



MEDICAL AND SURGICAL TREATMENT OF PARKINSON DISEASE WITH MOTOR FLUCTUATIONS AND DYSKINESIA

This is a summary of the American Academy of Neurology (AAN) evidence-based guideline reviewing all of the evidence to determine which medications reduce off time and dyskinesia; their relative efficacy in reducing off time; whether deep brain stimulation (DBS) reduces off time, dyskinesia, medication usage, and improves motor function; and which factors predict improvement after DBS.

Please refer to the full guideline for detailed findings and supporting evidence at www.aan.com.

RECOMMENDATIONS FOR MEDICATIONS THAT REDUCE OFF TIME FOR PATIENTS WITH MOTOR FLUCTUATIONS

Strong Level A evidence	The following medications should be offered to reduce off time in Parkinson disease (PD) patients with motor fluctuations: <ul style="list-style-type: none"> • Entacapone • Rasagiline
Good Level B evidence	The following medications should be considered to reduce off time in PD patients with motor fluctuations: <ul style="list-style-type: none"> • Pramipexole • Tolcapone (should be used with caution and requires monitoring for hepatotoxicity) • Ropinirole • Pergolide (should be used with caution and requires monitoring for valvular fibrosis)
Weak Level C evidence	The following medications may be considered to reduce off time in PD patients with motor fluctuations: <ul style="list-style-type: none"> • Apomorphine <i>injected subcutaneously</i> • Cabergoline • Selegiline
Weak Level C evidence	The following medications may be disregarded to reduce off time in PD patients with motor fluctuations: <ul style="list-style-type: none"> • Sustained release carbidopa/levodopa • Bromocriptine

* Strength indicates level of supporting evidence, not a hierarchy of efficacy.

RECOMMENDATIONS FOR THE RELATIVE EFFICACY OF MEDICATIONS THAT REDUCE OFF TIME FOR PATIENTS WITH MOTOR FLUCTUATIONS

Weak Level C evidence	Ropinirole may be chosen over bromocriptine to reduce off time in PD patients with motor fluctuations.
Insufficient Level U evidence	There is insufficient evidence to support or refute the use of any other agent over another.

RECOMMENDATIONS FOR MEDICATIONS THAT REDUCE DYSKINESIA

Weak Level C evidence	Amantadine may be considered for patients with PD with motor fluctuations in reducing dyskinesia.
Insufficient Level U evidence	There is insufficient evidence to support or refute the efficacy of clozapine in reducing dyskinesia. Clozapine's potential toxicity including agranulocytosis, seizures, myocarditis and orthostatic hypotension with or without syncope, and required white blood cell count monitoring must be considered.

RECOMMENDATIONS FOR DEEP BRAIN STIMULATION (DBS)

	Recommendation for efficacy	Factors that predict improvement after DBS
DBS of the subthalamic nucleus (STN)	DBS of the STN may be considered as a treatment option in PD patients to improve motor function and to reduce motor fluctuations, dyskinesia and medication usage (Level C). Patients need to be counseled regarding the risks and benefits of this procedure.	Based upon two Class II studies, preoperative response to levodopa is probably predictive of post-surgical improvement. Preoperative response to levodopa should be considered as a factor predictive of outcome after DBS of the STN (Level B). Based on one Class II study, younger age and shorter disease duration (less than 16 years) is possibly predictive of greater improvement after DBS of the STN. Age and duration of PD may be considered as factors predictive of outcome after DBS of the STN. Younger patients with shorter disease duration may possibly have improvement greater than that of older patients with longer disease duration (Level C).
DBS of the globus pallidus interna (GPi)	There is insufficient evidence to make any recommendations about the effectiveness of DBS of the GPi in reducing motor complications or medication usage or in improving motor function in PD patients (Level U).	There is insufficient evidence to make any recommendations about factors predictive of improvement after DBS of the GPi in PD patients (Level U).
DBS of the ventral intermediate (VIM) nucleus of the thalamus	There is insufficient evidence to make any recommendations about the effectiveness of DBS of the VIM nucleus of the thalamus in reducing motor complications or medication usage or in improving motor function in PD patients (Level U).	There is insufficient evidence to make any recommendations about the effectiveness of DBS of the VIM nucleus of the thalamus in reducing motor complications or medication usage or in improving motor function in PD patients (Level U).

Copies of this summary and additional companion tools are available at www.aan.com or through AAN Member Services at (800) 879-1960.

View the following AAN movement disorder guidelines at www.aan.com.

Jan 2002	Initiation of Treatment for Parkinson Disease (UPDATED)
April 2006	Diagnosis and Prognosis for New Onset Parkinson Disease
April 2006	Neuroprotective Strategies and Alternative Therapies for New Onset Parkinson Disease
April 2006	Evaluation and Treatment of Depression, Psychosis and Dementia in Parkinson Disease
April 2006	Medical and Surgical Treatment of Parkinson Disease with Motor Fluctuations and Dyskinesia

This is an educational service of the American Academy of Neurology. It is designed to provide members with evidence-based guideline recommendations to assist with decision-making in patient care. It is based on an assessment of current scientific and clinical information, and is not intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on the circumstances involved. Physicians are encouraged to carefully review the full AAN guidelines so they understand all recommendations associated with care of these patients.

This guideline summary is evidence-based. The AAN uses the following definitions for the level of recommendation and classification of evidence. **Class I:** Prospective, randomized, controlled clinical trial with masked outcome assessment, in a representative population. The following are required: a) primary outcome (s) is/are clearly defined, b) exclusion/inclusion criteria are clearly defined, c) adequate accounting for drop-outs and cross-overs with numbers sufficiently low to have minimal potential for bias, d) relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences OR a statistical, population-based sample of patients studied at a uniform point of time (usually early) during the course of the condition. All patients undergo the intervention of interest. The outcome, if not objective, is determined in an evaluation that is masked to the patients' clinical presentations. **Class II:** Prospective matched group cohort study in a representative population with masked outcome assessment that meets a-d above OR a RCT in a representative population that lacks one criterion a-d OR a statistical, non-referral-clinic-based sample of patients studied at a uniform point in time (usually early) during the course of the condition. Most patients undergo the intervention of interest. The outcome, if not objective, is determined in an evaluation that is masked to the patients' clinical presentations. **Class III:** All other controlled trials including well-defined natural history controls or patients serving as own controls in a representative population, where outcome assessment is independently assessed or independently derived by objective outcome measurement. **Class IV:** Evidence from uncontrolled studies, case series, case reports, or expert opinion OR Expert opinion, case reports or any study not meeting criteria for class I to III. ***Objective outcome measurement:** an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data) OR a sample of patients studied during the course of the condition. Some patients undergo the intervention of interest. The outcome, if not objective, is determined in an evaluation by someone other than the treating physician. ***Recommendation Level:** "Level" refers to the strength of the practice recommendation based on the reviewed literature. **Level A**=Established as effective, ineffective, or harmful for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.) **Level B**=Probably effective, ineffective, or harmful for the given condition in the specified population. (Level B rating requires at least one Class I study or at least two consistent Class II studies.) **Level C**=Possibly effective, ineffective, or harmful for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.) **Level U**=Data inadequate or conflicting; given current knowledge, treatment is unproven.