Annotated Bibliography

Peer Reviewed Sources

1. Chandra, Ramesh, Jeffrey D. Lenz, Amy M. Gancarz, Dipesh Chaudhury, Gabrielle L. Schroeder, Ming-Hu Han, Joseph F. Cheer, David M. Dietz, and Mary Kay Lobo. “Optogenetic Inhibition of D1R Containing Nucleus Accumbens Neurons Alters Cocaine-Mediated Regulation of Tiam1.” *Frontiers in Molecular Neuroscience* 6 (May 24, 2013). <https://doi.org/10.3389/fnmol.2013.00013>.

Tiam1 is implicated in structural rearrangement and plasticity following exposure to stimulants. In self administration paradigms, the authors demonstrate lowered expression of Tiam1 in the NAc following cocaine exposure. The authors found that Tiam1 expression was down regulated and that D2 receptor activation did not change Tiam1 expression. Optogenetic inhibition of the D1R expressing neurons prevented the Tiam1 downregulation and blunted the locomotor effects of cocaine.

1. Covington, Herbert E., Mary Kay Lobo, Ian Maze, Vincent Vialou, James M Hyman, Samir Zaman, Quincey LaPlant, et al. “ANTIDEPRESSANT EFFECT OF OPTOGENETIC STIMULATION OF THE MEDIAL PREFRONTAL CORTEX.” *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience* 30, no. 48 (December 1, 2010): 16082–90. <https://doi.org/10.1523/JNEUROSCI.1731-10.2010>
This paper looked into indicators of activity in the post mortem tissues from the prefrontal cortex of clinically depression patients. The human tissues showed reductions in markers for cellular activity. In a mouse model of depression, researchers expressed channel rhodopsin 2 to drive burst firing in the medial prefrontal cortex. Animals that suffered depressive like states showed similar reductions in the markers for cellular activity while optogenetic stimulation of the mPFC showed strong anti-depressant qualities.
2. Galvan, Adriana, William R. Stauffer, Leah Acker, Yasmine El-Shamayleh, Ken-ichi Inoue, Shay Ohayon, and Michael C. Schmid. “Nonhuman Primate Optogenetics: Recent Advances and Future Directions.” *The Journal of Neuroscience* 37, no. 45 (November 8, 2017): 10894–903. <https://doi.org/10.1523/JNEUROSCI.1839-17.2017>.

Nonhuman primate research allows for many of the closest comparison to human experiments in preclinical settings. Optogenetics being utilized in primates allows researchers to take advantage of the inherent qualities of primate research like brain size and combine it with the level of synaptic control given by the light controlled cells and circuits. This review discusses the technicalities and advantages of long term primate research in these animals, including specific cell population targeting and minimizing tissue damage.

1. Kim, Christina K., Avishek Adhikari, and Karl Deisseroth. “Integration of Optogenetics with Complementary Methodologies in Systems Neuroscience.” *Nature Reviews. Neuroscience* 18, no. 4 (March 17, 2017): 222–35. <https://doi.org/10.1038/nrn.2017.15>.
Modern techniques allow multiple layers of control and tracing within tissues. This allows for a wider array of potential methods for any given experiment and more specialized techniques for previously impossible experiments. Allowing the integration of anatomical tracing, electrophysiology, and activity dependent monitoring gives a more complete picture of the neural circuits and neural activity.
2. Lenz, Jeffrey D., and Mary Kay Lobo. “Optogenetic Insights into Striatal Function and Behavior.” *Behavioural Brain Research*, Optogenetics, 255 (October 15, 2013): 44–54. <https://doi.org/10.1016/j.bbr.2013.04.018>.
This review of striatal experiments highlights the ways that optogenetics has been employed to tease apart previously unknown and unidentifiable functions of the circuits contained in the structure. Optogenetic stimulation and inhibition have allowed for the anatomical tracking of structures as well as the behavioral functions that the circuits control. This has given new insights into reward behavior, addiction pathologies, depression and anxiety behaviors, and some aspects of motor behavior.
3. Lobo, Mary Kay, Herbert E. Covington, Dipesh Chaudhury, Allyson K. Friedman, HaoSheng Sun, Diane Damez-Werno, David Dietz, et al. “Cell Type Specific Loss of BDNF Signaling Mimics Optogenetic Control of Cocaine Reward.” *Science (New York, N.Y.)* 330, no. 6002 (October 15, 2010): 385–90. <https://doi.org/10.1126/science.1188472>.
The BDNF receptor TrkB differentially affects cocaine reward when selectively deleted from D1 or D2 expressing neurons in the NAc. Optogenetic stimulation of D2 expressing neurons in the NAc was shown to mimic the effects of TrkB loss and suppress cocaine reward, with the opposite result being shown in D1 expressing neurons. The function of BDNF in these circuits with respect to cocaine reward highlights the opposing nature of their activity, and potentially how adjusting the activity in one will allow for modulation of the other in future treatments.
4. Lobo, Mary Kay, Eric J. Nestler, and Herbert E. Covington. “Potential Utility of Optogenetics in the Study of Depression.” *Biological Psychiatry* 71, no. 12 (June 15, 2012): 1068–74. <https://doi.org/10.1016/j.biopsych.2011.12.026>.
This review of techniques highlights the usefulness of circuit and cell level control in the studies of depression. Given the in vivo applications of optogenetics, behavioral experiments with depression models is possible, allowing for immediate circuit level control of critical areas associated with depression like behavior. By highlighting the improvements of this technique compared to previous generations of techniques and its tie ins to related neuroimaging studies, the paper gives a promising future direction in identifying and modulating cell and circuit level activities with the hopes of improving and potentially preventing the development of depression.
5. Soper, Colin, Evan Wicker, Catherine V. Kulick, Prosper N’Gouemo, and Patrick A. Forcelli. “Optogenetic Activation of Superior Colliculus Neurons Suppresses Seizures Originating in Diverse Brain Networks.” *Neurobiology of Disease* 87 (March 2016): 102–15. <https://doi.org/10.1016/j.nbd.2015.12.012>.

Seizures result as a result of overactive firing in many regions of the brain. The deep layers of the superior colliculus have been shown to counteractive seizure activity by regulating the hypeactive firing in these brain areas. By inducing seizure from multiple pathways and optogenetically stimulating the DLSC, the researchers demonstrate a potential target and mechanism of stopping these seizure activities and potentially showing a neuroprotective mechanism of preventing them.

1. Thanos, Panayotis K, Lisa Robison, Eric J. Nestler, Ronald Kim, Michael Michaelides, Mary-Kay Lobo, and Nora D. Volkow. “Mapping Brain Metabolic Connectivity in Awake Rats with MicroPET and Optogenetic Stimulation.” *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience* 33, no. 15 (April 10, 2013): 6343–49. <https://doi.org/10.1523/JNEUROSCI.4997-12.2013>.
Glucose metabolism can be tracked in the brain as an indicator of activity using Positron Emission Tomography (PET). Optogenetic stimulation of the NAc induced changes to this metabolism, and researchers highlighted several other areas that had similar changes induced by this stimulation in the NAc, including the globus pallidus and the hippocampus. These changes were verified by increased levels of cFos expression. This experiment demonstrates not only the usefulness of optogenetics in elucidating network connectivity but PET monitoring of glucose metabolism in awake animals.
2. Wright, Katherine N., Amanda M. Dossat, Caroline E. Strong, Lindsay L. Sailer, Samantha M. Pavlock, and Mohamed Kabbaj. “Optogenetic Inhibition of Medial Prefrontal Cortex Projections to the Nucleus Accumbens Core and Methyl Supplementation via L-Methionine Attenuates Cocaine-Primed Reinstatement.” *Integrative Zoology* 0, no. ja. Accessed November 13, 2018. <https://doi.org/10.1111/1749-4877.12365>.

L-methionine has been shown to methylate DNA that has been demethylated following exposure to drugs of abuse, indicating a potential insight into the cause of relapse. Animals were put through a cocaine self-administration protocol. Using optogenetic modulation of the prefrontal cortex and nucleus accumbens circuit and treatment with L-methionine, the animals were shown to have less cue induced cocaine consumption following a prolonged abstinence period. This would indicate that epigenetic modification within the PFC-NAc circuit plays critical a role in relapse.

Website Sources

1. Optogenetics: Controlling the Brain with Light
<https://www.youtube.com/watch?v=QA67v4vSg00>
This is an MIT-TV video showing the basic concepts of neural circuits and the idea behind optogenetics. It demonstrates the genetic material sourcing of the light sensitive ion channels and how the technique can be applied with microsecond precision within cell circuits.
2. Lighting Up the Brain with Optogenetics
<https://www.labroots.com/trending/videos/11448/lighting-up-the-brain-with-optogenetics>
This is a easy to understand website breaking down advanced techniques to new audiences. With cartoon diagrams of ion channels, viral infection, and behavior experiments, it give a simple and concise explanation of the ins and outs of the techniques and what it can be used for.
3. Optogenetics: Harvesting the Power of Light for Neuronal Control
<https://www.technologynetworks.com/neuroscience/articles/optogenetics-harvesting-power-light-neuronal-control-284926>
A technical overview of the procedure, including the history of its development, its applications, and the potential pitfalls of using it. It includes references for the original publications on optogenetics and some of the newer applications that have been noted as successful in laboratory settings.
4. Optogenetics
<https://www.britannica.com/science/optogenetics>
Written by developer Karl Deisseroth, this is a brief but thorough explanation of the technique. The link includes videos made by the developers and links to background information on each individual component of the technique.
5. Let There Be Light: A Tutorial on Optogenetics
<https://www.researchgate.net/publication/263894386_Let_There_Be_Light_A_tutorial_on_optogenetics>
This is a published tutorial on the development of the optogenetics, how to design your own experiment using optogenetics, and potential medical research utility that can come from optogenetic techniques. It includes diagrams of specific circuits and pathways implicated in specific disease pathologies.
6. Open Optogenetics Video Tutorials
<http://www.openoptogenetics.org/index.php?title=Videos>
This is a collection of videos on the topic of optogenetics. These include TED talks, technical application, lectures, how to videos, and MIT research releases concerning the topic.
7. MIT Explained: Optogenetics
<https://www.youtube.com/watch?v=Nb07TLkJ3Ww>
Edward Boyden, one of the original developers of the technique, gives a brief talk about the development and utility of optogenetics. It goes into the methods of aiming light wavelengths at specific tissues within the brain and the limitations with regard to human patients.
8. NeuroWiki: Optogenetics
[http://neurowiki2013.wikidot.com/individual:optogenetics:basics](http://neurowiki2013.wikidot.com/individual%3Aoptogenetics%3Abasics)
A University of Toronto created wiki of neuroscience techniques, with diagrams for the stereotaxic surgeries, molecular targets, and viral constructs. A complete list of sources is included with the page.
9. Nanalyze: Optogenetics Explained (for Investors)
<https://www.nanalyze.com/2016/11/optogenetics-explained-simply-investors/>
This is an out of the science fields source, giving explanations of the technique and its potential utility and value to investors. An important read for those who might be going into industry or attempting to market the potential applications.
10. Neuro Transmissions: What Are Optogenetics

<https://www.youtube.com/watch?v=-8bMMuvpbkg>

A quick and easy breakdown of the technology that makes the techniques possible. This includes simple demonstrations and animations of the molecular mechanism, as well as clips of videos of animal behavior demonstrations.