Brain Tissue Response to Implanted SU-8

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Abstract

The last few decades has seen a tremendous increase in the research of brain-machine interfaces (BMI). The materials used are however not always long-term stable and must be studied thoroughly before a completely biocompatible solution can be found. One of these materials is the epoxy SU-8 which has the potential to become one of the first long-term implantable materials.

Introduction

Neural devices may come to play an important role in diagnostics and therapies for a number of clinical conditions such as chronic pain and an assortment of motor symptoms. They may also be used for control of prosthetic limbs[1, 2], increasing the life quality of many disabled patients.

Electrodes intended for neural implants must however fulfill certain criteria. They should be long-term stable, biocompatible and be able to stimulate as well as record signals from multiple nerve cells. If these criteria are not met, the resulting inconveniences may indeed lower the subject's life quality instead of increasing it.

Studies investigating the response of reactive astrocytes to the insertion and continuous presence of an implant have shown that a continuous, albeit loosely organized, sheath of cells surround the insertion site at 2 weeks. By 6 weeks the surrounding sheath is highly compacted and continuous, thereby isolating the probe from the brain. The perpetual presence of the probe also appears to result in a sustained response that both produces and maintains this compact sheath, keeping the probe isolated from the brain[4].

The biocompatibility of SU-8, a material that though frequently used, is not widely researched. To further investigate SU-8 and its usefulness in bio-implants the material was subjected to different hard baking times to see if the material itself was affected, at any hard baking temperature, by the brain's environment and if there was any leakage of material. The biocompatibility of the SU-8 was also investigated by analyzing tissue reactions to the implants through staining with antibodies.

Materials & Methods

To test whether or not the SU-8 has a negative/positive effect, the tissues were evaluated by cell staining after 6 weeks. The staining was for: astrocytes which provide nutrition to the cells; microglia that are the macrophages of the brain; neuronal cell bodies and for DNA (general cell bodies). It is not only the tissue however that may be affected; the epoxy might be affected by the exposure to the brain environment. To assess the stability of SU-8 in a brain-like environment it was subjected to a saline solution at 37 °C and then studied using mass spectrometry.

Results & Discussion

One gathers that SU-8 might not be as biocompatible as earlier studies have implied[3]. For instance, the epoxy might fragment already at implantation due to its inherent fragility, causing a prolonged damage response visible in the controls, see Figure 1, where the green represents microglia, the red astrocytes and blue cell bodies. For a stab wound of 6 weeks, no sign should be visible of any trauma, but here we see both astrocytes and microglia.

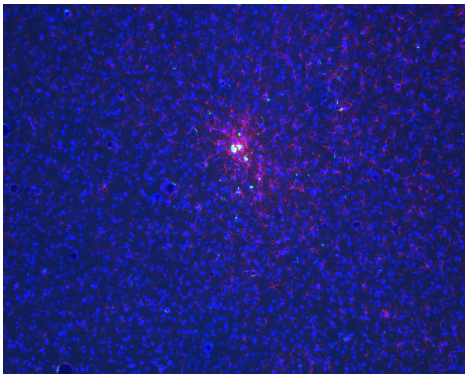

Figure 1: A control section stained against microglia, astrocytes and cell bodies

An amplification of astrocytes is apparent for both controls and implants, indicating large and sustained damage response, not merely to the implants, but to the procedure itself. Leakage from the needles could of itself explain the upregulation in the implants, something that can be corroborated by the mass spectra which shows a significant leakage of material from the needles. But to explain the same behavior in the controls one must assume it is the act of implantation that causes the response. A theory that would fully support the increase of activated astrocytes in both groups would be that the needle design creates a wound so severe the response to insertion can be seen for an extended amount of time. An example of a wound can be seen in Figure 2.

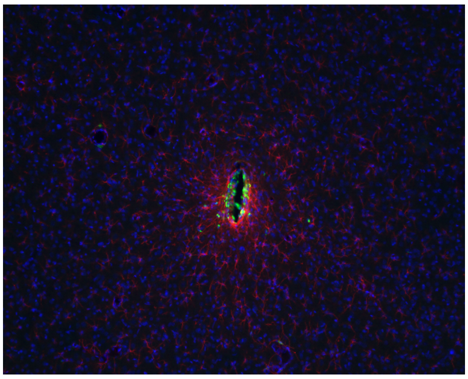

Figure 2: An example of an implant wound stained against microglia, astrocytes and cell bodies

Conclusions

If this study is to be believed, SU-8 is not the smash hit it was expected to be. According to the mass spectra, the needles may pose a threat to the sensitive environment they are meant for by releasing too many contaminants. This theory is supported by the unexpected upregulation of astrocytes that can be seen through the entirety of the brain. However, if one looks at the controls, where the tissue was only exposed to the epoxy for approximately $2\ \mathrm{min}$, one sees the same kind of upregulation of astrocytes, indicating that it might not be due to material leakage. Instead it may be because of the slicing effect of the sharp tip, or because some SU-8 was left behind after needle retraction. None of this can be deduced from the performed tests documented in here and so new tests need to be designed for this purpose.

References

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