

“Optogenetics and Deep Brain Stimulation as Novel Treatments for Essential Tremor: A Comparison”

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Abstract:

Essential tremor is a nervous system disorder that causes rhythmic shaking, and while treatable, it is not yet curable. Medication is the first line of treatment. If drugs do not work, deep brain stimulation is a viable option commonly used today. However, optogenetics, an emerging technology that uses light to alter neurons, may soon replace deep brain stimulation as the preferred form of treatment for essential tremor. Optogenetics offers high temporal precision, high cell type specificity, and is able to induce both excitation and inhibition (Liu, et al. 2016), which deep brain stimulation lacks. When used in conjunction with deep brain stimulation, optogenetics appears to even make the effects of treatment last longer (Creed, et al. 2019). Optogenetics is not currently used in the clinical setting, however, in the lab setting it is showing incredible potential to change people's lives once it can be integrated into clinical practice. Like deep brain stimulation, optogenetics would not be used as a stand alone treatment, but would be used in adjunct with other treatments and therapies. The goal would be the same as deep brain stimulation, which is to reduce severity of tremors, improve daily functioning, and improve quality of life. Currently, both optogenetics and deep brain stimulation are very invasive techniques, although strides are currently being taken towards making optogenetics much less invasive. In the upcoming years it is plausible that optogenetics could replace or be used with deep brain stimulation as a treatment for essential tremor.

Introduction:

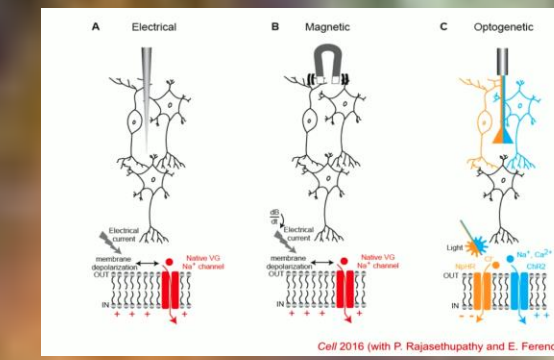
- Essential Tremor (ET), nervous system disorder causing rhythmic shaking.
- Different from Parkinson's and other diseases:
 - ET: no associated symptoms, occurs during volitional movement.
- ET is chronic and worsens with age.
- DBS: approved treatment for ET by FDA
- Optogenetics has shown promise in laboratory settings.
- Both operations are very invasive.
- Optogenetics can be much more accurate.
- Optogenetics is not currently used clinically.

Methods:

- Peer-review studies were compiled and analyzed.
- Some key words used in search: “optogenetics essential tremor deep brain stimulation” “optogenetics”, “optogenetics deep brain stimulation chronic pain” “essential tremor”
- Professional webinars and videos were utilized
 - (In lieu of hands on mentor time).
- Keywords in video search: “optogenetics lecture”, “optogenetics essential tremor lecture”, “Deep brain stimulation essential tremor lecture”, and “noninvasive optogenetics lecture”
- Telephone interview was conducted with Dr. Phil Albrecht, PhD.
- Zoom Meeting was conducted with Heidi Tucker, MS.

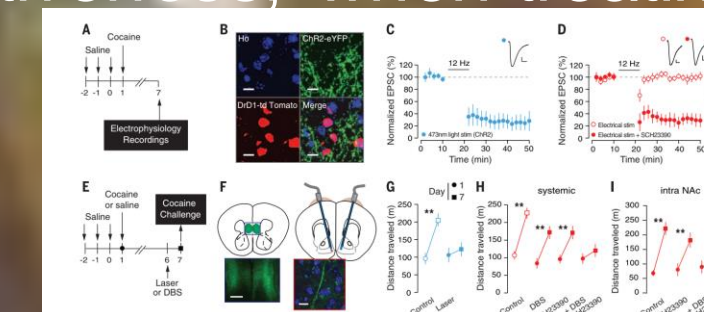
Results:

The different ways a neuron can be stimulated



(Blavatnik School of Government, 2019, *Illuminating the Brain*)

When used in addition to DBS, optogenetics have been seen to prolong treatment effectiveness, when treating addiction



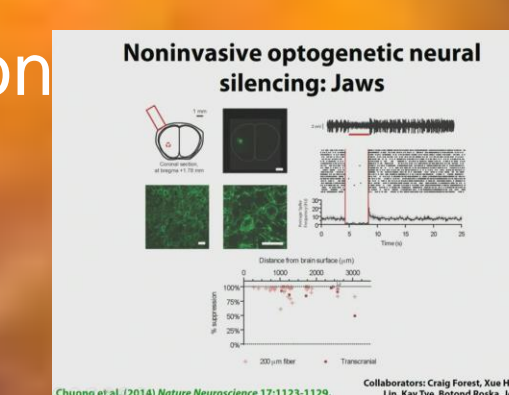
(Creed, et al. 2019)

NexFrame use in DBS



(Stanford Health Care, 2015, *Current and Expanding Surgical Treatments for Essential tremor*)

Optogenetics has been done in laboratories.



(Harvard Medical School, 2019, *Optogenetics: Illuminating the Path toward Causal Neuroscience*)

Interviews:

Dr. Phil Albrecht, PhD,

- Optogenetics is in a very early stage. Technologies in science evolve quickly.
- Common targets for DBS: Globus Pallidus internus (GPI), Subthalamic Nucleus (STN), and Ventralis Intermedius Nucleus (VIM).
- Gabaergic circuits in the GPI- gaba ureic transmission issues can lead to tremor.
- FDA looks for 2 things-> is it really safe, was it efficacious.
- Both treatments are more or less trial and error as of now.
- The hard part with optogenetics and injecting the opsins is if only some of the same kind of cells are targeted, but we don't know how to only target or even identify those specific cells (could further limit target compounds, but science may not necessarily there yet, addressing proteins are currently being used)

Heidi Tucker, MS,

- Patients and prescribers may be averse to optogenetics for the simple reason that permanent foreign gene expression is associated with opsins used.
- DBS has a long way to go, many possibilities with DBS have not even been explored yet.
- DBS is reversible, a major advantage.
- There is a long way to go and a lot of theoretical hurdles for optogenetics to be widely accepted in a clinical setting.
- There is much more that can improve the methods and delivery of DBS.
- There are conflicting results for everything, even the most common target in DBS there are conflicting reviews.

Discussion/Questions:

- Optogenetics can induce both cell excitation and inhibition.
 - Optogenetics also has high cell type specificity (Liu, et al. 2016)
 - DBS has multiple deep brain nuclei available for treatment.
1. Could DBS alter the action in a diazo bridge reaction to aid in the treatment of Chronic Pain?
 - Diazo bridge= location where reactions with diazo compounds (Any molecule with the general formula R-N=N-R.) occur.
 1. Could optogenetics be a possible treatment for other movement disorders, like Parkinson's Disease or Multiple Sclerosis?
 2. Could there be potential problems from injecting opsins into cells?

Conclusion:

- Optogenetics could become a treatment for Essential Tremor. This could occur as either a replacement for DBS or in addition to DBS.
- Years in the future, when more is known.
 - New treatment need to overcome many hurdles,
 - Optogenetics is no exception.
 - If it is proven that optogenetics has a longer effect, or that it can be done noninvasively, there would be a more compelling reason to push for optogenetics to be used clinically.
 - More research needs to be done on DBS as well,
 - The full potential of DBS is not yet known.

Future Directions:

1. Doing hands on work with DBS/optogenetics.
2. Researching optogenetics as a possible treatment for other movement diseases/disorders like Parkinson's Disease or Multiple Sclerosis.
3. Looking into if DBS could alter the action in a diazo bridge reaction to aid in the treatment of Chronic Pain.

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