Design Brief

Using Optogenetics to Reduce Parkinsonian Symptoms

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By using optogenetics to change the way particular neurons function, we can develop a new solution to many neural diseases. By changing neural pathways and certain rates of communication, alterations can be made as to which neurons are active versus inactive. One disease that optogenetics can be used to reduce or eliminate is Parkinson's disease, due to the relatively simple target activity of the neural circuits.

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Background

The brain is an amalgam of pathways and circuit patterns that not only allow a person to function but also have designated roles in various parts of the brain. But many factors can damage the fragile circuitry that we rely on such as genetic defects, blunt trauma, and various substances. For instance, we can lose muscle control, cognitive abilities and in the worst cases, our lives if issues are not resolved within the basal ganglia. Fortunately modulating certain neural pathways in particular areas of the brain can alleviate the symptoms of a disease by activating needed pathways or silencing an area of interference (Kravits et al. 2010). Optogenetics is a method of manipulating neural tissue by using light to control when and which neurons fire. It works by using viral vectors to deliver opsin genes, originally from algae in DNA, to allow protein channels of individual neurons to be controlled, thus allowing the experimenter to dictate when neurons fire[5] based on where the light hits (Berger et al. 2010). Although optogenetics is a novel concept, its testing has been well established within the neuroscience community and its principles have highlighted new understandings about how the mind works. The brain is structured based on the patterns of neurons (Liam et al. 1996; Berger et al. 2010; kravitz et al. 2010) and, with increased activity, large amounts of activity strengthen those particular pathways and allow for that structure to be maintained. Based on the Hebbian model of synaptic plasticity neurons that wire together, fire together to increase synaptic efficacy (Liaw et al. 1996) Optogenetics utilizes light to control which neurons fire and when, thereby regulating brain activity and this can be used to study and influence the way parts of the brain interact and function. Optogenetics can more precisely affect the brain than many other methods since it does not cause side effects and can directly control specific neurons without having to worry about various limitations such as the blood brain barrier or metabolism.

Systems Level

Based on mouse trials optogenetics can be used to reduce neurodegenerative symptoms by suppressing indirect pathway medium spiny neurons (MSNs) in the basal ganglia and increasing the activity of direct pathways (Kravitz et al. 2010) Indirect pathways are neuronal circuits through the basal ganglia which help prevent unwanted muscle contractions from competing with voluntary movements. Direct Pathways facilitate the initiation and execution of voluntary movement. By devel-

oping new biotechnology we can change how the brain communicates to provide better inter-neuron communication throughout a person afflicted with a neurodegenerative disease like Parkinson's disease. Direct-pathway activation significantly reduce deficits in freezing, bradykinesia, and locomotor initiation (Kravitz et al. 2010). Establishing a critical role for basal ganglia circuitry in the bidirectional regulation of motor behaviour and indicating that modulation of direct-pathway circuitry may be the newest and most effective therapeutic method in comparison with current treatments. Computers can store neural activity patterns once the information is gained (from electrodes) and the brain can be changed based off of the stored information from another or prior subject in addition with the already mentioned heuristic algorithm that can compensate for differences and the non-linear nature of neurons. A compatible neurotypical patient with a similar neural pathway structure and rates of activity can give the blueprints of what to change for an abnormal subject. The expected outcome is that the neurons will retain the level of activity that was used with an optogenetic session and the new rates of activity and structure of the neural pathways will be consolidated within the patient after a certain period of time.

Device Level

Beams of electromagnetic energy can transfer energy between coupled coils allowing for the transfer of energy and oscillating magnets can extract power from a low-level AC field removing the need for wires (Du et al. 2018) The magnetic fields can be modified to go through human tissue while remaining at safe non-ionizing levels and can be modified depending on human risk or other standards of safety (Du et al. 2018). Various frequencies of the electromagnetic beam can be sent to allow for different distances (Du et al. 2018) that would be needed to transfer the energy to allow the patient to lead a normal life. Lastly, the energy used from the coupling can be used to power small LEDs that would be used on the implants. After the duration of a few months, an electrode cap can be placed to see how pathways have changed. An algorithm will reprogram the implants based on the new heuristic model which will be constantly improving the best method to maintain an ideal system in which implants turn on and off in order to get or keep the brain operating in the ideal system. This design eliminates the need to replace implants unless there is mechanical damage or incorrect installation of the device. There should be a portable device with the patient that will house the hardware necessary for the algorithm's software and hardware requirements (as well as the algorithm itself), a Graphic User Interface (GUI) for the user and the necessary transmitters to control the implants on the patient.

Parts Level

Various types of opsin genes will be applied in the host sporting an array of different colours in order to allow for different wavelengths of light to activate to allow for finer control. There are various solutions to manipulating several engrams at once in a more complex brain, such as using a system of light emitters and various types of opsin genes.

Safety

Optogenetics has side effects and risks that are mainly the byproduct of improper administration, however the current methods for treating the disease are not as effective or safe. Carbidopa, Dopamine agonists, and Catechol O-methyltransferase (COMT) inhibitors are some of the drugs that are used in treating Parkinson's symptoms but they all share the issue in that they do not stop the underlying issue completely and they have various side effects. The drugs have side effects ranging from restlessness, confusion, nausea, and involuntary movements,etc. Transcranial Magnetic Stimulation (TMS) has a lot of potential for treating Parkinson's symptoms but has a variety of shortcomings which is why optogenetics should be preferred. It is not uncommon for TMS to cause some sort of localized pain for patients or some other discomfort, patients with ear implants are not able to pursue it, and lastly despite its success with depression and other neurological conditions it has not shared the same success with Parkinson's (Greb 2018) These methods all are capable of reducing the symptoms in varying degrees, but optogenetics can offer much more potential in treating Parkinson's. Extensive testing will have to be done, and due to some success with rodents, moving to extensive testing on primates could be used to confirm that indirect pathways are the issue and that treatments are effective with no unforeseen consequences in a more similar brain. After more human trials and the new device's finalization, we can apply the concepts on a mass scale so it can be used to enhance the lives of those who suffer from various debilitating neurodegenerative brain conditions by analyzing which neurons are problematic or need more expression and subsequently activating or deactivating them. Human trials will have volunteers with Parkinson's have their neurons spliced with opsin gene by using a viral vector (or CRISPR if by that time it has been approved and is a standard means of editing genetics). Data will be gleaned from how humans' indirect and direct pathways interact by having neurotypical volunteers have their brains studied by using electrode caps, and MRIs will verify the hypothesis that changing indirect pathways will prevent symptoms from appearing. Testing will be finalized by the application of the information of the neurotypical studies on the volunteers with Parkinson's, as the optogenetic equip-

ment begins to activate and deactivate certain pathways depending on the patient and studying the effects on the symptoms.

Discussions

The main point of contention with this model is the difficulty of tailoring the implants to specific hosts, the cost of the device and materials, and the difficulty in adapting the software to truly be able to dynamically assist a human and learn from the input that it is given. To mitigate these concerns new technologies will need to be oriented to assist in these issues. In order to reduce costs and allow for tailoring implants and other necessary devices for the user, using 3-D printing could be a common procedure in order to custom-make devices easily and efficiently. Having software that can adapt to the human brain easily may require the studying of multiple client's brains for a certain period of time beforehand so data can be compiled, studied, and averaged to make a widely applicable baseline for the heuristic algorithm before further sessions of re-evaluation of neural activity right before and for the time after applying the optogenetic equipment. Optogenetics seem to be applicable to many other neurological diseases such as epilepsy, Parkinson's disease, Alzheimer's disease, multiple sclerosis and spinal cord injuries.

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