Supplementary Material Contents

Abbreviations

ACSF = artificial cerebrospinal fluid
CFM = carbon fiber microelectrode
DBS = deep brain stimulation
ET = essential tremor
FSCV = fast scan cyclic voltammetry
MRI = magnetic resonance imaging
WINCS = wireless instantaneous neurotransmitter concentration sensing

eAppendix - Supplementary Methods

1.1 Consent process to recruit participants

The research protocol was approved by Mayo Clinic IRB (Institutional Review Board). Out-patients in our neurosurgery clinic were given the opportunity to consent to the study before surgery. The procedure description and patient education and counseling took approximately 20 minutes with an additional 10 minutes for questions and answers. A mandatory waiting period of one night prior to their scheduled surgery was instituted to allow patients to withdraw if they elected to do so. The following was ensured:

1. Participants can knowledgeably discuss the consent document with their physician (assure understanding) and whomever else they turn to for advice (e.g., family members).

2. Participants understand that no services, treatments, or benefits will be withheld if they do not participate in the research. They also understand that their consent to the study will not directly benefit them.

Deep Brain Stimulation Surgery (DBS) protocol inclusion/exclusion criteria:

Inclusion: Adult patients with medically intractable ET who have been approved for DBS surgery by the interdisciplinary Mayo DBS committee.

Exclusion: Pregnant patients, prisoners, children (under 18 years of age), and any patients identified by the Mayo Clinic DBS committee as unsuitable for the study protocol

1.2 DBS neurosurgery in human subjects

Written informed consent was obtained from all patients prior to surgery. Under local anesthesia, an MRI-compatible stereotactic head frame was fixed to the patient's head. A localizer box created nine fiducials as reference points to enable localization of MR images in stereotactic space. The patient was then transported to the MRI scanner. MR imaging was conducted using a General Electric Signa 1.5 T MRI clinical system operated

by EchoSpeed LX Version 9.1. The human DBS imaging protocol consists of MP-RAGE sequences using 1.5 mm slice thickness and 24 cm field of view. Using COMPASS navigational software, MRI data were merged with the human Schaltenbrand and Wahren stereotactic atlas, and stereotactic coordinates for DBS electrode implantation for ET patients in the ventral intermediate (VIM) thalamus were identified. The patient was then returned to the operating suite where, under local anesthesia, a skin incision in line with the trajectory coordinates was made followed by a 5-10 mm burr hole made in the skull using a high-speed drill. Microelectrodes for standard electrophysiological recording and for the FSCV recording using a CFM were implanted simultaneously through 5-trajectory guide canula system that was attached to the alpha- omega microdrive system. As cellular activities were measured through the center trajectory to define the target, FSCV recording was performed in a 2 mm anterior path from the center of the 5-trajectory guide canula system. Once brain mapping was successfully performed, the electrophysiological recording electrode was replaced with the DBS electrode (Medtronics 3387). Electrochemical recordings utilizing the CFM were obtained to evaluate the concomitant neurochemical changes.

To document potential microthalamotomy effects, the frequency and amplitude of hand tremor were recorded using a wireless accelerometer which patients held in their extended hand during surgery. To obtain a baseline, accelerometer recordings were made 20 seconds before DBS electrode implantation. Following DBS electrode implantation, hand tremor was also recording for over 30 seconds during which time, the optimal clinical stimulation parameters were determined (see Table 1). During this DBS surgery in the operation room, FSCV recordings were performed by the CFM using the WINCS system. There were no complications following DBS surgery and concurrent electrochemical recording.

1.3 Fabrication of CFM for human use

In accordance with the Mayo Clinic IRB guidelines, CFM fabricated in the same laboratory as those for use in animals were considered unsafe for human application. To avoid possible animal contamination, a separate clean room was secured in the clinical area, and all new equipment was bought in to fabricate new CFMs. Recently, Clark et al.[24] reported on the construction of durable chronic microsensors for FSCV recording using carbon fiber. For human recording, both disc and columnar shaped CFMs have been developed. Disc shaped CFM was fabricated by modifying the tip of a human electrophysiologic electrode (Neuroprobe 366-000080-00, Alpha Omega Engineering, Nazareth, Israel) to which was affixed a short segment of 30 μm carbon fiber (eFigures 2A and 2C). In addition, the tip was insulated with silicone (Silgard 184 Silicone Elastomer, Dow Corning. Co., Midland, MI). In a columnar shaped CFM, the sensing tip and insulating material consisted of a 7 μm carbon fiber and polyamide, respectively (eFigures 2B and 2D). To achieve the maximum safety, carbon fibers were cut to provide a limited exposure. Stainless-steel ring on a sheath of a commercially available electrode (Neuroprobe 366-000080-00) was utilized as a reference (eFigures 2A and 2B).

1.4 Fast scan cyclic voltammetry (FSCV) recording in humans

To perform FSCV recording, WINCS (eFigure 1) and WincsWare (in-house designed software) were utilized. WINCS is a battery powered electrochemistry device, combining digital telemetry with amperometry and FSCV for real-time chemically resolved measurements from an implanted microelectrode. It measures neurotransmitter activity, including alterations in dopamine, adenosine, and serotonin.[10, 11, 25] WincsWare, an in-house-designed software, runs on a base-station computer, controls the wireless patient module, filters and processes the received data stream, and displays the results in nearly real time. For FSCV, the potential at the CFM was linearly scanned at 400

V/second in a triangular waveform from -0.4 V to 1.5 V and back to -0.4 V at 10 Hz as described by Cechova and Venton for adenosine detection and dopamine co-monitoring.[20] The WincsTrode rests at a bias potential of −0.4 V between scans.

1.5 WincsTrode and WINCS sterilization

Prior to implantation in patients, every effort was made to ensure safe and sterile implantation. Steps included utilizing a clean room dedicated to electrode construction for human use only. WINCS unit was sterilized by the Sterrad®hydrogen peroxide gas plasma process. CFM and its accessory wires were sterilized with an ethylene oxide treatment. Ethylene oxide, the most common chemical sterilization method used, is used for over 70% of all sterilizations and for 50% of all disposable medical devices. Ethylene oxide treatment was carried out for 24 hours out at 60 °C with relative humidity above 30% and a gas concentration between at 200 mg/l. This process was followed by a 72 hour decay period in which the sterilized electrodes were quarantined. Because the pre and post-sterilization calibrations were nearly identical, it appeared that the ethylene oxide sterilization did not affect the structure and characteristics of the CFM.

There were no electrode breakage, infection, or hemorrhage related to WINCS measurements. However, there was 1 patient who had infection at the battery site, and required removal of the DBS system.

1.6 Detrending algorithm

Acquiring FSCV data during human neurosurgery is challenging due to the time limitation. Because the amplitude of the raw background FSCV current is larger than the subtracted current by a factor of 100, it is necessary to obtain a stable background current during FSCV recordings. This can be accomplished by preconditioning the FSCV electrode by applying the intraoperative FSCV waveform to the electrode, a procedure that takes approximately 20 minutes. However, in the operating theatre during human surgery, those 20

minutes of electrode stabilization are prohibitive. Fortunately, the background current drifts with a predictable pattern (eFigure 9), and can be estimated mathematically and corrected using detrending algorithms based upon well-established linear regression [1]. The detrending algorithm can be applied to compensate for either cyclic voltammogram drifting (ICV) or current drifting (ICT) with time. The CV detrending algorithm is more reliable than that of CT, because the pattern of drift is not linearly time dependent at all points in time.

The linear regression for the CV detrending algorithm can be described as follows:

$$\hat{A}_j = \alpha_j + \beta_j x \qquad [1]$$

where, x is a drift pattern cyclic voltammogram which can be obtained from cyclic voltammograms, recorded before and after an interval when the data of interest is collected,

α_j and β_j regression parameters at j time, and the estimated $\hat{A}_j$ voltammogram.

$\min_{\alpha,\beta} Q_j(\alpha_j, \beta_j)$, where

$$Q_j(\alpha_j, \beta_j) = \sum_{i=1}^{m} (A_{j,i} - \hat{A}_{j,i})^2 \qquad [2]$$

where, we find α_j, β_j in order to minimize Q_j which is the square of the difference of voltammogram A_j to be detrended and the estimation $\hat{A}_j$ at j time points. At last, the detrended FSCV can be obtained by the subtraction of $\hat{A}_j$ from A_j.

The linear regression for the CT detrending algorithm is the same procedure with the exception of x which is the time at two time points of interest, and A_j is the current change during same time period at a specific voltage.

1.7 *In vitro* rat slice experiment

Sprague-Dawley rats (3 to 5 weeks old) were used for this study. Animal care followed the Mayo Clinic Animal Care and Use Committee guidelines which are in accordance with National Institute of Health guidelines for use of animals in teaching and research. After deep anesthesia using ketamine (1.6 g/kg i.p.), the brain was rapidly removed and transferred into ice-cold slicing solution, in which NaCl was replaced with sucrose while maintaining an osmolarity of 307 mOsm to increase tissue viability. The hemispheres were separated with a midline incision. Four hundred-micron thick slices were obtained using a vibratome (VT-1000S, Leica, Germany) in a coronal plane. During slice preparation, the tissue was kept in a chilled slicing solution (4 ºC). After cutting, slices were transferred into a pre-chamber (Harvard Apparatus, Inc.) and maintained at room temperature for at least one hour. The bath was perfused with artificial cerebrospinal fluid (ACSF) which contained (in mM): NaCl, 126; KCl, 2.5; $MgSO_4$, 1.2; NaH_2PO_4, 1.25; $CaCl_2$, 2; $NaHCO_3$, 26; d-glucose, 10 and was aerated with 95% O_2, 5% CO_2 to a final pH of 7.4. For the first 20 minutes of perfusion, the bathing medium contained an equal mixture of ACSF and the slicing solution.

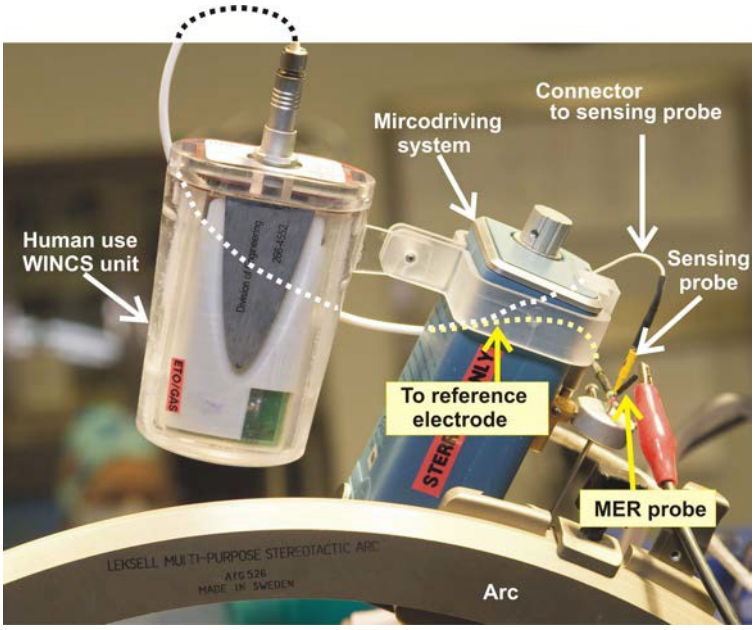
Electrode insertion was applied with a motorized micromanipulator. Once the final position of the stimulation electrode was determined, the electrode automatically and repetitively was implanted into the programmed position. The stimulation electrode was made by pulling the glass capillary out (TW-100-4, World Precision Instruments, Sarasota, FL). The tip resistance of the stimulating electrode was 5- 6 MΩ with 5 mV voltage step pulse.

For FSCV recording, a glass-insulated CFM was constructed by aspirating a single carbon fiber (7 μm diameter) (T-300, Cytec Industries Inc., Woodland Park, NJ) into a borosilicate glass capillary (TW-100-4, World Precision Instruments, Sarasota, FL) and

pulling it to a microscopic tip using a pipette puller (P-97, Sutter instruments, Novato, CA). The exposed carbon fiber was cut to a length of approximately 50 μm, under a dissecting microscope. Chloridized silver (Ag/AgCl) wire was utilized as a reference electrode in the animal research. The same triangle-shape protocol used in human FSCV recording was then applied to collect the alterations in electrochemical signals caused by the electrode insertion.

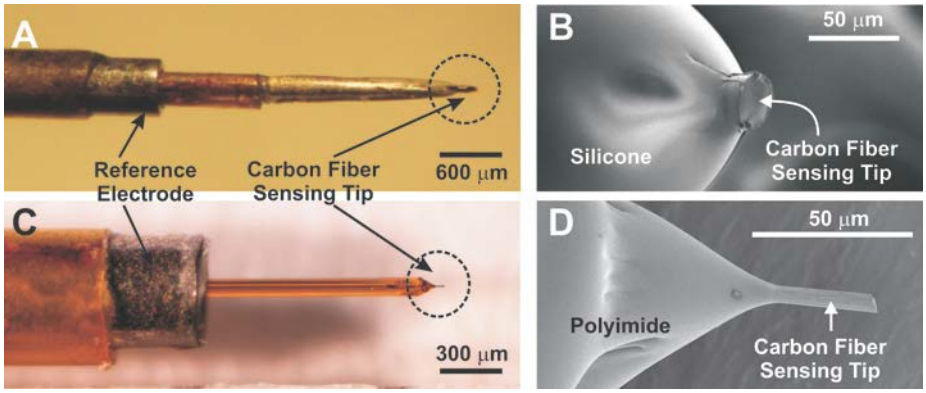
1.8 Drugs

ARL 67156 and other chemical components for solutions were purchased from Sigma-Aldrich, and TTX was purchased from Alomone, Inc. (Jerusalem, Israel).



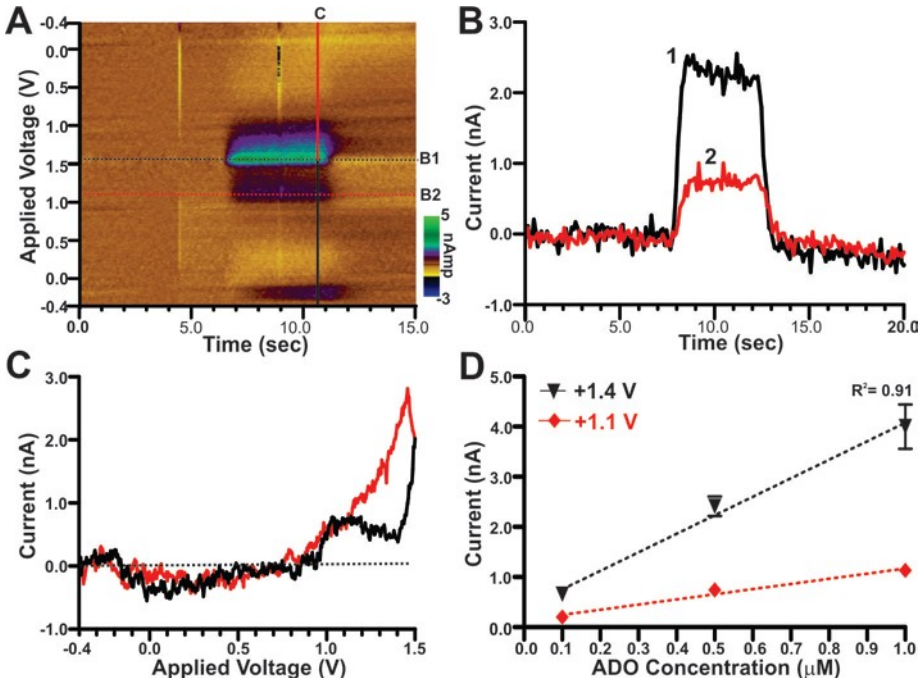
eFigure 1. Intraoperative electrochemical recording using the Neurotransmitter Concentration Sensing (WINCS) system.

Instrumental set-up for real-time electrochemical recording during human DBS surgery using WINCS (secured to an electrode microdrive system and attached to the arc of the stereotactic head-frame). The accessory wire from the WINCS unit divides to connect to the working microelectrode and the reference electrode. The microelectrode recording electrode [7] for electrophysiological recording and the electrochemical sensing electrode (WincsTrode) were implanted simultaneously and attached to a micro-driving system.

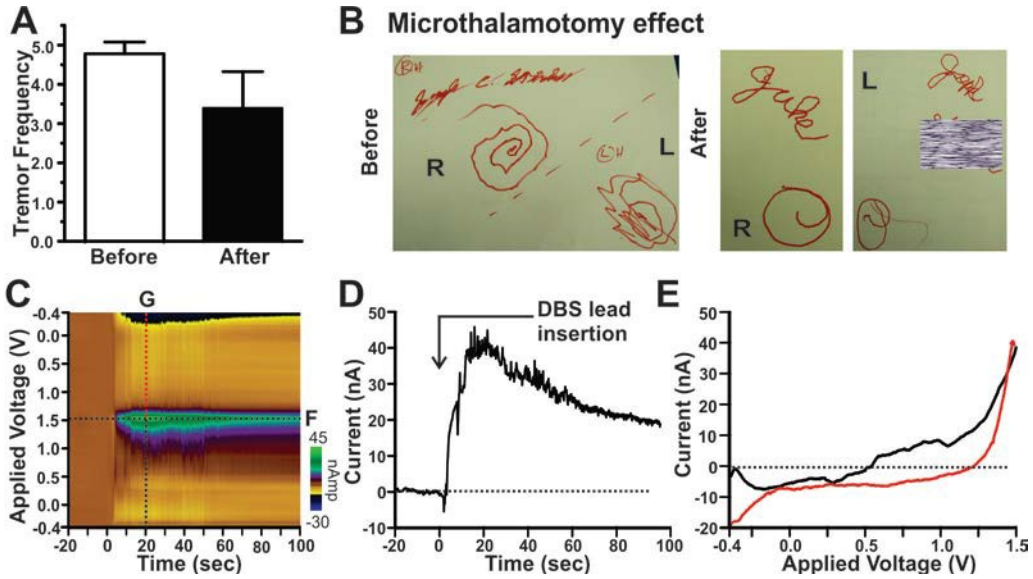


eFigure 2. Human applicable CFM for FSCV.

(A) Disc shaped CFM for FSCV in the human brain; carbon fiber diameter 30 μm. (B) Scanning electron microscopy image (SEM) of the sensing tip of (A). (C) Columnar shaped CFM for FSCV in the human brain showing that the length of the exposed carbon fiber (7 μm diameter) extends less than 50 μm. (D) SEM of the tip of (C).

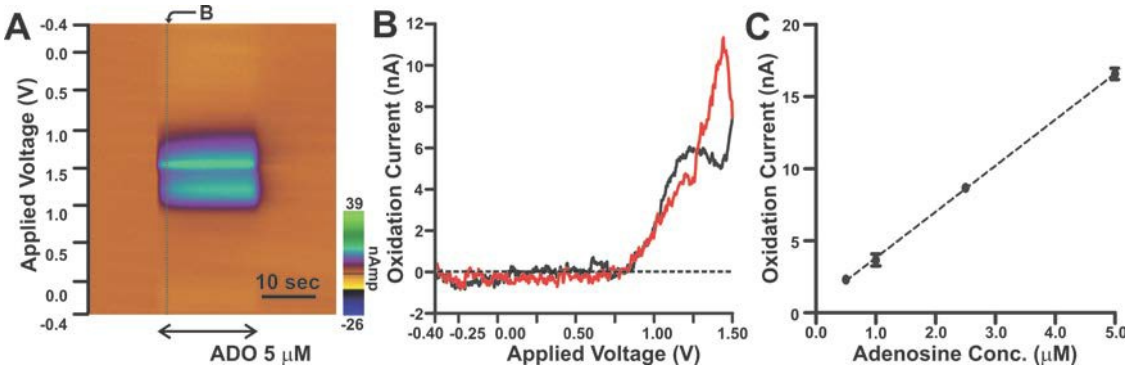


eFigure 3. Adenosine detection with FSCV in an *in vitro* flow cell analytical system. (A) Representative pseudocolor plot showing adenosine (0.5 µM) in an *in vitro* flow cell analytical system. The x-, y-, and color gradient axes represent time, the applied voltage, and resulting current changes respectively, as detected by the CFM. The two oxidation currents detected at +1.4 and +1.1 V, respectively, represent the 1st and 2nd oxidation peak current of adenosine; (B) Oxidation current versus time plot of the 1st and 2nd oxidation peak currents of adenosine (0.5 µM); back line (1) represents the 1st oxidation current at +1.4V; red line (2) represents the 2nd oxidation current at +1.1 V. (C) Cyclic voltammogram obtained following injection of 0.5 µM adenosine as marked in (A). (D) Calibration curve obtained for adenosine (0.1 to 1.0 µM) with an indicated correlation coefficient (n = 3) using a stainless steel reference electrode.



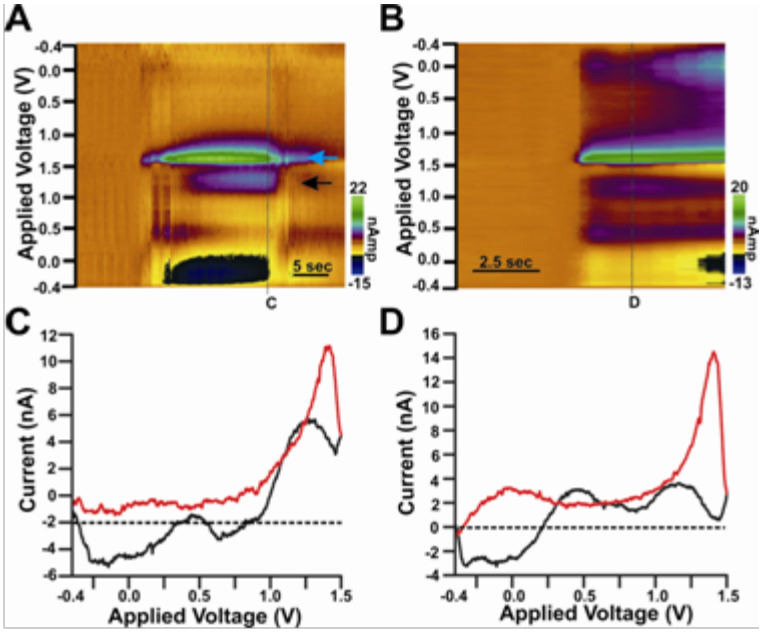
eFigure 4. Microthalamotomy effect during DBS surgery.

(A) Averaged (n = 7) tremor frequency recording during DBS shows no significant change in tremor frequency (3.4 ± 2.4 Hz, n = 7, p = 0.12). (B) Representative handwriting sample before and after DBS electrode implantation (L, left hand; R, right hand). (C) Pseudocolor plot showing an instantaneous increase at around +1.45 ± 0.03 V upon electrode insertion. (D) Representative current versus time plot as depicted at letter D in (C). (E) Background subtracted cyclic voltammogram at E in (C); the solid black line indicates the current detected during the ascending portion of the applied voltage waveform; the red line, by reverse-going voltage protocol.



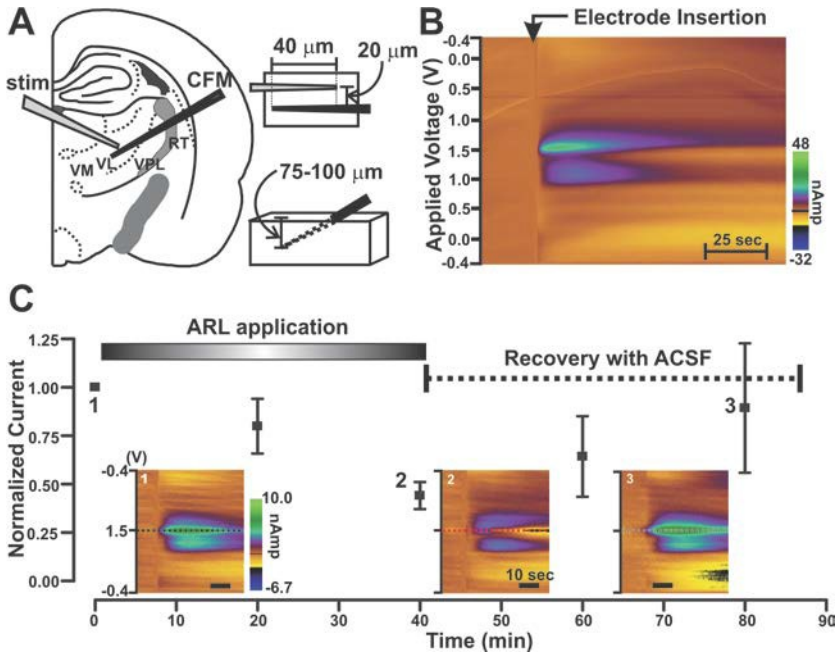
eFigure 5. Post-calibration of columnr shaped CFM with adenosine.

(A) Representative pseudocolor plot obtained by post-calibration of WincsTrode with adenosine (5 µM) following human DBS surgery. The x-, y-, and color gradient axes represent time, the applied voltage, and detected current, respectively. Note the two oxidation peaks detected at +1.4 and +1.1 V represent, respectively, the 1st adenosine oxidation peak and the 2nd adenosine oxidation peak, a product of the initial adenosine oxidation. (B) Cyclic voltammogram obtained following injection of 5 µM adenosine as marked in (A). (C) Calibration curve obtained for adenosine (0.5 to 5.0 µM) with an indicated correlation coefficient (n = 3 trials with 1 electrode) using reference electrode of stainless steel.

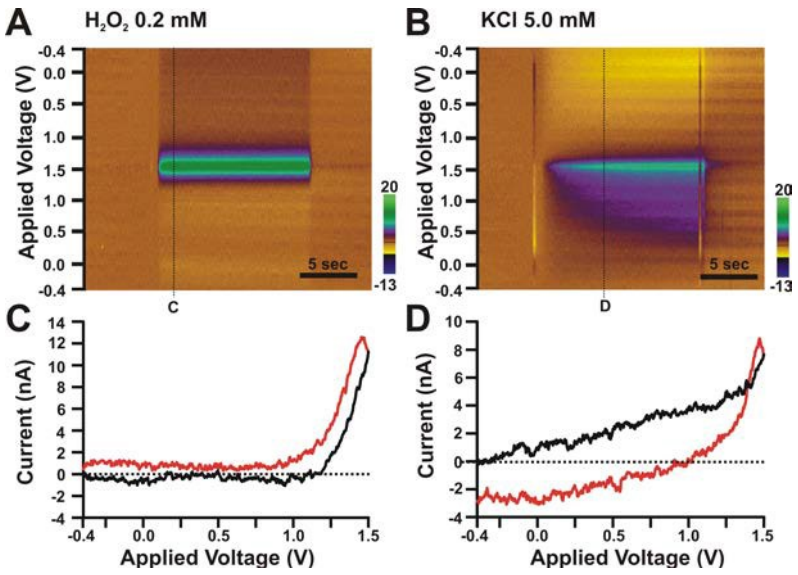


eFigure 6. FSCV recording showing adenosine release induced by CFM and DBS electrode implantation in human patients with ET.

(A) Pseudocolor plot of oxidation peak currents at +1.4 V and +1.1 V concurrent with WincsTrode insertion into VIM thalamus showing that the potentials match those for adenosine oxidation peak. (B) Pseudocolor plot obtained from a patient under general anesthesia, which show the appearance of oxidation currents immediately upon DBS electrode implantation. (n = 1). (C) Representative cyclic voltammograms obtained upon sensing electrode, WincsTrode, implantation (A) showing two significant oxidation peak currents at +1.1 V (black arrow) and +1.4 V (blue arrow). (D) Representative cyclic voltammograms obtained following DBS implantation (B) showing significant oxidation peak current at +1.4 V (blue arrow), but not at +1.1 V (black arrow). The solid black line indicates the current detected by forward-going voltage protocol; the red line, by reverse-going voltage protocol.

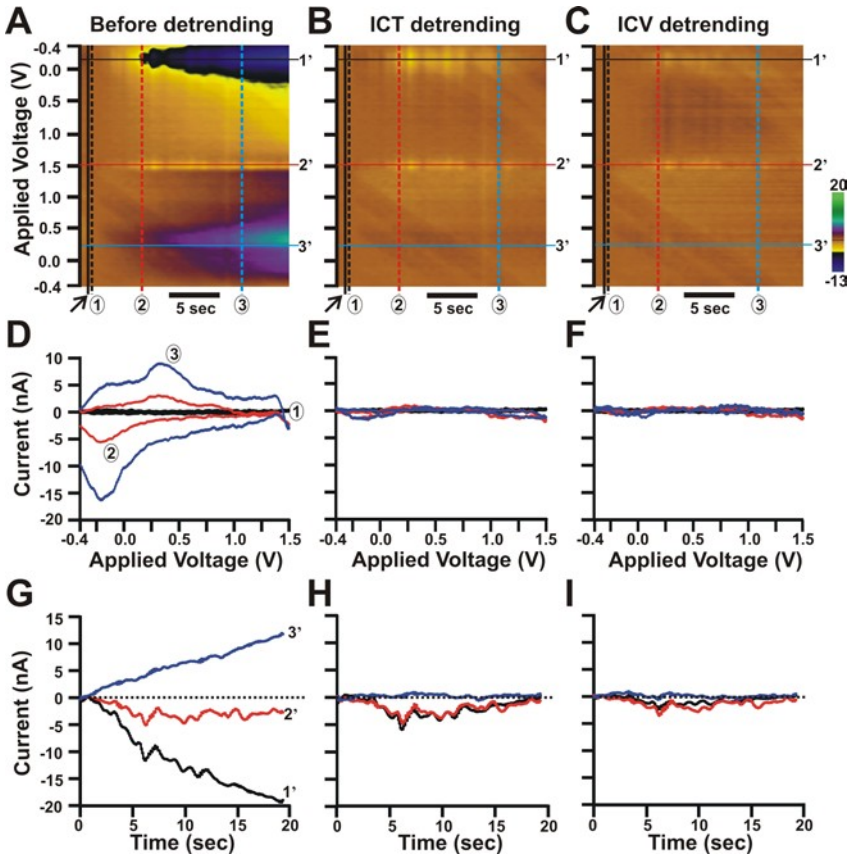


eFigure 7. Signal evaluation with a pharmacological method in *in vitro* rat slice (A). Diagram of electrode positions (VL, ventrolateral; VM, ventromedial; VPL, ventroposterior lateral; RT, reticular thalamic; stim, glass capillary for mechanical stimulation; CFM, carbon fiber microelectrode). (B) Adenosine release evoked by electrode insertion (arrow). (C) Pseudocolor plot depicting reduction in adenosine concentration with application of an ectonucleotidase inhibitor, ARL-67156 50□M (n=4, $P < 0.05$). Normalized 1st oxidation peak currents of adenosine induced by electrode insertion were plotted via time (average ± SEM).



eFigure 8. FSCV of alternate molecules.

Pseudocolor plots from hydrogen peroxide (A) and potassium ion (B) both of which are similar to the adenosine signal and for which a triangular waveform similar to the one used for human recording was applied, ramping from -0.4 V to +1.5 V and back at 400 V/sec, every 100 ms. (C) Cyclic voltammogram depicting that hydrogen peroxide can be identified by one oxidation peak current at +1.4 V. (D) Cyclic voltammogram depicting bolus injection of 5 mM potassium ion using *in vitro* flow cell analysis system generated one broad peak current at +1.4 V. The solid black line indicates the current detected by forward-going voltage protocol; the red line, by reverse-going voltage protocol.



eFigure 9. Detrending methods to correct background current drift prior to FSCV recording during human DBS surgery.

(A) Representative color plot shows accumulation of background changes from disc-type sensing electrode with a baseline adjusted by a detrending algorithm which can compensate for either cyclic voltammogram drifting or current drifting (CT) with time on the x axis (the time at which the control current to be subtracted was obtained is indicated by an arrow). (B) Background current shift with time (ICT) following detrending. (C) Cyclic voltammogram showing drifting with time (ICV) following detrending. (D), (E), and (F) Subtracted FSCV current at three different time points showing an increase in current with time. (G), (H), and (I) Current vs time plots before detrending (D and G) and after ICT (E and H), and after ICV (F and I).

To be completed by IRB office:
IRB # 09-007441 00
Consent form approved March 18, 2010;
This consent valid through March 17, 2011;

1. General Information About This Research Study

Study Title: "Neurotransmitter Measurements Using Wireless Instantaneous Neurotransmitter Concentration System (WINCS) During Deep Brain Stimulation Neurosurgery"

Name of Principal Investigator on this Study: Dr. K. Lee and Colleagues

A. Study Eligibility and Purpose

You are being asked to take part in this research study because you are scheduled for Deep Brain Stimulation (DBS) surgery. In this study, we are investigating the usefulness of monitoring dopamine and adenosine in patients with medically intractable Essential Tremor, Parkinson's Disease, and Dystonia. Currently, we use electrical activity to determine where to place the DBS electrodes in the brain. We are investigating the changes in dopamine and adenosine in response to DBS.

As you read this form describing the study, ask any questions you have. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you decide. If you decide to participate, you may stop participating at any time during the study. You may decide not to participate. If so, none of your current benefits or normal health care will be affected in any way. When you feel comfortable that all your questions have been answered, and you wish to take part in this study, sign this form in order to begin your participation. Your signature means you have been told about the study and what the risks are. Your signature on this form also means that you want to take part in this study.

B. Number of Participants

The plan is to have 15 people take part in this study at Mayo Clinic Rochester.

2. What Will Happen To You While You Are In This Research Study?

If you agree to be in the study, you will be asked to participate in the following:

This study will take place while you are at Saint Mary's Hospital. After you have been determined to be an appropriate candidate for DBS surgery, you will undergo identical procedure for the DBS surgery with the addition of an extra electrode that would be placed into your brain that would measure neurotransmitter levels related to DBS.

If you decide to take part in this study, the electrodes we will place and the data recording system have been specially designed to gather information for this study. There is no difference in the evaluation, surgery or risks with the use of these study electrodes compared to the standard electrodes.

The device used in this study is considered investigational, which means it has either not been approved by the Food and Drug Administration (FDA) for routine clinical use or for the use described in this study.

3. How Long Will You Be in This Research Study?

You will be in this study for the duration of your surgery; there will be no prolonged follow-up.

4. Why You Might Want To Take Part In This Research Study

This study will not make your health better. It is for the benefit of research.

5. What Are the Risks Of This Research Study?

The study will be performed after the DBS electrodes have been implanted. The study will not interfere with your doctor's ability to perform the DBS surgery. It is unlikely, but not known if the addition of the extra recording electrode is a risk. Further, the procedure will prolong your anesthesia time by 15 to 30 minutes; the risk of this additional anesthesia time is minimal.

Pregnancy and Birth Control:

1) Will women of child-bearing-potential be allowed to participate in this study?

Yes: Women of child-bearing-potential will be able to participate in this.

2) Will pregnant and/or nursing women be allowed to participate in this study?

No: Pregnant and/or nursing women will not be allowed to participate in this study.

3) Do you need to have a pregnancy test done to be part of the study?

No: A pregnancy test will be done as part of your normal clinical care.

4) Will men who are able to father a child be allowed to participate in this study?

Yes: Men who are able to father a child are allowed to take part in this study.

Risk summary

The risks of this research study are what you would experience during deep brain stimulation surgery. However, you will be undergoing monitoring of neurotransmitter (brain chemical) levels during DBS surgery that will require implantation of monitoring electrode that is similar to the electrophysiologic electrode that is used routinely during DBS surgery. The therapeutic mechanism of action of DBS is currently unknown. This study may provide important new information concerning how DBS may work

6. What Other Choices Do You Have If You Don't Take Part In This Research Study?

This study is only being done to gather information. You may choose not to take part in this study.

7. Are There Reasons You Might Leave This Research Study Early?

Taking part in this research study is voluntary. You may decide to stop at any time. You should tell the researcher if you decide to stop and you will be advised whether any additional tests may need to be done for your safety.

In addition, the researchers or Mayo may stop you from taking part in this study at any time:

- if it is in your best clinical interest,
- if you do not follow the study procedures,
- if the study is stopped.

8. Will You Need To Pay For Any Of The Tests And Procedures?

You will not need to pay for any tests and procedures which are done just for the purpose of this research study. These tests and procedures are:

- neurochemical/neurotransmitter monitoring during deep brain stimulation surgery.

However, you and/or your health plan will need to pay for all tests and procedures that you would normally have as part of your regular medical care.

If you have study related questions regarding billing, insurance or reimbursement, stop by: Admission and Business Services office, or call Patient Account Services at (507) 287-1819.

9. Will You Be Paid For Participating In This Research Study?

You will not be paid for taking part in this study.

10. What Happens If You Are Injured Or Ill Because You Were In This Research Study?

If you have side effects from taking part in this study, you need to report them to the researcher and your regular physician, and you will be treated as needed. Mayo will give medical services for treatment for any bad side effects from taking part in this study. Such services will be free if not covered by a health plan or insurance. No additional money will be offered.

11. What Are Your Rights If You Are In This Research Study?

Taking part in this research study will not change your rights and benefits. Taking part in this research study does not give you any special privileges. If you decide to not participate in this study, or stop in the middle of the study, no benefits are taken away from you. Specifically, you do not have to be in this research study to receive or continue to receive medical care from Mayo Clinic.

You will be told of important new findings or any changes in the study or procedures that may affect you or your willingness to continue in the study.

12. What About Your Privacy?

Authorization To Use And Disclose Protected Health Information

Your privacy is important to us, and we want to protect it as much as possible. By signing this form, you authorize Mayo Clinic and the investigators to use and disclose any information created or collected in the course of your participation in this research protocol. This information might be in different places, including your original medical record, but we will only disclose information that is related to this research protocol for the purposes listed below.

This information will be given out for the proper monitoring of the study, checking the accuracy of study data, analyzing the study data, and other purposes necessary for the proper conduct and reporting of this study. If some of the information is reported in published medical journals or scientific discussions, it will be done in a way that does not directly identify you.

This information may be given to other researchers in this study, or private, state or federal government parties or regulatory authorities in the USA and other countries responsible for overseeing this research. These may include the Food and Drug Administration, the Office for Human Research Protections, or other offices within the Department of Health and Human Services, and the Mayo Clinic Office for Human Research Protections or other Mayo groups involved in protecting research subjects.

If this information is given out to anyone outside of Mayo, the information may no longer be protected by federal privacy regulations and may be given out by the person or entity that receives the information. However, Mayo will take steps to help other parties understand the need to keep this information confidential.

This authorization lasts until the end of the study.

The study does not end until all data has been collected, checked (or audited) and analyzed. Sometimes this can be years after your study visits have ended. For example, this could happen if the results of the study are filed with a regulatory agency like the Food and Drug Administration.

You may stop this authorization at any time by writing to the following address:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
200 1st Street SW
Rochester, MN 55905

If you stop authorization, Mayo may continue to use your information already collected as part of this study, but will not collect any new information.

13. What Will Happen to Your Samples?

No biological samples will be collected as part of this research study.

14. Who Can Answer Your Questions?

You can call …	At …	If you have questions or concerns about …
Principal Investigator: Dr. Kendall Lee **Study Coordinator:** Deb Gorman	**Phone:** 507-284-2511	**Questions about the study tests and procedures** **Research-related injuries or emergencies** **Any research-related concerns or complaints**
Mayo Clinic IRB **Research Subject Advocate:**	**Phone:** 507-266-4000 **Toll-Free:** 866-273-4681	**Rights of a research subject** **Use of Protected Health Information** **Any research-related concerns or complaints**
Research Billing	**Rochester:** 507-287-1819	**Billing / Insurance Questions**

MAYO CLINIC

15. Summary and Enrollment Signatures

You have been asked to take part in a research study at Mayo Clinic. The information about this study has been provided to you to inform you about this study.

- I have read the whole consent form, and all of my questions have been answered to my satisfaction.
- I am satisfied that I have been given enough information about the purpose, methods, risks, and possible benefits of the study to decide if I want to join.
- I know that joining the study is voluntary and I agree to join the study.
- I know that I can call the investigator and research staff at any time with any questions or to tell them about side effects.
- I know that I may withdraw from the study at any time.
- A copy of this form will be put in my medical records and I will be given a copy of this completed form.

Please sign and date to show that you have read all of the above guidelines. Please do not sign unless you have read this entire consent form. If you do not want to sign, you don't have to, but if you don't you cannot participate in this research study.

(Date / Time)	(Printed Name of Participant)	(Clinic Number)

(Signature of Participant)

(Date / Time)	(Printed Name of Individual Obtaining Consent)

(Signature of Individual Obtaining Consent)