

Lepmkal, S.F., Johnson, M.D., Miocinovic, S., Vitek, J.L., McIntyre, C.C. (2010). Current-controlled deep brain stimulation reduces in vivo voltage fluctuations observed during voltage-controlled stimulation. *Clinical Neurophysiology*, 121(12): 2128-2133.

### **Background of the Study**

Deep brain stimulation (DBS) is a surgical treatment used to relieve some of the most debilitating symptoms of advanced Parkinson's disease (PD). The treatment helps to control motor symptoms of PD using a surgically implanted *DBS medical system*, a device that sends electrical stimulation through electrodes (metal conductors) to specific parts of the brain that control movement.

Currently, two types of DBS systems are available for DBS therapy:

- **Voltage-controlled (VC) systems:** DBS systems that control the stimulation delivered to the brain by adjusting the *volts*, or the force that “pushes” electricity from the device
- **Current-controlled (CC) systems:** DBS systems that control the stimulation delivered to the brain by adjusting the *current*, or the rate that electricity flows from the device.

Although DBS therapy traditionally uses voltage-controlled systems, a major concern with VC stimulation is that tissue buildup on the electrodes can cause electrical resistance changes that alter the *voltage* (or “intensity”) of the stimulation reaching the brain. As a result, patients with VC systems may:

- Experience unwanted side effects due to overstimulation
- Need their stimulation settings reprogrammed several times in order to feel the benefits of DBS.

However, a recent study by researchers of the Cleveland Clinic in Ohio establishes that the use of newer, current-controlled DBS systems can minimize the voltage fluctuations produced by tissue-related resistance changes and--as a result--help to reduce the side effects of DBS therapy and the amount of time needed to program each device. This suggestion based on a comparative analysis of the voltage fluctuations occurring during voltage-controlled and current-controlled DBS.

### **Purpose of Study**

The purpose of the study was to examine fluctuations in the voltages produced in the brain during voltage-controlled and current-controlled DBS and to evaluate the potential advantages of using CC systems instead of VC systems.

### Study Subjects

During the study, researchers compared the voltages produced in the brains of two laboratory primates during voltage-controlled and current-controlled DBS. These primates included two macaque monkeys, ranging from 8 to 10 years of age and weighing approximately 11-13lbs.

### Study Methods

In order to evaluate the potential advantages of using current-controlled systems over voltage-controlled systems for DBS therapy, researchers used the following methods:

- First, to deliver DBS therapy to the brains of the macaque monkeys, researchers surgically implanted 3 DBS electrodes into target DBS regions of each monkey's brain (i.e. *globus pallidus*, *subthalamic nucleus*, and *thalamus* regions of the brain).
- Next, to monitor the voltage of stimulation produced in the brain, researchers implanted recording electrodes 2mm away from each DBS electrode. These recording electrodes included:
  - Single-channel recording electrodes with one recording location
  - Multi-channel recording electrodes with several recording locations.
- Afterwards, to compare the voltage fluctuations produced during voltage-controlled and current-controlled DBS, researchers connected each monkey's DBS electrodes to a VC and CC system and conducted the following experiments examining:
  1. **Voltage changes after DBS electrode implantation:** To examine how tissue buildup after electrode implantation can affect the voltages produced during voltage-controlled DBS, researchers:
    - Compared the *peak* (maximum) voltages recorded in each monkey's brain on day 1 and day 7 after implantation.
  2. **Voltage changes during voltage-controlled DBS:** To examine how continuous stimulation can affect the voltages produced during voltage-controlled DBS, researchers:
    - Performed a set of four experiments to compare the peak voltages recorded in each monkey's brain during 60 minutes of VC stimulation.
  3. **Voltage changes over the course of voltage-controlled vs. current-controlled DBS:** To examine the differences in the voltage fluctuations produced over the course of voltage-controlled and current-controlled DBS, researchers:
    - Conducted a set of three experiments to compare the peak voltages recorded after initial (1-second) VC and CC stimulation and after continuous (60-minute) VC and CC stimulation.
- Lastly, to monitor tissue-related resistance changes that could affect the voltages recorded during each experiment, researchers measured:

- The electrical resistance of each DBS electrode several times during each experiment
- The electrical resistance of the recording electrodes at the start and end of each experiment.

### Study Results

In response to the potential advantages of using current-controlled systems over voltage-controlled systems, the study data suggests that--unlike VC stimulation--voltages produced in the brain during current-controlled DBS are minimally affected by tissue-related resistance changes. This suggestion was based on an analysis of the resistance changes and voltage fluctuations produced in the brains of two macaque monkeys: 1) after DBS electrode implantation, 2) during continuous voltage-controlled DBS, and 3) over the course of voltage-controlled vs. current-controlled DBS.

According to the tissue-related resistance changes and voltage recordings in each monkey's brain, researchers found that:

- From day 1 to day 7 after DBS electrode implantation:
  - The peak voltage produced in the brain during voltage-controlled DBS decreased by an average of  $38.6 \pm 10.6\%$
  - The electrical resistance of the DBS electrodes increased by an average of  $298 \pm 136\%$ .
- During 60 minutes of continuous voltage-controlled DBS:
  - The peak voltage produced in the brain rapidly increased during the first 10-15min of stimulation, increasing by an average of  $19.3 \pm 6.2\%$  after a full hour of VC stimulation
  - The electrical resistance of the DBS electrodes rapidly decreased during the first 10-15min of stimulation, decreasing by an average of  $47.9 \pm 16.7\%$  after a full hour of VC stimulation.
- Over the course of initial (1-second) to continuous (60-minute) voltage-controlled DBS and current-controlled DBS:
  - The peak voltage produced in the brain during voltage-controlled DBS increased significantly by an average of  $54.8 \pm 54.5\%$
  - The peak voltage produced in the brain during current-controlled DBS increased minimally by an average of  $6.5 \pm 1.1\%$
  - The electrical resistance of the DBS electrodes decreased by an average of  $48.9 \pm 30.1\%$ .

Altogether, these findings suggest that: 1) tissue buildup after DBS electrode implantation causes an increase in the electrode resistance that corresponds with a decrease in the voltages produced during voltage-controlled DBS, 2) continuous stimulation through DBS electrodes reverses some

of the tissue buildup and causes a decrease in the electrode resistance that corresponds with an increase in the voltages produced during voltage-controlled DBS, and 3) resistance-related voltage fluctuations observed over the course of voltage-controlled DBS are significantly reduced during current-controlled DBS.

### **Study Discussion & Implications**

While tissue around the DBS electrodes naturally changes as a result of the body's reaction to a foreign object (i.e. implant) or as a consequence of prolonged stimulation, these tissue changes can alter the electrical resistance of the DBS electrodes and produce voltage fluctuations during DBS therapy that may contribute to:

- The appearance of unwanted side-effects during DBS
- Difficulties in the clinical programming of DBS systems.

Overall, the study found that changes in the DBS electrode resistance significantly affect the voltages produced in the brain during voltage-controlled DBS. However, these resistance-related voltage fluctuations can be minimized with the use of current-controlled DBS. This outcome is evident by the significant variability of the voltages produced in the macaque monkeys' brains during VC stimulation, and, in contrast, the relative stability of the voltages produced in the monkeys' brains during CC stimulation.

Based on these study results, researchers recommend that current-controlled systems should replace voltage-controlled systems as the standard, clinical hardware for DBS therapy. The adoption of CC systems may provide three advantages over VC systems: 1) allow for a more accurate comparison of stimulation settings across PD patients, 2) reduce unwanted variables when researching the behavioral and functional benefits/side effects of electrical stimulation, and 3) provide a more reliable stimulation effect while programming the DBS hardware. However, since the study was only performed on an animal model and involved only a small number of subjects, additional studies should be conducted to explore the potential advantages of current-controlled DBS systems in a larger, human study sample.