Abstract

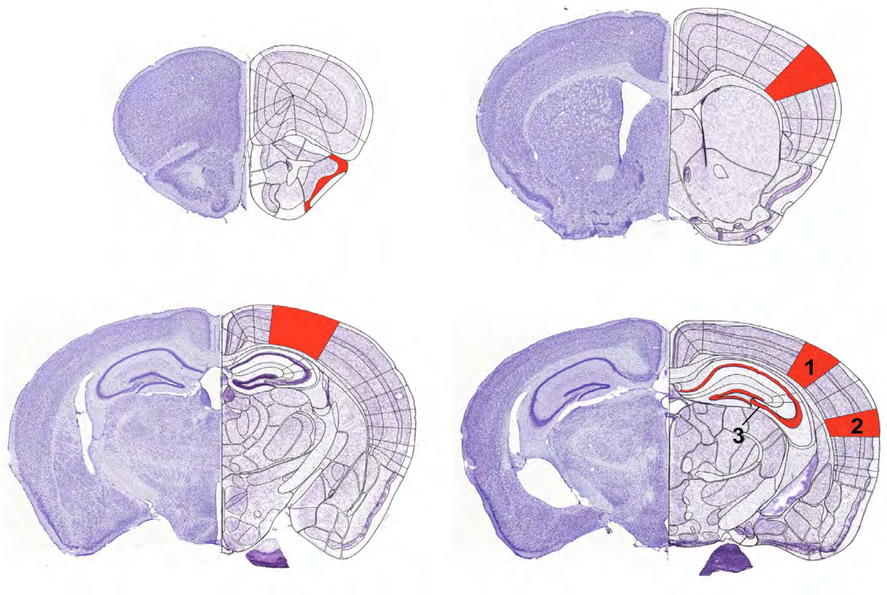
The C57BL/6 mouse has been the strain of choice for brain research studies but synaptic plasticity, such as long-term depression (LTD) or long-term potentiation (LTP) is difficult to induce in these mice.

A largely ignored fact is that C57BL/6 mice become progressively deaf starting in early adulthood. Having recently observed that early blindness in mice results in deficits in hippocampal synaptic plasticity and changes in cortical and hippocampal receptor expression, we wondered whether deafness in C57BL/6 mice also has consequences for the efficacy of their brain function in comparison to CBA/J (develop hereditary blindness) and CBA/CaOlaHsd mice (no reported deficits in sensory modalities).

Related publications:

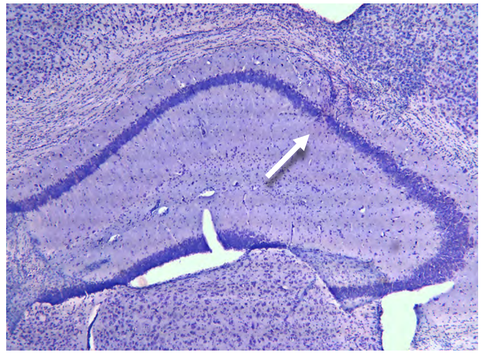
- Goh and Manahan-Vaughan, Hippocampus (23), 2013
- Feldmann et al., Cerebral Cortex (29), 2019

Methods

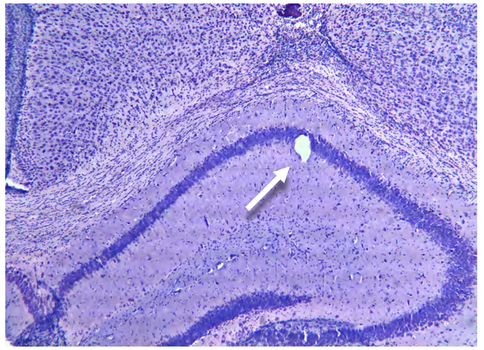


Areas selected for immunohistochemical analysis
(1) visual cortex
(2) auditory cortex
(3) hippocampus

- Implantation of recording and stimulation electrodes in the CA1 region of the hippocampus of C57BL/6, CBA/J and CBA/OlaHsd mice
- Examination of LTP induced by high-frequency stimulation at different ages
- Comparison of receptor expression in C57BL/6 and CBA/CaOlaHsd mice

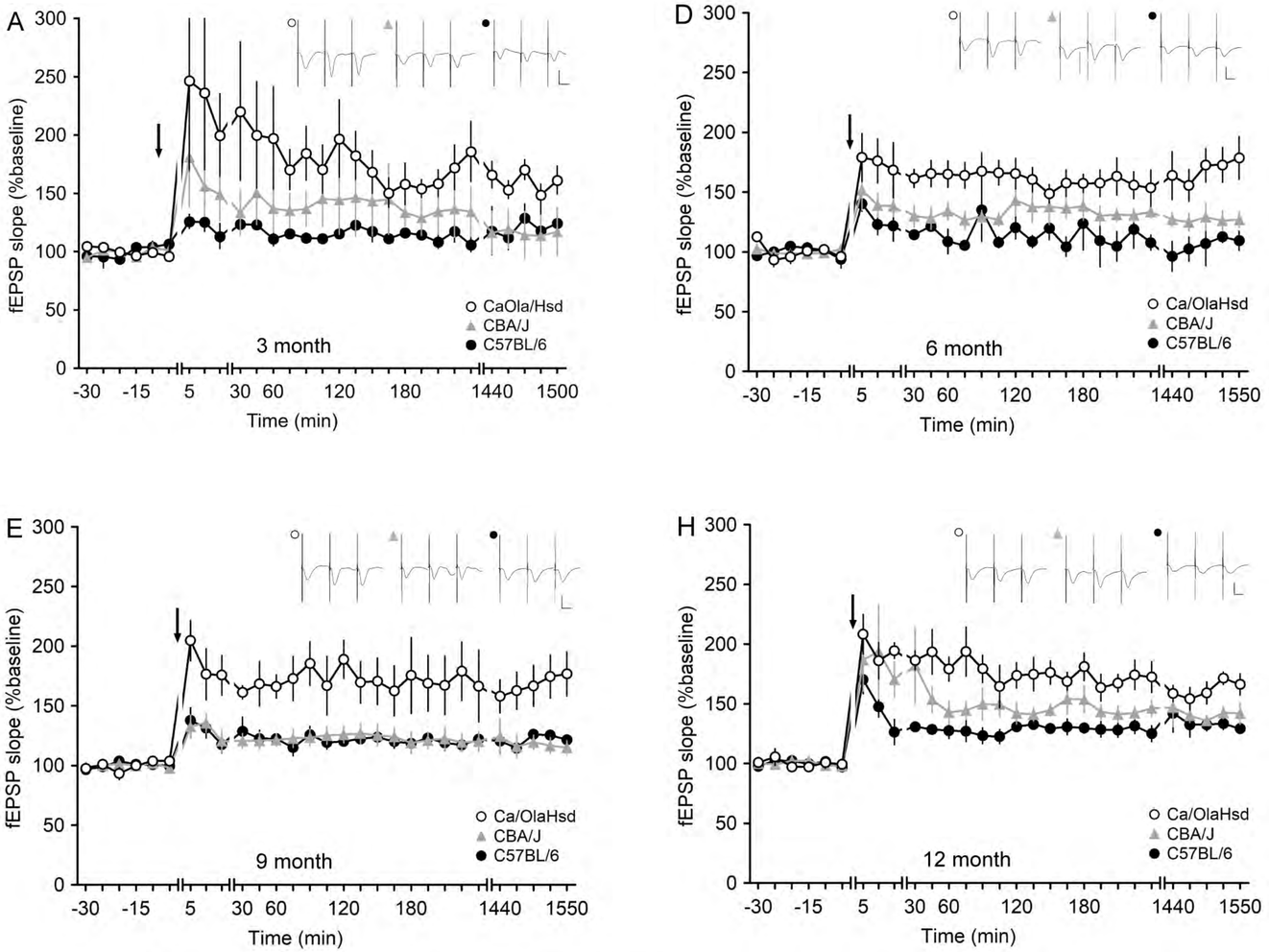


Placement of stimulation electrode



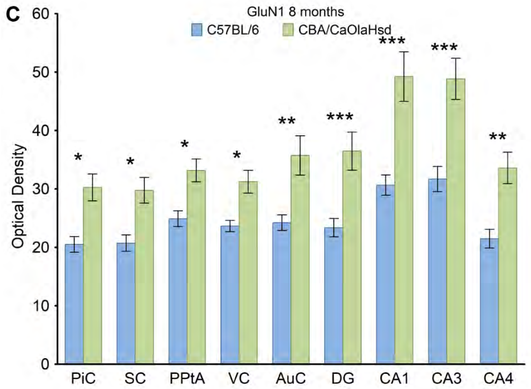
Placement of recording electrode

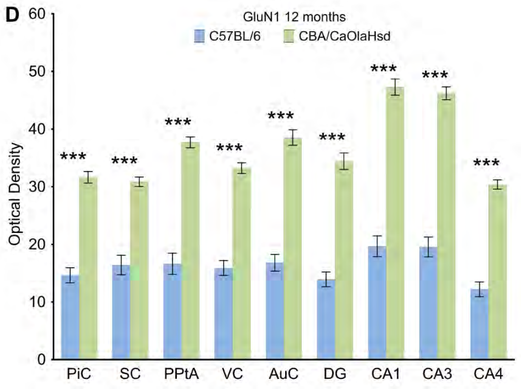
Results

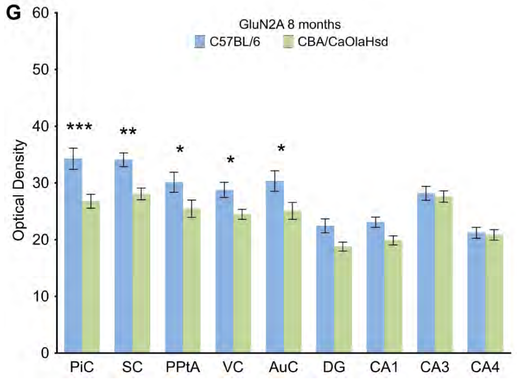


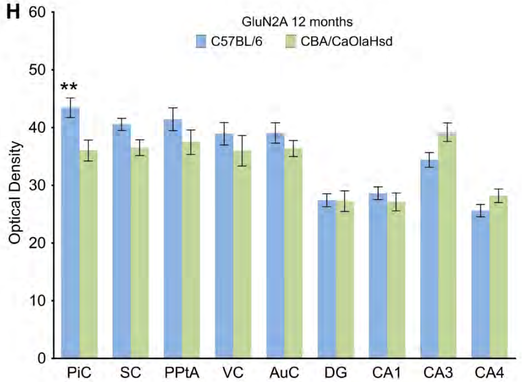
- Hippocampal synaptic plasticity was persistently compromised, with effects being more severe in deaf mice (C57BL/6) compared to blind mice (CBA/J) and mice without sensory deficits (CA/OlaHsd).

Results

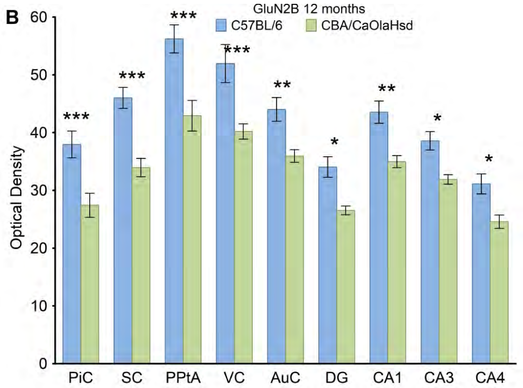


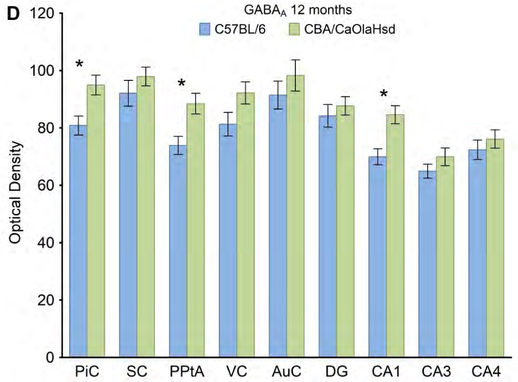






- NMDA receptor subunit and GABA receptor expression constantly changes throughout adulthood in blind (CBA/J) and deaf (C57BL/6) mice
- GluN1 subunit expression was reduced and the GluN2A:GluN2B ratio was persistently altered in cortex and hippocampus
- GABA receptor expression was decreased





Conclusion

- Cortical adaption due to loss of sensory input is sustained throughout adulthood
- Thus, the cortex remains in a state similar to critical period of postnatal cortical development
- The brain responds in equivalent manner regardless of sensory modality and degree of loss
- Hippocampal synaptic plasticity is persistently debilitated following permanent sensory loss, probably causing cognitive deficits due to progressive sensory loss
- The constant flux in NMDAR and GABAR expression results in impoverished LTP in blind (CBA/J) and deaf (C57BL/6) mice

→ Cortical and hippocampal adaptation to sensory loss progresses into advanced adulthood and is a process that chronically affects hippocampal function