OPTOGENETICS TO INSPIRE DEEP BRAIN STIMULATION: A NOVEL TREATMENT APPROACH FOR BEHAVIOURAL BRAIN DISEASES

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Behavioral brain disorders, such as addiction depression or obsessive compulsive disorder, are characterized not by death of neurons, but by functional disturbances in the brain's reward circuits. For example, exposure to addictive drugs (such as cocaine) increases the strength of neural connections in the nucleus accumbens – a key hub in the reward circuit. Optogenetics is a powerful technique that allows the control of specific populations of neurons with light in mice. Using this technique, we could selectively drive activity of neurons at low frequencies in order to weaken neural connections, thereby normalizing neural communication after cocaine exposure. This procedure also reversed pathological behavior induced by cocaine exposure, such as drug-sensitization and drug-seeking. While optogenetics is a powerful technique to causally link changes in neural activity and neuronal communication to behavior, it is not a technique that can be applied to patients anytime soon. Instead, we develop deep brain stimulation (DBS) for addition, a surgical therapy whereby electrodes are implanted into the brain and electric current is applied to stimulate discrete brain areas. This therapy has been successfully used to treat patients with movement disorders (ie. Parkinson's disease) for over 20 years. In the case of movement disorders, DBS is applied at very high frequencies (> 100 Hz) and is only effective at treating symptoms of the disease when the stimulation is turned on. Moreover, unlike optogenetic manipulations, DBS is highly non-specific; all types of neurons may be affected by electrical stimulation. To overcome these limitations, we combined our low-frequency DBS with tailored pharmacology in order to counter the non-specific effects of electrical stimulation. We refer to this approach as optogenetically-inspired DBS (OiDBS). In these conditions, a 10 minute application of OiDBS completely reversed cocaine-evoked neuronal changes and abolished drug-adaptive behavior. Crucially, unlike classical, high-frequency DBS, the effects of our acute OiDBS protocol lasted for over 1 week. Our work provides a blueprint for how we can use insight from mechanistic studies of neural circuits to develop novel, clinically-relevant treatments for behavioral brain diseases.