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Proceeding Paper

Characterization of Spinal Cord Stimulation Electrode for Chronic Implant in Animal Models †

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Abstract: Spinal cord electrical (SCS) stimulation alleviates motor deficits in rodent and primate models of Parkinson due to a suppression of synchronous corticostriatal low-frequency oscillation. Limited epidural space requires resistant biocompatible microelectrodes to deliver efficiently electrical currents through a metal-cellular interface. Platinum (Pt) microelectrodes may lead to material degradation and topography modification under prolonged electrical stimulation. Thus, microstimulation performance over time can deteriorate and affect functional recovery produced by SCS. To investigate electrodes commonly implanted in epidural space of rats, Pt microelectrodes immersed in physiological saline underwent 48 h of electrical stimulation (100 Hz, 1.0, 1.3, 1.6 mA). A wettability test was performed to characterize the interaction of the contact angle before and after stimulation, where there was an increase in this angle after the stimulation. An electrical impedance test showed that electrochemical interactions caused an increase in impedance after the stimulation. A roughness analysis also showed an increase in roughness after stimulation. Pt electrodes under chronic electric stimulation are susceptible to degradation, and further studies can improve electrode stability and efficacy as new sensor technologies become available.

Keywords: invasive microeletrode; spinal cord stimulation; platinum; microelectrode; wettability; roughness

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1. Introduction

Spinal cord electrical stimulation (SCS) was first used in 1967 to inhibit severe diffuse pain in the chest and abdomen [1,2]. Since then, SCS has emerged as a potential neuromodulation method for pain relief and motor disorders. More recently, SCS in mice [3] and marmoset models of Parkinson disease reduced akinesia [4], a significant step toward alternative therapies for PD, since subthalamic nucleus (STN) deep brain stimulation (DBS) eligibility is limited to 1.6 to 4.5% of PD patients [5].

Recent findings support the neurophysiological mechanism of SCS on PD motor symptoms, such as desynchronizing the corticostriatal oscillation to improve movement control [3,4].

Despite the lack of a complete neurophysiological mechanism describing SCS effects on akinesia, other aspects, such as electrode geometry, stimulation parameter, and spinal cord stimulation level are critical to understanding different outcomes [1,6].

One of the most critical issues concerning implantable devices is biocompatibility. Biocompatible materials are used to reduce the intensity and time duration of the inflammatory processes. However, the implanted material interacts with physical, biological, and chemical agents over time and may change its composition, surface, biocompatibility, and electrochemical property. Platinum is extensively used as a biocompatible metal for mechanical and electrical applications. Nevertheless, when platinum is used at thin thicknesses, its structure may be disrupted after several cycles of stimuli [7]. Another critical factor is impedance. Since a low value of the electrochemical impedance between the electrode and the electrolyte (tissue) is a vital and necessary condition to reduce tissue damage during stimulation. The reduction of these lesions contributes directly to an increase in the longevity of the electrode [8–10].

A well-characterized and fully functional electrode leads to an optimized electrode-tissue interface coupling. The electrode characterization contributes to chronic SCS studies for motor symptoms in PD [3] since this technique still needs a standardized method for its therapeutic consistency. This characterization supports the robustness of electrode behavior throughout chronic use and as a preliminary approach to providing safety and effectiveness for its use in animal models.

Here, we present a characterization with wettability, impedance and roughness tests on electrodes that underwent electric current stimulation in vitro. A wettability characterizes the interaction between electrode-electrolyte; impedance testing indicates the resistance to flow current between electrode-tissue; and roughness evaluates the surface texture that interfaces with tissue. These tests can assist in predicting the behavior of the electrode submitted in vivo.

2. Materials and Methods

2.1. Manufacture of Electrodes

Platinum foil (99.9% purity) was used for two rectangular electrical contacts measuring 1.0 × 0.8 mm (25 µm thick). These contacts were micro-welded to stainless steel wires ø25.4 µm, with welding alloy (PbSn). NuSil MED2-4420 (ratio 1:1) medical silicone was used to insulate the welding surface of pairs of platinum contacts, resulting in a 100 µm total thick paddle electrode.

Dimensions of platinum contacts are based on rats spinal cord anatomy, at high thoracic level, accordingly to previous successful results [3,4,11]. The rectangular contacts are placed side by side spaced by 0.4 mm (center-center distance is 1.2 mm), and their longer dimension runs longitudinally to the spinal cord. This electrode geometry intends to deliver electrical current to stimulate dorsal column fibers and to avoid side effects resulting from the activation of the dorsal root fiber.

2.2. Wettability Test

Wettability test can be performed as an indicator of biocompatibility, and it consists of a technique to measure surface energy of a material sample. This energy is given as a function of the interaction between surface and a liquid with a known surface energy, such as water, for example. This interaction can be numerically associated to the measurement of the contact angle existent between the liquid droplet and the material surface [12]. If a material has a low wettability, it means hydrophobicity and thus it would not recruit cells in a biological environment, once there is no water adhered to it in first place [13]. However, considering stimulation electrodes inserted in a fluid, the target is a minimal inflammatory response and an optimal interface between solid and liquid surfaces to facilitate charge transfer [14]. Thus, the characterization of the wettability of platinum electrodes is necessary to verify their ability to conduct charges through the fluid, where it is desired that it be hydrophilic.

Our method was based on wettability test technique shown in Mittal [15]. Sessile drop measurement was performed with an adapted apparatus coupled to an automatic injector system (Robot Stereotaxic, NEUROSTAR) to precisely deliver pure water droplets of

0.5 µL using a Hamilton syringe over the platinum contacts and silicone paddle (substrate) (Figure 1a).

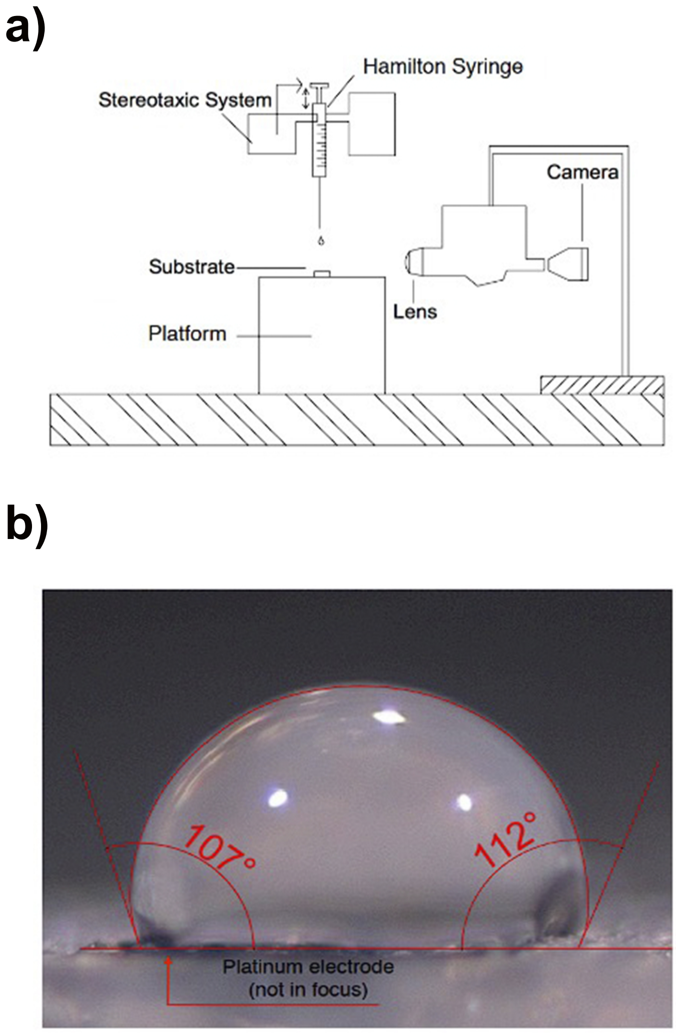

Figure 1. (**a**) Schematic representation for the setup of wettability test. (**b**) Example of contact angle measurement by AutoCAD geometry drawing tools.

Images were captured within 5 s after droplet met the surface of the substrate using a digital camera (AxioCam MRc, Zeiss) attached to a microscope, which was tilted to obtain images of the droplet accordingly to previous procedures shown in Mittal [15]. Temperature room was maintained at 17 °C in order to avoid rapid water evaporation and contact angles were computed offline using Auto-CAD Autodesk software (Figure 1b).

2.3. Electrical Impedance Measurement

Impedance meter (SIGGI II, Falk Minow) was used at frequency of 100 Hz (same frequency of stimulation). Electrodes to be measured were dipped into saline solution (0.9%) with reference wired to its metallic beaker (circuited with the saline) and the system was properly grounded.

Stabilization for the measurement was observed after a period of accustoming to the electrolyte in use. Electrode is meant to have its electrical potential but if it reaches a value of 300 mV the electrode is considered faulty. Measurements occurred when electrical potential was lower than 1 mV (following specifications by the impedance meter manufacturer).

For each electrode three measurements were taken before and after stimulation cycles for posterior calculation of their average.

2.4. In Vitro Electrical Stimulation

STG 4004 stimulator (Multichannel Systems) was used to generate bipolar square wave signal at 100 Hz, 1.6 mA, 500 µs pulse width to continuously stimulate the electrodes dipped in saline solution 0.9% for 48 h, generating over 1.7 × 107 pulses which is at least 2 times more than previous study with SCS in PD [11].

2.5. Stimulation Characterization

The Shannon [16] limit was used to characterize the electrical stimulation performed by the electrode. Based on past neural stimulation results in cats, Shannon made a chart with upper limits for safe electrical stimulation. Shannon proposed that the maximum stimulation limit was k = 1.5. However, because this value is restrictive, a value of 1.75 was considered by the literature, slightly below the appearance of tissue damage [17]. The values obtained without damage by McCreery [18] can be obtained from:

$$Log(D) = K - Log(D) \tag{1}$$

where D is charge density in µCoulombs/cm^2/phase and Q is charge in µCoulombs/phase. $D = Q/A$, where A is the electrode surface area in cm^2. The formula can be expressed as

$$Log(\frac{Q}{A}) = K - Log(Q) \tag{2}$$

From Equation (2), K calculations were made for the stimulation analyzed in vitro. The surface contact area of the electrode is A = 0.008 cm², whereas the charge is Q = 0.8 µC. Where Q is the product between 1.6 mA and 500 µs. The influence of other K values on the change in the surface of the electrodes was carried out to analyze of roughness before and after in-vitro electrostimulation. Electrostimulations were performed with loads of 1.6 mA, 1.3 mA and 1.0 mA, respectively representing K = 1.90, K = 1.75 and K = 1.50.

2.6. Roughness Analysis

The roughness of the electrodes was measured through analysis by the atomic force microscope (AFM). Three pairs of electrodes were characterized at room temperature (25 °C) using 11 N/m spring cantilevers, 10 nm tip radius of curvature, 10:1 aspect ratio and 150 kHz resonance frequency. In all measurements, two measurements were performed per sample to be scanned and data collected. The surface scan was performed perpendicular to the cantilever axis and with a scan area of 5 × 5 µm. The evaluation of the roughness used to compare the samples was the mean squared deviation (Rq), provided by the equipment.

3. Results and Discussion

3.1. Electrode and Impedance Characterization

Three pairs of electrodes were manufactured, tested and stimulated for uninterrupted 48 h. Average of each electrode measurements taken before and after electrical stimulation cycles are presented graphically as shown in Figure 2. Overall electrical impedance showed an increase of 7.8% (from 5.1 kΩ to 5.5 kΩ after stimulation), and the two pairs (1 and 3) have presented significant increase in impedance value ($p < 0.05$).

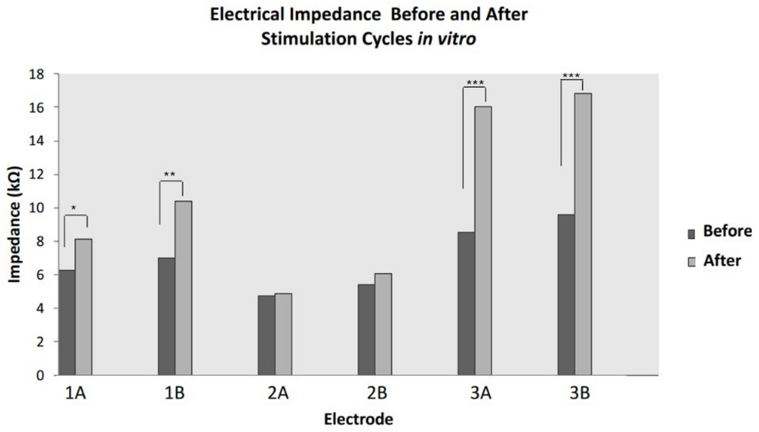

Figure 2. Electrical impedance measurements of three pairs of electrodes. Contacts were numbered 1 to 3 and A and B means left and right, respectively. Dark bars are from measurements before stimulation and light bars, after stimulation.

Impedance results were higher after stimulation compared to before. This is due to the oxidation of the platinum with the values of $k > 1.75$ and thus, having superficial changes in the electrode interface increasing its contact angle. This increase in the contact angle generates a different solid-liquid interaction and increases the impedance. Nevertheless, the average increase was within the experimental measure's acceptable range of 10%, thus electrodes were considered robust in their electrical behavior throughout experiencing electrical stimulation over more than 1.7×10^7 pulses (2.4 times more than used in Yadav et al. [11]). It is important though to highlight that different results are expected if other frequencies are used once capacitive polarization in an electrode-electrolyte interaction is frequency-dependent accordingly to Fricke's Law [19].

The characterization of the stimulation resulted in $k = 1.90$, above the limit of $k = 1.75$ proposed by Shannon as safe and incapable of generating damage to the tissue where it is implanted [16]. The increase in the impedance of the electrodes after the stimulation tests can be attributed to the value of $k = 1.90$. The platinum used for electrical stimulation with the values of $k > 1.75$ and an environment with available oxygen, ends up suffering surface oxidation. This oxidation can generate an increase in impedance due to the superficial change of the electrode, as well as a release of platinum oxide, which in large quantities it can cause damage to the tissue where it was implanted [14].

3.2. Wettability Test and Roughness

The wettability test showed average contact angles of 106º and 120º, for the platinum contacts before and after stimulation and 130º for the silicone pad. These values showed that the electrodes had increased hydrophobic properties, which is not desirable for stimulation electrodes. The value of $K = 1.90$ was obtained according to Equation (2). This characterization is necessary to predict wheter the electrode will cause tissue damage through electrical stimulation. With this result, we enter the level of tissue damage and platinum degradation.

Contact angle was measured before and after stimulation and showed an increase compared to the measurement before stimulation. This change occurs in the oxidation of platinum, due to changes in the electrode surface, thus increasing its roughness resulting from stimulation with values of $K > 1.75$. Correlating roughness and wettability is not a simple association. Traditionally, the theories of Wenzer and Cassie-Baxter explain the moistening of rough interfaces. According to Wenzer's theory, a smooth surface, which is hydrophobic, will increase its contact angle if a roughness is added. This statement is also valid for a smooth hydrophilic surface, with its contact angle reduced if a roughness is added [20]. Cassie-Baxter's theory considers gas bubbles that are trapped in the solid and liquid phases [21]. Thus, with the increase in the contact angle due to the degradation of the platinum, there was an increase in the impedance, due to a greater hydrophobicity of the electrode. Figure 3 shows an increase in roughness after stimulation, thus increasing the contact angle.

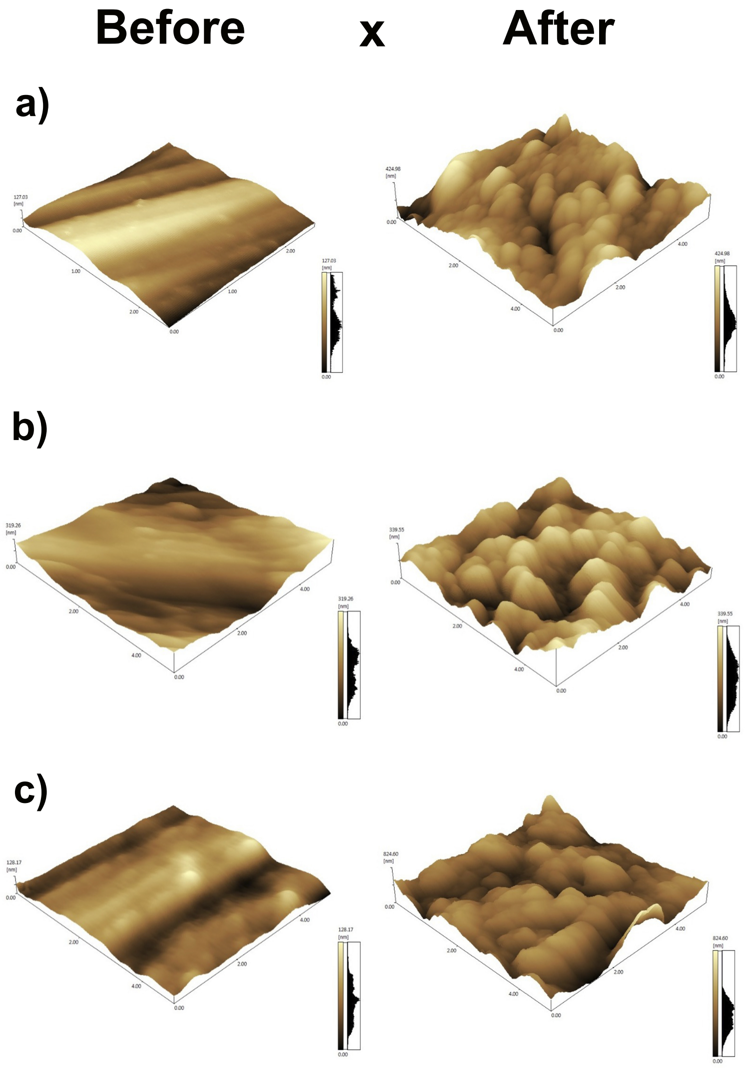

Figure 3. (**a**) Electrode before and after stimulation with a load of 1.0 mA ($K = 1.50$). (**b**) Electrode before and after stimulation with a load of 1.3 mA ($K = 1.75$). (**c**) Electrode before and after stimulation with a load of 1.6 mA ($K = 1.90$).

This study examined three different electrostimulation loads to assess their effect on the surface roughness of electrodes. The loads of 1.6 mA, 1.3 mA, and 1.0 mA were chosen, corresponding to K values of 1.90, 1.75, and 1.50, respectively, based on the Shannon parameter [16]. Surface changes before and after in vitro electrostimulation were compared using the difference in current, and mean square deviation was used to quantify roughness in both conditions. Results showed an increase in roughness of up to 371% (Table 1 compared to the initial condition, with the greatest increase observed at the highest load of 1.6 mA corresponding to $K = 1.90$. The increase in roughness was found to be directly linked to the increase in the applied load during in vitro electrostimulation. However, it is noteworthy that the coefficient was above the safety threshold proposed by Shannon, indicating a potential risk of damage to the tissue where the electrode is implanted. The electrostimulation loads of 1.3 mA and 1.0 mA, corresponding to K values of 1.75 and 1.50, respectively, were within the safety range for electrostimulation, but still resulted in an increase in roughness of 212.3% and 181.5%, respectively. The oxidation and modification of the platinum electrode's surface was also observed even within the safe electrostimulation parameters. This oxidation can lead to the formation of platinum oxide, which in large amounts can cause tissue damage [14].

Table 1. Roughness of platinum electrodes before and after electrostimulation.

Current	Roughness before Stimulation (Rq)	Roughness after Stimulation (Rq)	Percentage Change
1.0 mA	32.08 ± 5.61	90.32 ± 31.76	181.5%
1.3 mA	37.47 ± 11.79	115.73 ± 30.35	212.3%
1.6 mA	18.48 ± 4.73	86.89 ± 32.86	371.2%

4. Conclusions

In conclusion, the characterization of invasive electrodes is crucial to ensure safe and effective use in chronic experimentation. Consistent with existing literature, our study showed that the electrostimulation of platinum electrodes results in increased roughness, even at lower loads within the safe electrostimulation parameters. The roughness modification can form platinum oxide, which may cause tissue damage in large amounts. Therefore, it is crucial to consider the electrostimulation parameters used in medical devices, considering the potential risks of tissue damage caused by roughness modification in platinum electrodes. Finally, the potential of SCS to reduce the invasiveness of several therapies for neurological disorders is advancing. Furthermore, this characterization in animal models supports further human studies in neuromodulation.

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