***The absence of SV2A in interneurons leads to Epilepsy***

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**Abstract (max 250words):**

The SV2A protein is a glycoprotein present in the membranes of most synaptic vesicles whose physiological role remains unknown. However, it has been demonstrated that levetiracetam, an effective anti-epileptic drug, binds to SV2A. Moreover, SV2A expression is down-regulated in epileptic foci resected in humans with temporal lobe epilepsy, and *SV2A* full knock-out mice exhibited seizures around post-natal day 7 (P7) and die around P15.

AIMS: This project aims to understand how SV2A protein may be involved in epilepsy. First, we wanted to test if the absence of SV2A could lead to seizures appearance after complete brain development. Next, we wished to unravel the sub-population of neurons responsible for seizures onset.

METHODS: We induced recombination in UbiquitinERT2:SV2A-cKO mice at P70 and observed the obtained phenotype. Next, we compared the phenotype of Dlx5,6:SV2A-cKO (targeting GABAergic interneurons) with Nex:SV2A-cKO (targeting glutamatergic neuron) mice.

RESULTS: UbiquitinERT2:SV2A-cKO mice recombinated at P70 presented seizures and died one to two months after while WT mice behaved normally. Then, we observed that Dlx5,6:SV2A-cKO mice exhibited lethal spontaneous seizure while Nex:SV2A-cKO had no evident phenotype. Furthermore, Dlx5,6:SV2A-cKO mice present a significant decreased of PV neuron density in the hippocampus. Mass spectrometry analysis revealed that Dlx and Nex:SV2A-cKO synaptosomes present the same modification compared to WT.

CONCLUSIONS: Our results show that the absence of SV2A can lead to seizures after the complete brain development. We also observed that GABAergic neurons are sufficient to induce seizures in mice although they seem to bear the same molecular defect as glutamatergic neurons.