Damages to mammalian neural activity treatment

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Utilizing Prokaryotic Channels, Organic Biometric Neurons and Mammalian Target of Rapamycin to Reverse and Repair Damages to Mammalian Neural activity

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Introduction

One of the most detrimental conditions that a patient can acquire is damage to the nervous system. Major damages can include vascular disorders, congenital, degenerative disorders and trauma. These damages and disorders often involve abnormal neurochemical and electrical signaling (Purves et al. 2012). There are currently many treatments available for patients suffering damage to the nervous system. These possible treatments can range from surgery, physical therapy and medications for autoimmune diseases which can help a patient adapt to or possibly provide a small fix for their individual situation but the underlying problem may still subsist. The damages caused to mammalian axons in the central nervous system (CNS) fail to regenerate or repair after injury with issues such as traumatic brain injury (TBI) or demyelinating conditions such as multiple sclerosis (MS) leading to affected nerve fibers which will no longer work correctly as shown by Mierzwa et al. (2015). This can leave sites of injury in patients unmanageable and without a clear path to recovery. To remedy this, a toolbox has been proposed utilizing a series of recent research. Nguyen et al. (2016) describe a method which would allow for direct enhancement of electrical excitability in human cells through the overexpression of voltage-gated sodium channels (VGSC). Simon et al. (2015) developed an organic electronic biometric neuron, which has the capacity to integrate within a malfunctioning signaling pathway. Lim et al. (2016) present that through stimulating neural activity and the cell-growth-promoting pathway of mammalian target of rapamycin (mTOR), retinal ganglion cells (RGCs) in mice which their visual neurons silenced would see RGC axons regenerated and re-innervated. Utilizing these tools; engineered prokaryotic channels to increase tissue excitability, organic electronic biomimetic neurons to mimic the function of physiological neurons and bridge the affected zone to the rest of the nervous system, and utilizing visual neural stimulation along with activation of the mTOR pathway to stimulate axon regeneration, it opens up the possibility to reverse and repair conditions caused by damages and afflictions to the nervous system.

Prokaryotic Channels

Voltage-gated sodium channels (VGSCs) are fundamental to cell-to-cell communication in the nervous system, and their loss of function can lead to a variety of different disorders (e. g. neuronal, cardiac and skeletal muscular). These VGSCs, in electrically excitable tissues, allow for the firing and spread of action potentials. Ren et al. (2001) along with Koshi et al. (2003) had provided novel insight into the structure and biophysical properties of VGSCs and a large bacterial family of VGSCs called $BacNa_V$. Utilizing this bacteria Nguyen et al. (2016) established a platform to enable stable conversion of primary human fibroblasts into action potential conducting cells which can slowly recover conduction in tissues with pathological conditions. Versatility was shown as Nguyen et al. with applying this technology to human ventricular fibroblasts (HVFs), human astrocytes

(Has) and HECK293s into " engineered electrically excitable cells (E-HVFs, E-HAs and E-HEK293s, respectively)" (Nguyen et al.). Though this study only focused on the alteration of specific amino acid residues in BacNa $_{V}$, E43 and D60, a variety of possible combinations can be explored to further expand the possibilities of this approach.

Organic Biometric Neurons

Currently most neurological therapies are based in and rely on medication and electrical stimulation. Larsen et al. (2013) presented how a newer class of technology called iontronics, which is based on polyelectrolytes and Ï€-conjugated semiconducting polymers, can work as organic electronic electrophoretic transport devices. Iontronics exhibit a unique combination of ionic and electronic properties, enabling transduction between electronic impulses and biochemical signals. Applying this, Simon et al. (2015) presented an organic electronic biomimetic neuron or artificial neuron with the hopes it can be used to restore use to malfunctioning signaling pathways. These artificial neurons are based on the basic chemical-electrical-chemical signal transduction like projected neurons use in communication with one another hoping to find a potential for long-range neuronal signaling. Simon et al. had concluded their results offered a novel means for " auto-regulated neuromodulation based on endogenous substances, enabling malfunctioning neuronal signaling pathways to be restored or augmented", thus returning the damaged area to a chemically and electrically balanced healthy state. The artificial neurons also present a conversion of glutamate-induced descending neuromuscular signals into acetylcholine-mediated muscular activation signals may be obtained, applicable for bridging injured sites and active prosthetics (Simon et al.).

Neural Activity Combined with Activated Mammalian Target of Rapamycin

Focusing on the eye-to-brain pathway which consists of " RGC connections to subcortical targets [as] a widely used model for studying vertebrate CNS regeneration" (Vidal-Sanz et al. 1987) (Park et al. 2008), Lim et al. (2016) shows how that the stimulation of RGC activity leading to their axons regeneration and by looking at axon damage in the CNS they observed avenues in which they can regenerate and restore correct connectivity patterns. Lim et al. had found that " enhancing neural activity and mTOR signaling in RGCs, we observed long-distance, target-specific RGC axon regeneration in adult mice" showing a mechanistic combination that can lead to axon regrowth and repair. This research may prove informative for devising treatments for the damaged visual system, spinal cord or other CNS regions in patients suffering from neurodegenerative diseases or physical trauma (Lim et al.).

Proposed Method of Combination Therapy and its Prospect of Neuromodulation Through its Application/Discussion

There are important functional implications for the anatomical regeneration of the different parts of the nervous system. Utilizing a combination of these tools that these research teams worked on, it's possible to come up with a possible combination therapy to reverse or repair serious damages when it comes to the nervous system. A treatment involving these tools would be a personalized therapy requiring costume gene editing for the prokaryotic channels, specialized artificial neurons for the site of damage and while using out-patient or in-patient therapy to stimulate neural activity and enhance mTOR. If done together the possibility is open for neuronal regeneration and chemical and electric stabilization, for affected tissue and site of injury.

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