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A Novel Contrast-Enhanced Brain Mimicking Hydrogel for Testing Implantable Brain Electrodes

得獎獎項

Engineering First Award

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Abstract

Paralysis is a debilitating disorder that does not currently have safe and effective treatments. Implantable brain electrodes can be used to read brain waves and convert them into a corresponding motor function to restore movement in paralyzed patients. Tissue deformation induced around the implant site is believed to reduce their viability through the foreign body response. Developing electrodes that minimize deformation is challenging because the mechanical aspects of deformation are not fully understood and non-animal tissue models for testing electrodes are unavailable. Development of pre-clinical models for *in vitro* testing of the mechanical properties of electrodes can lead to a better understanding of this prevalent problem. The objective of this study was to construct a novel contrast-enhanced, brain mimicking hydrogel using photopolymerizable polyethylene glycol (PEG) polymer that contains alginate microspheres with enclosed gadolinium (Gd) contrast agent. 1.5% alginate microspheres were constructed with enclosed Gd-DTPA-BSA contrast agent and successively added into 10% PEG. Then, this mixture was photopolymerized using a 5 mW/cm^2 UV lamp to result in a successful brain mimicking hydrogel. Rheological testing showed that its elastic modulus was approximately 1.5 kPa, which is similar to that of a normal human brain. The model is valuable because the presence of the contrast agent in the hydrogel resulted in distinct bright spots on the MRI. This can facilitate the visualization of tissue deformation caused by electrode insertion via comparison of pre-insertion and post-insertion images. This brain-mimicking model has the potential to improve understanding of neural deformation from electrode implants in order to assist patients suffering from paralysis.

ABSTRACT OF EXHIBIT

Caffeine is a widely consumed drug, taking in one form or another by 90% of the world. Recently, it has been demonstrated that certain drugs of abuse (e.g., alcohol, nicotine), in addition to other known actions, act via induction of endogenous morphine release in animal tissue. It has also been shown that morphine exerts immunosuppressive actions (e.g., causing cellular rounding) which occur through induction of Nitric Oxide release. Caffeine too has been shown to exert immunosuppressive effects. Yet, caffeine's implications on the neuro-immune system have not been fully explicated.

The design of this study was to determine if a similar convergent relationship exists with caffeine, as observed between morphine and other drugs of abuse. The data was gathered through the use of hemocytes of *Mytilus edilus* (blue mussel). The hemolymph was extracted, and the cells were either left untreated with 10 mM caffeine. Other trials included naloxone (an opiate antagonist), morphine, morphine and naloxone, and caffeine and naloxone. After incubation, these cells were examined under computer-assisted microscopic image analysis to determine cellular roundness or Form Factor (where a value of 1 or close means a cell is round & stationary or "inactive" and a value close to 0 means a cell is amoeboid and motile, or "active"). This was done to establish a comparison between caffeine and morphine actions to cell activity. This information was analyzed (through the Holm-Sidak test for multiple variable comparison) to show the significance of the work. Caffeine was more similar to Morphine than the other 4 samples in terms of FF, as Caffeine and Morphine yielded FF values of 0.8250 and 0.82420, respectively, while naloxone + caffeine and naloxone + morphine gave significantly lower values. These values are too closely related to be purely coincidental ($P = <0.001$). This data supports the idea that caffeine and morphine are inter-related at the molecular level. The observed downregulatory effect of morphine was very similar to that of caffeine, which suggests a convergent pathway in which caffeine may be acting via endogenous morphine release. In this regard, naloxone was as effective in blocking caffeine as it was known to be effective in

blocking opiate alkaloids (i.e., morphine). This may lead to a novel approach in understanding addictions in general, and the possible role of caffeine in de-addiction in opioid addicts. Also, caffeine and morphine may have a synergistic effect, so they may be combined for pain management, allowing for smaller dosages of opioids to be used. Current testing is on: regarding caffeine's effects on certain cancer cell types, to determine what implications this may have, such as in U937 histiocytic lymphoma cells, and in neuroblastoma cells (SH-SY5Y). The next step is to detect and quantify changes in endogenous morphine levels in different cell types after caffeine treatment, by the use of high pressure liquid chromatography (HPLC).