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APO-THEOSIS

Imagine there's no APOE4, it's easy if you try. You may say I'm a dreamer—but what would be the functional consequences of genetically removing APOE4 from neurones in mice? In short, there is a significant reduction in tau pathology, gliosis, neurodegeneration, neuronal hyperexcitability and myelin deficits. The mice chosen for this honour were Human-APOE-expressing 'tauopathy model' mice. Researchers used single-nucleus RNA-sequencing to show that removing neuronal APOE4 greatly diminished

neurodegenerative disease-associated subpopulations of neurons, oligodendrocytes, astrocytes and microglia. Another suggestion that reducing total APOE protein levels may be beneficial in the hunt for the holy grail: Alzheimer prevention strategies.

Nat Aging (2023). doi:10.1038/s43587-023-00368-3.

MATEY MOUSE

Just as Mother always knew when judging A Fo Ben's potential partners—breeding matters. For

judgemental mothers, read clinical genetics, as genotype to phenotype is never a one-to-one match. A study of 33 strains looked at the impact of introducing the autism-associated gene, *Chd8*, to over 1000 mice. Favourite strains from the study included the CC10 (gentle giants who were docile enough to pet) but not the aggressive nippers CC57s. Some *Chd8* features were near universal, and *Chd8* mice were almost always distinguishable from wild type. *Chd8* mice

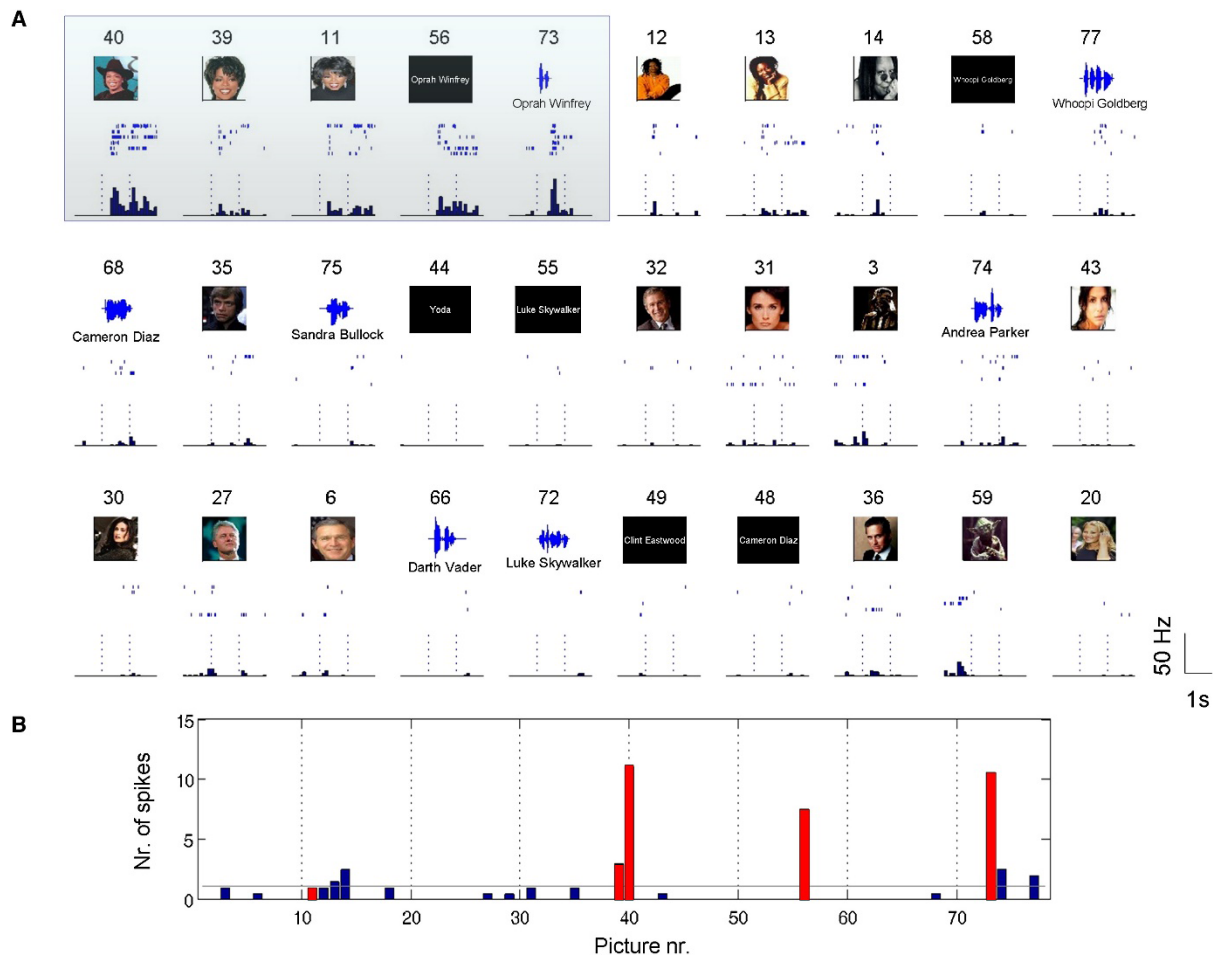


Figure 1 An Oprah Winfrey neuron from a nearly silent baseline (mean, 0.06 Hz; SD, 0.21 Hz), it responded with up to 50 Hz almost exclusively to the presentations of Oprah Winfrey, a nearly 1000-fold increase in its firing rate. To a lesser degree, the neurone also fired to the actress Whoopi Goldberg.

had larger brains, and tended to be more socially dominant when confronting another animal. It is important to remember that laboratory animals, are very much like A Fo Ben's school friends, aggressively inbred through generations of social engineering. In the same way that results from drug regulatory studies need confirmation in the 'real world' so too do murine models of neurogenetic disorders.

Neuron. 2023;111(4):539–556.e5.

THE OPRAH WINFREY NEURONE

A rose by any other name would smell as sweet, but would a neuron encode information about a rose similarly from visual text and sound stimuli? Using people who had depth electrodes in place for clinical reasons, they studied 7 subjects, and recorded from 750 medial temporal lobe (MTL) units. For example, [figure 1](#) shows a neuron in the left anterior hippocampus that fired selectively to three pictures of the television host Oprah Winfrey and to her written (stimulus 56) and

spoken (stimulus 73) name. The researchers repeat the trick with Saddam Hussain (!), to apparently show that single neurones in the human MTL respond selectively to representations of the same individual across different sensory modalities.

Curr Biol. 2009;19(15):1308–13.

HOW, WHY AND WHERE WOLF

If and when you develop psychosis, what would form the basis of your delusions? It is no secret that the residents near GCHQ in Cheltenham, UK have an excess of secret service-related hallucinosis. A recent case report details the mental illness associated with a 65-year-old man with Huntington's disease who become preoccupied with transgressive and apocalyptic ideas. His behaviour changed following admission to include acts where he would lunge at staff, and he'd refuse blood tests on the basis that he had no human blood in his veins. He had clinical lycanthropy, he believed he was transforming into

a werewolf. Culturally, a feature of werewolf stories is that full transformation into wolf form is associated with frenzied violence and sexual activity, followed by guilt and self-loathing once a human form is regained. As a window into what it may feel like to live with a neurodegenerative disorder and be aware of physical and emotional change that one cannot control, this is a sobering state in which to live.

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