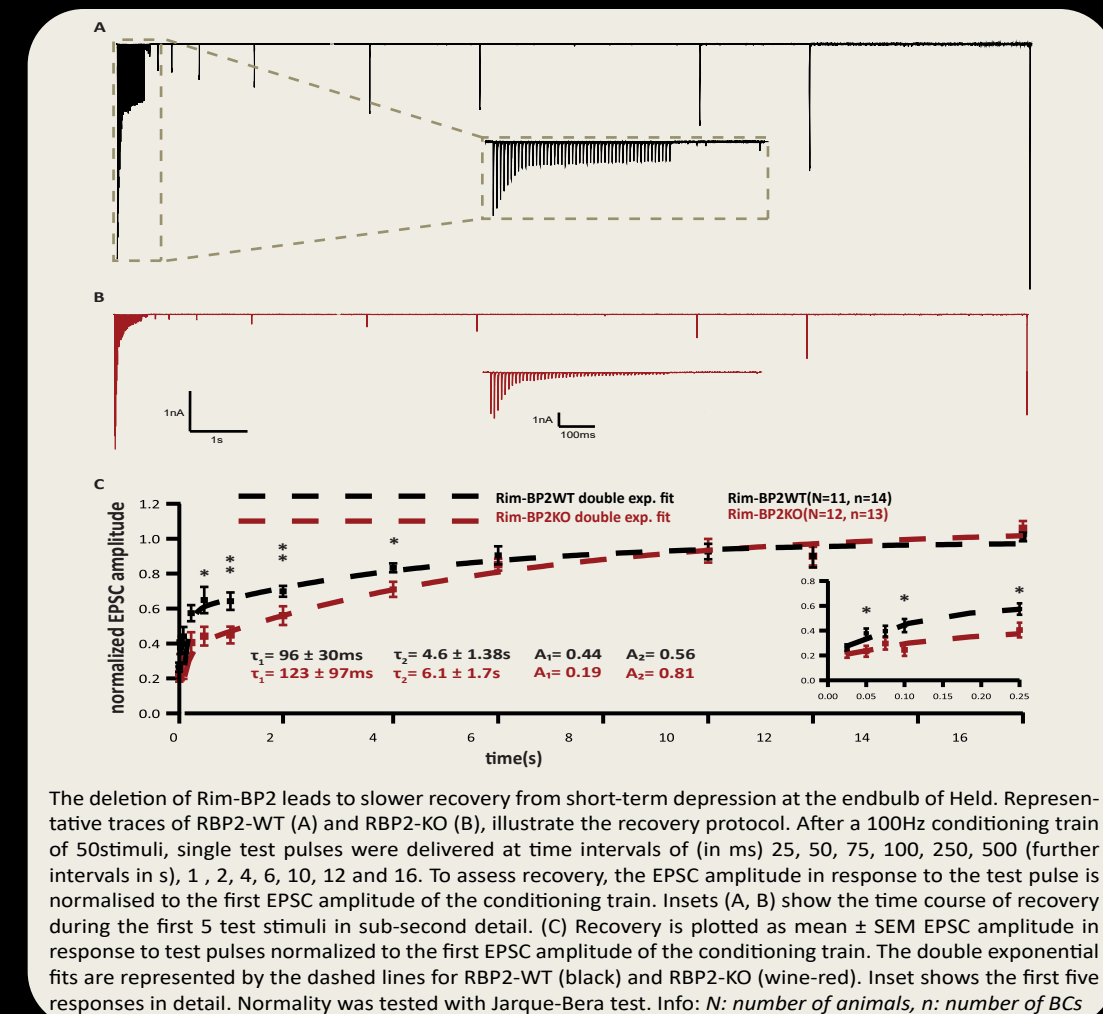
3. Unaltered CAZ molecular composition in Rim-BP2^{-/-}



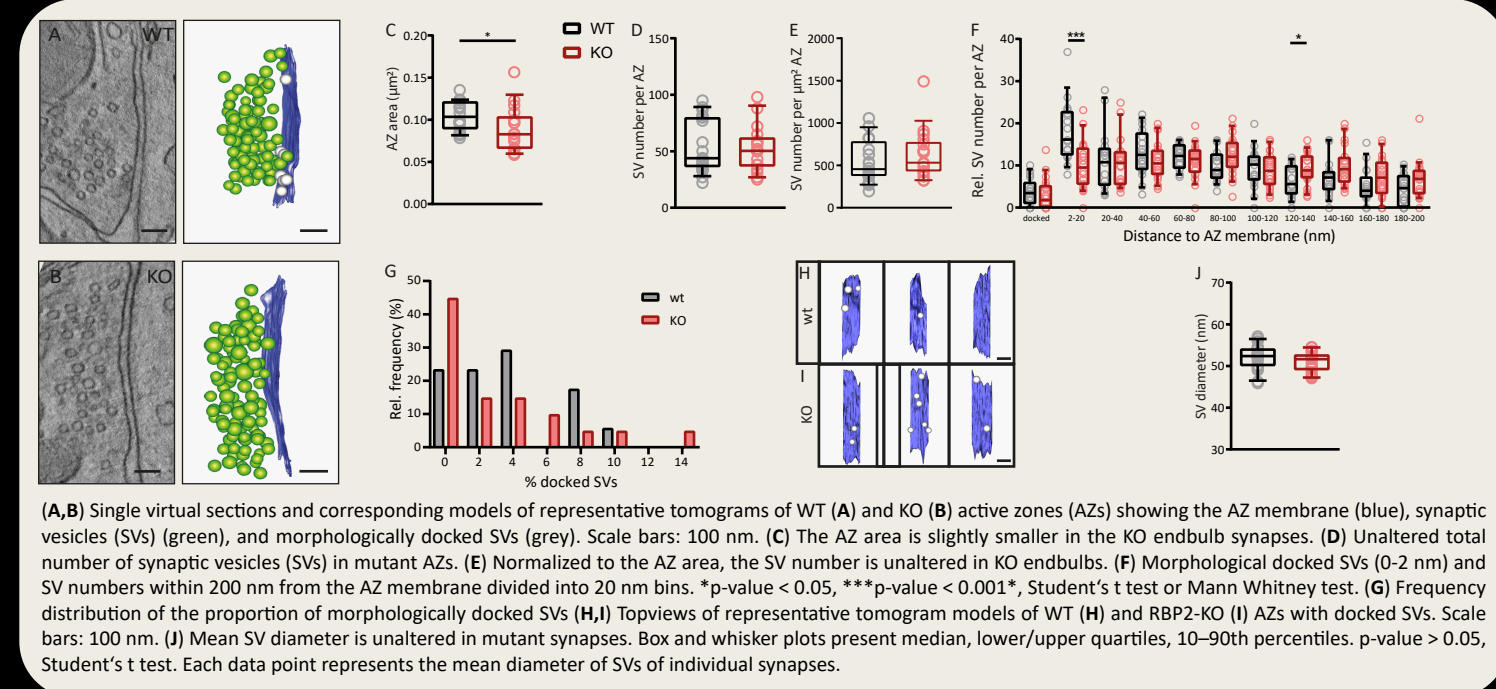
4. Reduced P_r rescuable at high Ca²⁺, where replenishment seems slower



5. Slowed recovery⁺ in the Rim-BP2^{-/-}



6. Vesicles located further from Active zone membrane at Rim-BP2^{-/-} endbulbs



7. The Rim-BP2 perturbation reduces the number of Ca_v particles per cluster in endbulb AZs

