*Movement Disorders*
Vol. 21, Suppl. 14, 2006, pp. S284–S289


# Basic Algorithms for the Programming of Deep Brain Stimulation in Parkinson's Disease

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**Abstract:** The clinical success of deep brain stimulation (DBS) for treating Parkinson's disease (PD) critically depends on the quality of postoperative neurological management. Movement disorder specialists becoming involved with this therapy need to acquire new skills to adapt optimally stimulation parameters and medication after implantation of a DBS system. At first glance, the infinite number of theoretically possible parameter combinations seems to make programming a complex and time-consuming art. This article outlines a stepwise and standardized approach, reducing the possible parameter settings in DBS to a few relevant combinations. The basic programming algorithms for thalamic, subthalamic, and pallidal stimulation in PD are explained and summarized in flowcharts. © 2006 Movement Disorder Society

**Key words:** deep brain stimulation; Parkinson's disease; programming

The programming of deep brain stimulation (DBS) is not a complex art, if one follows a standardized step-by-step approach. Using this basic programming algorithm will help to narrow down thousands of theoretical parameter combinations (pulse width, frequency, voltage) and multiple contact configurations to a few clinically useful alternatives. After the initial parameter setting is completed, only a few adaptations (mostly increases in amplitude) are necessary to stabilize the clinical benefit during long-term follow-up. However, major changes may be necessary when the electrode is not correctly placed or when stimulation-induced dyskinesia is difficult to manage.

Currently, Medtronic (Minneapolis, MN) is the only manufacturer providing approved DBS devices. The DBS systems consist of a quadrupolar electrode with an intercontact distance of 1.5 mm (model 3387) or 0.5 mm (model 3389), an extension cable, and an internal pulse generator (IPG) either controlling one (Itrel II, Soletra) or two (Kinetra) DBS electrodes. The relevant stimulation parameters, which can be controlled telemetrically by use of an external programmer (model 7432 or Envision), are electrode polarity, amplitude (V), pulse width (μs), and frequency (Hz). The patients may also be enabled to verify the status of the IPG and to turn it off or on by means of a handheld controller (model 7436 or Access for Kinetra and model 7438 or Access Review for Soletra). In addition, for the Kinetra model, the Access device may allow the patients to increase and decrease voltage, pulse width, and frequency according to the physician's discretion.

The following sections summarize for each adjustable parameter in DBS the neurophysiological effects, discuss device-related limitations, and give general suggestions for the initial parameter choice. Our suggestions are oriented toward three principal goals of DBS programming in their order of importance: to optimize clinical benefit, to minimize adverse effects, and to minimize current consumption (increasing the lifetime of the IPG battery).

## ELECTRODE POLARITY

Each electrode contact can be programmed as anode or cathode in bipolar settings or as cathode for monopolar stimulation against the IPG case. Monopolar stimulation provides a radial current diffusion, covering an

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**Published online in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/mds.20961**

approximately spherical space around the stimulating electrode. Bipolar stimulation creates a narrower and more focused current field with a maximal effect near the cathode.[1,2] By reducing diffusion into adjacent structures, it may be possible to avoid side effects of monopolar stimulation. However, monopolar stimulation is usually used because it requires lower stimulation intensity than bipolar stimulation to achieve approximately the same clinical benefit. Normally, a single cathode is chosen for DBS, although it may be useful in some cases to activate two adjacent contacts, providing partial benefit from each.

## AMPLITUDE

With increasing amplitude, neural elements are stimulated in a gradually increasing distance from the electrode. The exact current–distance relation of DBS is difficult to determine, because electrode design, tissue anisotropy, and biophysical properties of the neural elements mediating the behavioral effect (e.g., slow or rapid conducting axons, cell bodies) have a strong impact.[1–3] For standard stimulation parameters, however, a radial diffusion of 2 to 5 mm may be roughly estimated.

The IPGs provide constant voltage stimulation and allow the programmer to vary voltage in 0.1 V increments (Kinetra allows also 0.05 V changes) between 0 and 10.5 V. Therapeutic amplitudes for DBS normally range between 1 and 3.6 V (rarely above) for the different stereotactic targets. An important technical issue has to be considered, when programming an Itrel II or Soletra. The electrical current consumption of these neurostimulators is linear up to 3.6 V and rises abruptly above 3.6 and 7.3 V because a voltage doubler or tripler circuit is activated within the neurostimulator. Thus, whereas a mild amplitude increase from 3.6 to 3.7 V may only result in a minimal change of clinical efficacy, it significantly increases battery drain and shortens battery life by about one-half. Therefore, the voltage should not routinely be increased above 3.6 V unless absolutely necessary. Alternatively, the pulse width may be increased with a compensatory reduction of the amplitude. A different electrical circuitry provides a linear increase in current consumption throughout the full voltage range in the Kinetra IPG. Therefore, voltages greater than 3.6 will not affect the battery life significantly. However, it is worthwhile noticing that requirements of high voltage of stimulation more likely reflect suboptimal electrode positioning. In this situation, excessive increases in amplitude rarely add significant benefit, but rather increase the risk of stimulation-induced adverse effects.

## PULSE WIDTH

Medtronic IPGs allow varying pulse width (PW) in steps between 60 and 450 μs. The current required to stimulate a neural element decreases as pulse width increases. The nonlinear relation between the two variables is best described by an inverse exponential function.[1] The minimal amount of current necessary to excite a neural element at an infinitely long pulse width (PW) is termed rheobase current in neurophysiology. Chronaxie is a measure of the excitability of neural elements and has been defined as the pulse duration equivalent to the double rheobase current on the strength–duration curve. Axons have lower chronaxie than neuron bodies.[1] Chronaxies for DBS effects have been estimated to be around 65 μs for thalamic and around 75 μs for pallidal stimulation.[4,5] Chronaxies of rapid-conducting fiber tracts (e.g., the pyramidal tract) may be substantially lower. Selecting long pulse duration for DBS may bring the amplitude threshold for beneficial effects and side effects close to the rheobase current and therefore narrow the therapeutic window. Another aspect impacting on the initial choice of PW is the fact that amplitude can be adjusted on a much finer scale than pulse width with currently available IPGs, therefore allowing for a better fine tuning within the available therapeutic window. In addition, PW seems to have the least important role in improving clinical signs in subthalamic nucleus (STN) DBS,[6] although higher PWs (90–120 μs) may be more useful in ventral intermediate nucleus (Vim)[7,8] and globus pallidus internus (GPi)[9] stimulation. As a result, one should always start programming using the lowest possible pulse width of 60 μs. Reasons for increasing pulse width beyond the initial setting of 60 μs could be an unsatisfactory clinical response after increasing voltage to the limit of 3.6 V. In these cases, pulse width should be set to the next increment of 90 μs. The amplitude may need to be lowered in case of side effects.

In general, an optimally placed electrode will allow for the lowest amplitude and PW settings. As already pointed out for the voltage, the necessity to increase pulse width further due to unsatisfactory clinical results at maximal voltage levels usually indicates suboptimal targeting. The use of extremely high PWs together with high voltages for achieving additional clinical benefit should encourage the consideration of surgical repositioning of the electrode because battery drain increases proportionally and may cause frequent IPG exchanges.

## FREQUENCY

Pulse frequency can be set between 2 and 185 Hz in the Itrel II or Soletra and between 2 and 250 Hz in the Kinetra. The therapeutic effect of DBS is only observed

at high frequencies above 100 Hz with a fairly abrupt threshold.

The amplitude–frequency relationship has been studied systematically for the antitremor effect of thalamic stimulation[7,8] and the antiparkinsonian effect of subthalamic stimulation.[6] Low-frequency stimulation (<10 Hz) may aggravate the parkinsonian signs,[6] whereas higher frequencies (>50 Hz) improve symptoms at progressively lower stimulation intensity. The benefit increases linearly with increasing frequency and is almost maximal around 130 Hz. There is a further small nonlinear increase in efficacy above 130 Hz until a plateau is reached around 200 Hz. A further increase from 200 up to 10,000 Hz, using an external stimulator, does not further improve the antitremor effect of thalamic DBS.[7]

As a compromise between clinical efficacy and power consumption, one usually sets stimulation frequency to 130 Hz and keeps this parameter constant. Exceptional reasons for changing this fixed rate may be an unsatisfactory clinical response that cannot be improved by an increase in voltage or pulse width without causing side effects by unintended current spread. In these rare instances, a further increase in frequency may improve clinical benefit without increasing current diffusion into adjacent structures.

## BASIC ALGORITHM FOR DBS PROGRAMMING

### Initial Programming Session

The most important step during the postoperative programming is to determine the amplitude threshold for clinical benefits and side effects for each of the four electrode contacts. These initial test results will serve as a reference for all future adaptations of DBS parameters. The acute testing is usually a good predictor for the long-term clinical benefit and changes of the electrode configuration are rarely necessary if the initial testing is properly done and documented. The examination should take place in a stable *off* drug condition to have testable clinical symptoms and to prevent medication effects from interfering with DBS effects. The initial programming session is usually performed in the morning after an overnight medication washout. This timing reduces the discomfort of the patient during drug withdrawal and allows observation of the stimulation response during office hours after making the initial choice of parameters. The choice to start the stimulation soon after the IPG positioning or several weeks later depends on the patient's condition (the microlesioning effect after surgery may mask the actual benefit of the stimulation) and the surgical team's preferences.

The basic algorithm for evaluating each electrode contact is outlined in Figure 1. Pulse width is set to 60 μs and frequency to 130 Hz. Both parameters are kept constant throughout the testing period. Then, one determines for each electrode contact the amplitude threshold for inducing a clinical response and side effects using monopolar stimulation and a stepwise increase in amplitude (0.2–0.5 V).

The target signs that are examined after each increment may vary depending on the target and the individual clinical feature. Moreover, the time course of the stimulation response can differ substantially between signs and predispose some to more acute clinical testing than others. Bradykinesia and tremor in Parkinson's disease (PD) may respond with a variable time delay to effective STN DBS and their severity may be influenced by confounding factors such as fatigue, patient comfort, or training. In contrast, rigidity usually responds within seconds to STN or GPi stimulation and can be reliably examined, even if patient cooperation is poor. The Froment maneuver (contralateral finger tapping) may be used to increase or provoke rigidity, which can be best assessed by passive flexion/extension movements around the wrist joint. Effective STN or GPi DBS induces a marked (>70%) and abrupt decrease in muscle tone approximately 20 to 30 seconds after initiating stimulation. The examiner can easily feel this sudden drop in rigidity after little practice. Other standardized motor tasks such as alternating movements (items 23–26 of the Unified Parkinson's Disease Rating Scale motor scale) or tremor may be used as additional criteria in patients with little rigidity or tremor dominant PD.

In Vim stimulation, the benefit on tremor is immediate (within 5–30 s). Limb tremor may be examined in the three conditions, rest (with supported limbs), posture (wing-beating position), and action (finger-to-finger or finger-to-nose test), depending on the predominant activation mode. Especially in predominant action tremors, one may add functional tasks, such as water pouring or spiral drawing, to quantify the degree of tremor suppression. A provoking task (such as backward counting or mental calculation) may be useful if tremor severity fluctuates.

If a clinical response is observed before evoking side effects, the amplitude is further increased to determine the threshold for adverse effects. If no beneficial or adverse effects are observed within the available amplitude range, testing is discontinued and the next contact is selected. The electrode contact with the lowest threshold for inducing a benefit and the largest therapeutic width (i.e., highest threshold for side effects) is finally selected for chronic stimulation.

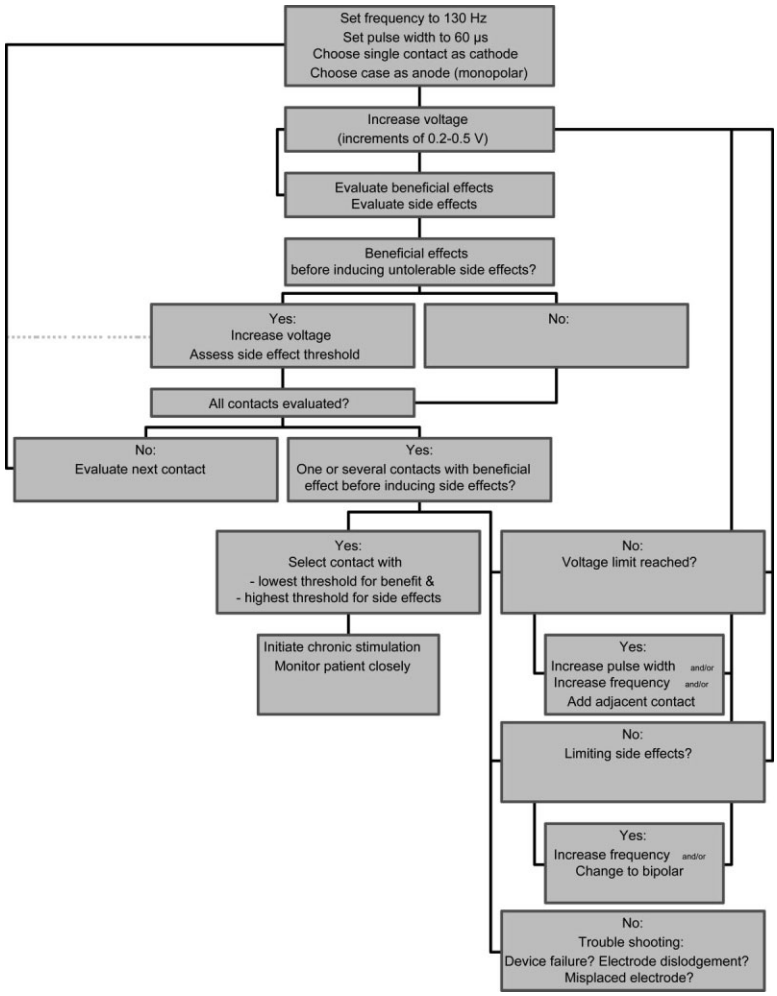


**FIG. 1.** Basic algorithm for the initial parameter setting in DBS

If this iterative approach does not lead to a satisfactory benefit or if side effects limit the amplitude range, additional steps for troubleshooting are necessary. In general, one will try to increase current diffusion or stimulation efficacy in case of an unsatisfactory benefit as long as side effects are tolerable. Increases in pulse width or frequency or the combination of two cathodes may be tried. In the latter case, the two best contacts will be stimulated together. In case of limiting side effects, one should focus the electrical field by selecting a bipolar configuration. For this purpose, the best contact will be chosen as the cathode and the second best one as the anode, because cathodic stimulation is more effective.[1,3] Alternatively, a higher frequency may be programmed to improve stimulation efficacy without significantly increased current diffusion.

Once again, the necessity to perform troubleshooting steps usually indicates a suboptimally placed electrode. Postoperative imaging may help to identify a misplaced electrode, but care must be taken when performing magnetic resonance imaging with implanted DBS systems and only approved MRI protocols should be used. A careful balance between actual clinical benefit, side effects, energy consumption, patient's satisfaction, and physician opinion should guide the decision to proceed with chronic stimulation or to consider surgical revision.

### Initiation of Chronic Stimulation

The initial setting for chronic stimulation is monopolar with a single cathode, 60 µs pulse width, 130 Hz frequency, and a variable amplitude.

Since delayed complications, such as severe STN stimulation dyskinesia, may occur hours after initiating the stimulation or increasing the amplitude or pulse width, one usually programs a low amplitude of 0.5 to 1 V to start stimulation. The amplitude is slowly titrated in increments of 0.2 to 0.5 V or more during the following days, depending on clinical efficacy and patient and

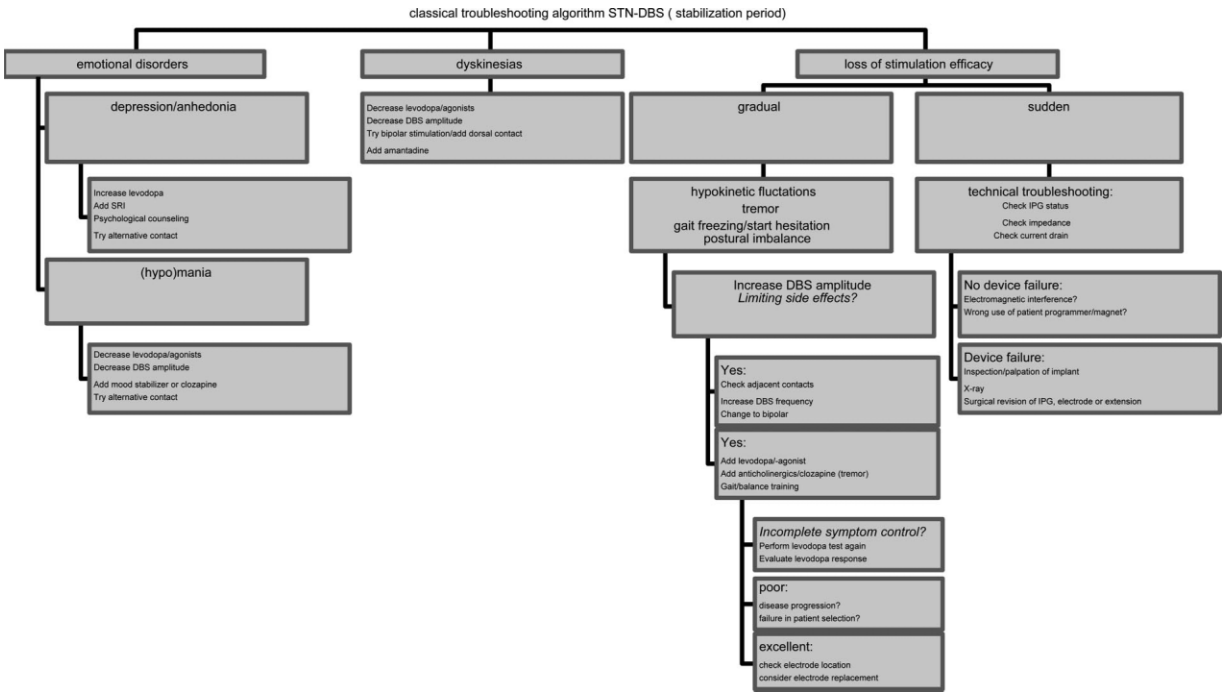


**FIG. 2.** Troubleshooting algorithm for subthalamic nucleus stimulation in Parkinson's disease (STN DBS).

physician availability. In patients implanted with a Kinetra system, the physician may set a voltage range and some or all of the gradual amplitude titration may be done by the patient using the Access patient programmer. As a rule, STN chronic stimulation should be initiated always in the morning, never in the evening or before weekends, unless the patient is under observation and the treating physician is available. The anti-PD medications will be progressively reduced, usually starting with COMT inhibitors, anticholinergic drugs, or amantadine and ending with levodopa and dopamine agonists.

The approach for programming thalamic or pallidal DBS may be somewhat different. Tremor suppression in thalamic DBS is almost immediate, allowing effective amplitudes to be programmed during the initial programming session. Pallidal DBS in PD may have a comparable immediate effect on dyskinesias. Some groups therefore program pallidal DBS in the *on* period, when dyskinesias allow monitoring of the intended clinical response.

## Stimulation Adjustment During the Stabilization Period

The stabilization period (first 3 to 6 months after surgery) is characterized by a gradual adaptation of medication and stimulation parameters. During the first weeks after surgery, the microlesioning effect of electrode implantation gradually disappears. This healing process usually requires a compensatory increase in stimulation amplitude to maintain the clinical benefit. Changes of other stimulation parameters or electrode configuration are seldom necessary.

Clinical problems during the stabilization period are mostly caused by the complex interaction of medication and stimulation. Figures 2 to 4 outline the troubleshooting steps for the most common postoperative problems in DBS of the STN, Vim, and GPi. A more complete and detailed survey of the postoperative neurological man-

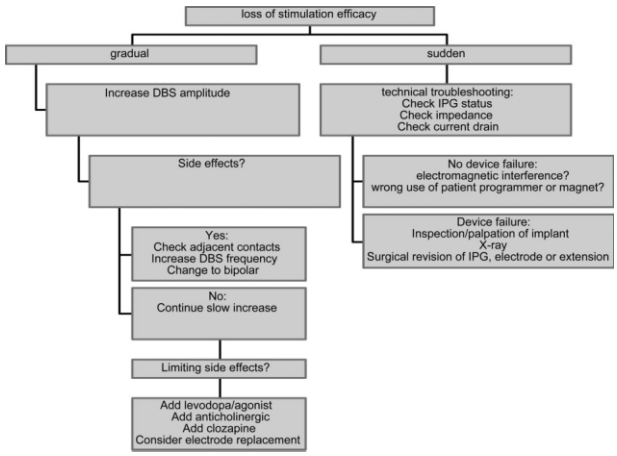


**FIG. 3.** Troubleshooting algorithm for thalamic deep brain stimulation (Vim DBS).

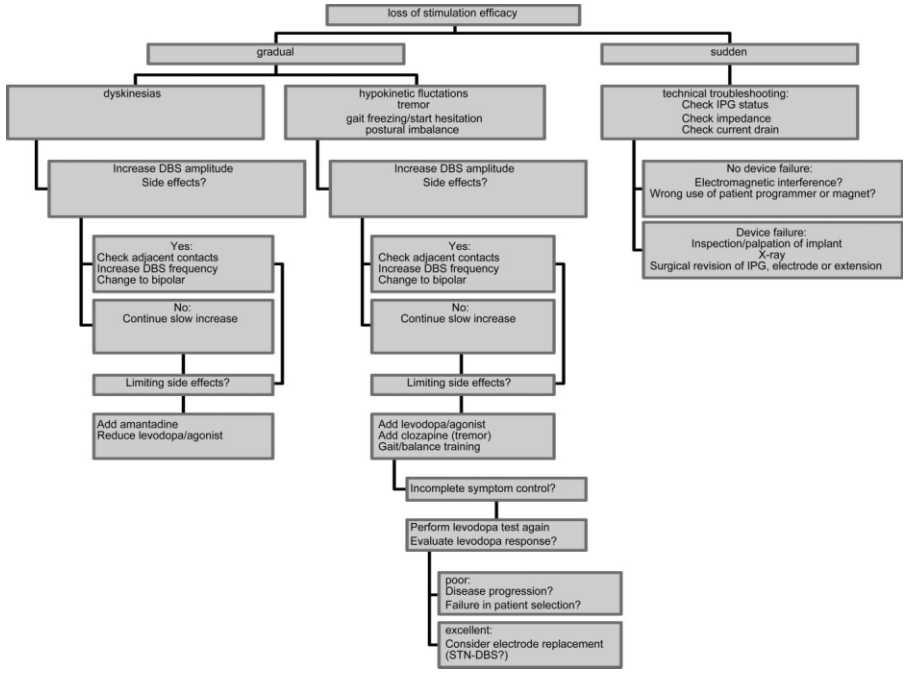


**FIG. 4.** Troubleshooting algorithm for pallidal deep brain stimulation in Parkinson's disease (GPi DBS).

agement after deep brain stimulation is provided in a companion article in this issue.[10]

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