

The effects of myelin loss, repair, and remyelination therapies on visual cortical function

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1. Key points

Abnormalities of the visual pathway are present in virtually all patients with multiple sclerosis (MS), often being the first symptom to manifest

We used longitudinal two-photon microscopy and acute Neuropixels recordings to evaluate how myelin loss and repair affect the visual cortex following cuprizone-mediated demyelination

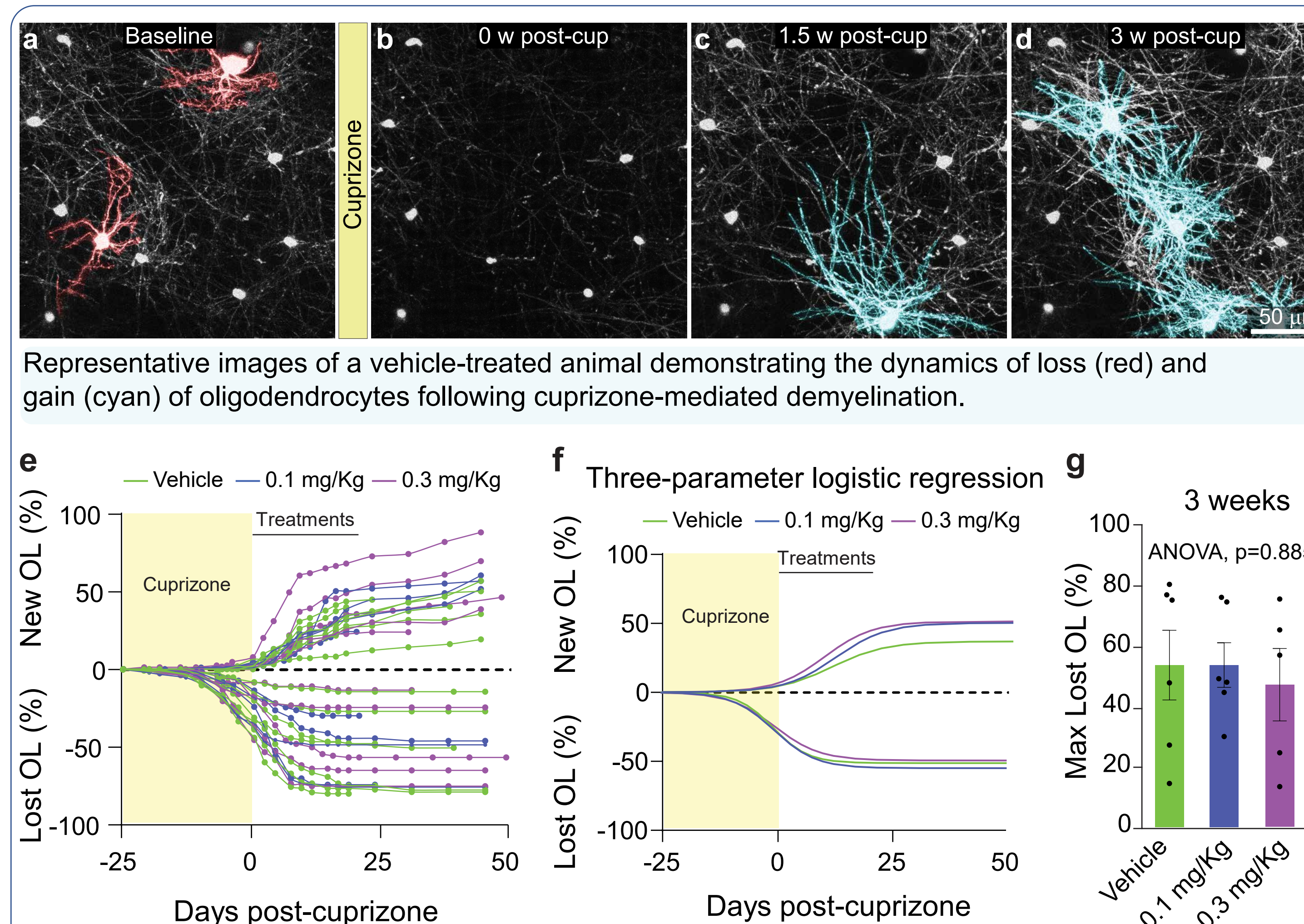
We tested the ability of the brain-penetrant thymomimetic (LL-341070, Autobahn Therapeutics) to improve oligodendrogenesis and visual cortex function

Cuprizone-induced demyelination led to increased latency in visual responses and reduction of P100 amplitude in the visually-evoked potential (VEP)

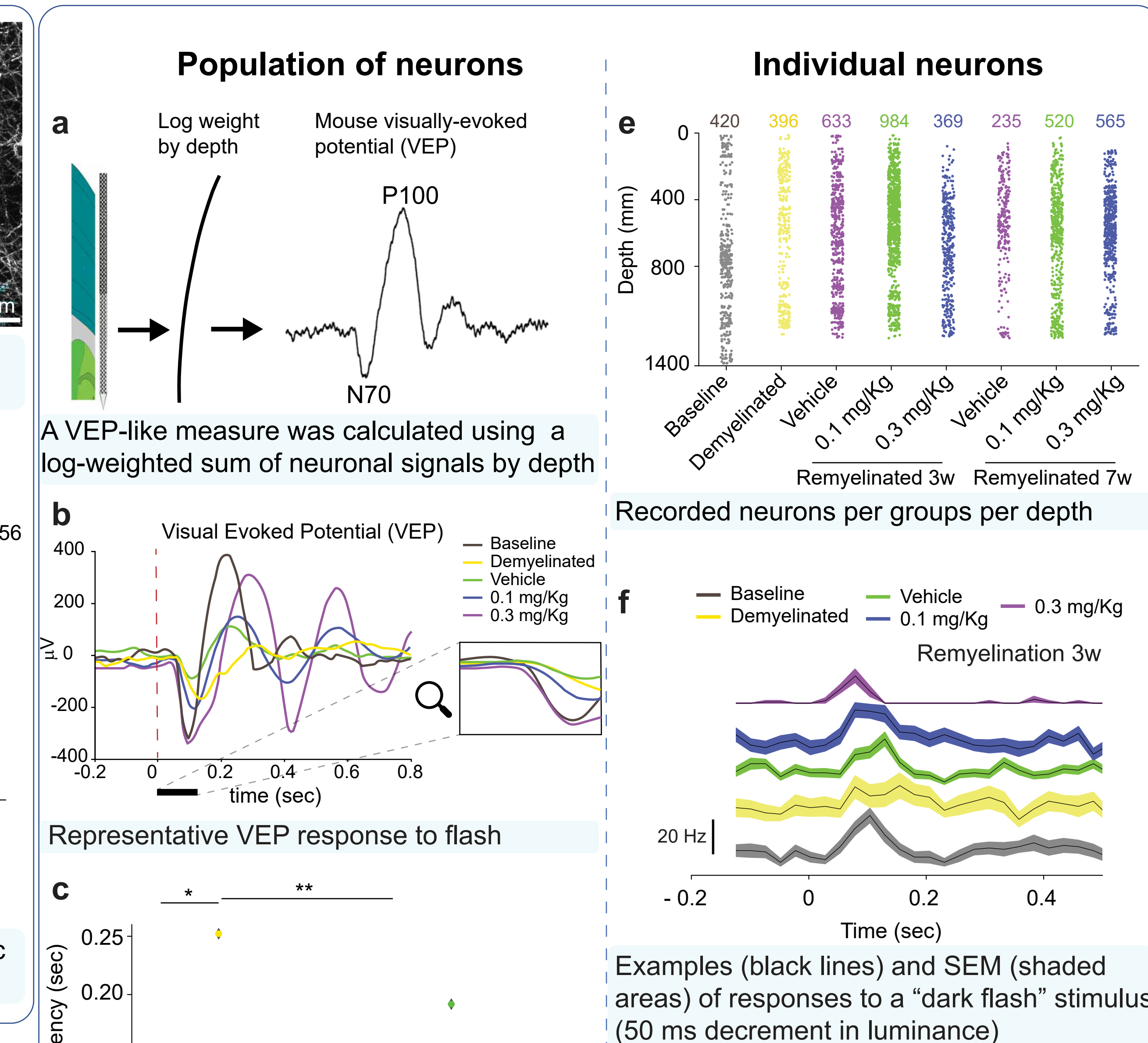
LL-341070 accelerated the dynamics of myelin repair, concomitantly rescuing the reduced P100 amplitude and the delayed latency of the visual response

Together, our results indicate that myelin loss impairs neuronal and network function in the visual system, which can be ameliorated by myelin repair and further enhanced by remyelination therapies, like LL-341070

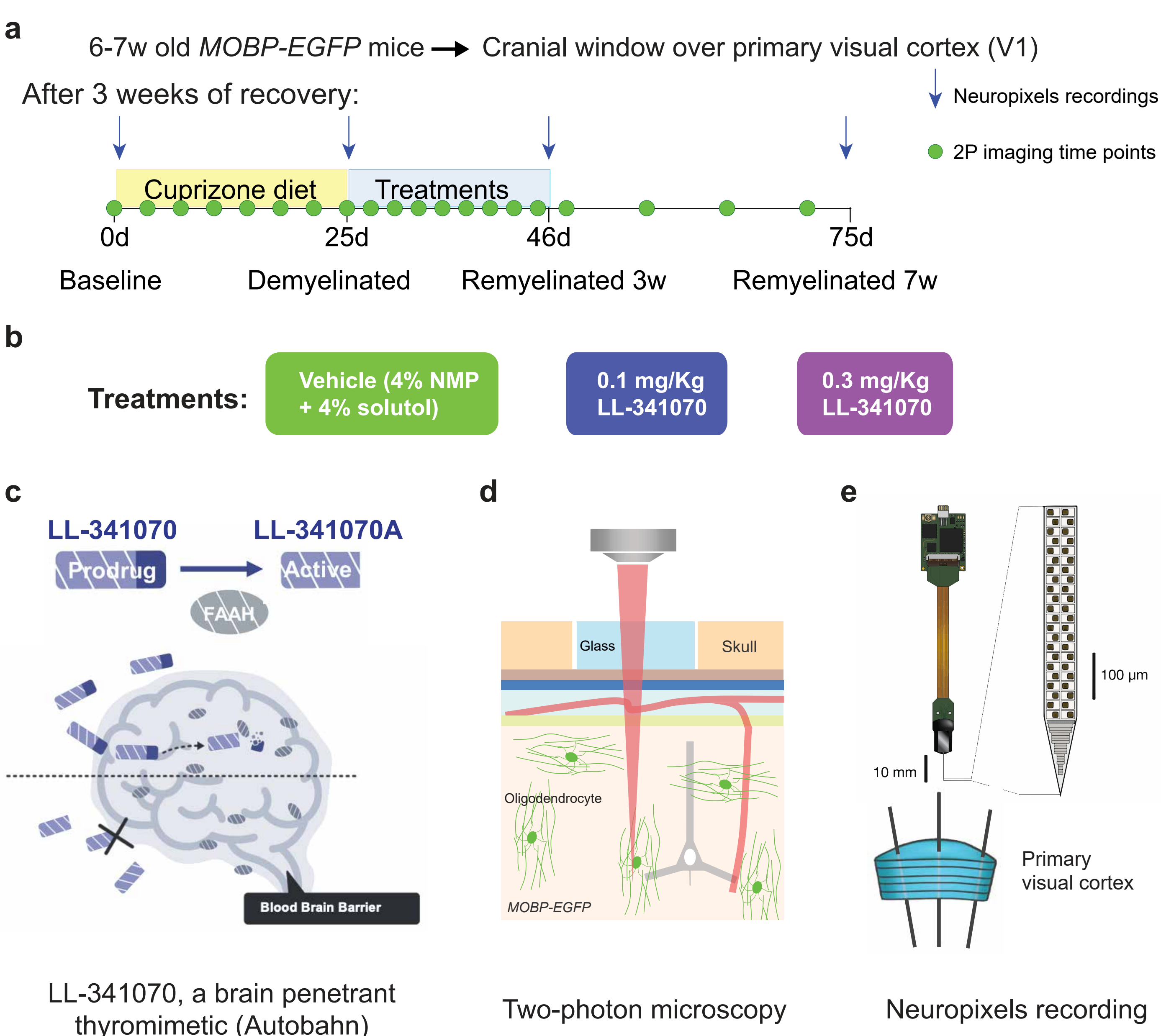
3. Dynamics of oligodendrocyte loss and repair in the visual cortex (V1)



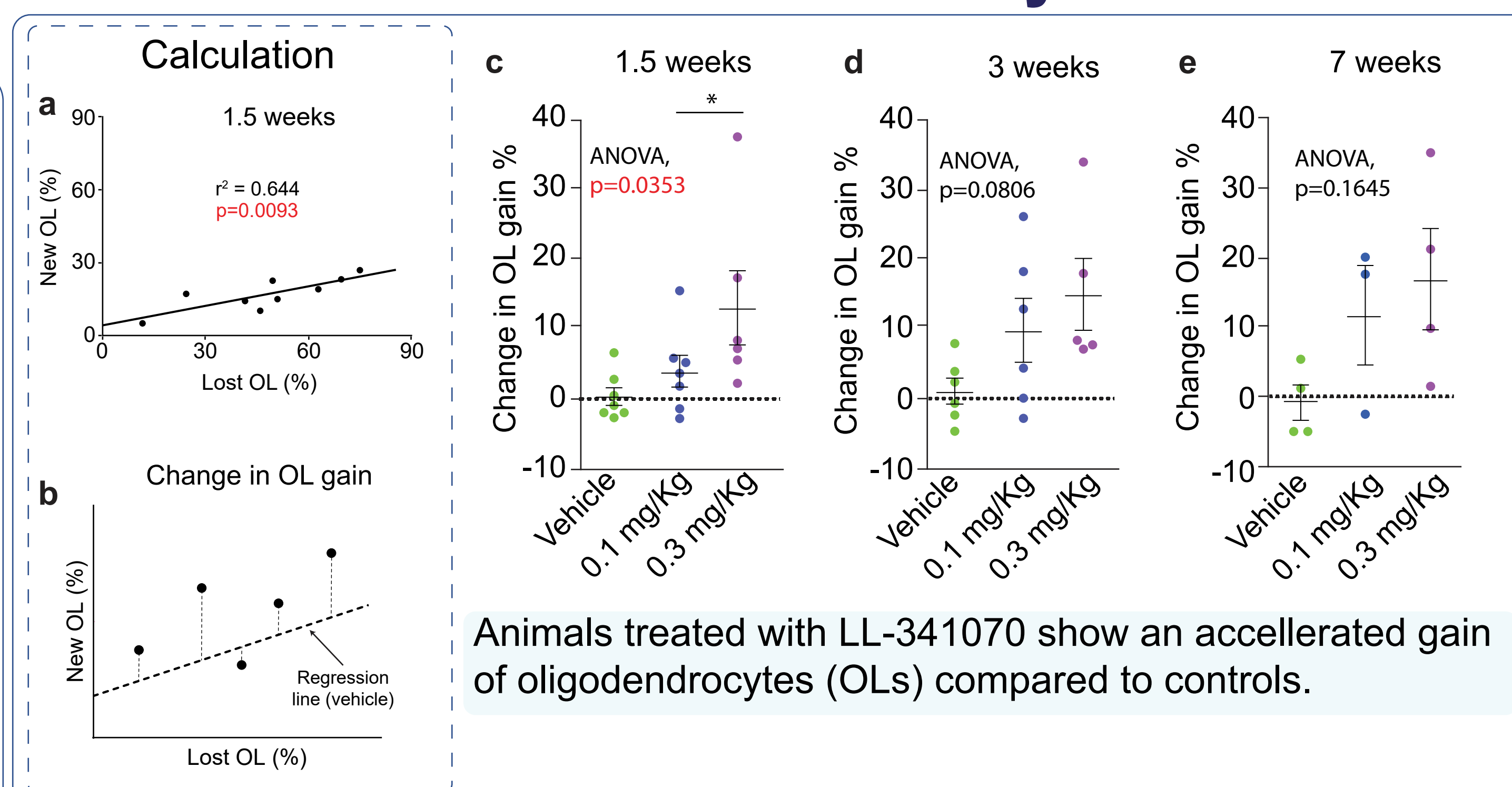
5. Accelerated myelin repair enhances recovery of visual function



2. Methods and experimental timeline



4. LL-341070 accelerates remyelination in V1



6. Conclusions

- 25 days of cuprizone induces significant loss of oligodendrocytes in V1
- Myelin loss impairs neuronal function in V1 resulting in delayed latency to visual response at population and single-neuron level
- Demyelination leads to a decrease in P100 amplitude in the VEP potentially via reduced synchrony in cortical visual processing
- Remyelination results in recovery of delayed latency in visual responses and of P100 amplitude
- The thymomimetic LL-341070 accelerates the dynamics of remyelination
- LL-341070 leads to faster recovery of delayed latencies in visual response and of reduced P100 amplitude