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Adaptive Deep Brain Stimulation in Advanced Parkinson's Disease: A Narrative Review of Motor Fluctuation, Speech and the Caregiver's Experience

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Abstract

Conventional deep brain stimulation runs continuously at settings chosen in clinic, while the disease it treats fluctuates hour by hour. Adaptive stimulation reads a brain signal and adjusts itself. The idea is two decades old; the randomised evidence for it currently rests on a handful of patients.

Objectives: *To review the published evidence on adaptive deep brain stimulation in advanced Parkinson's disease: what it changes in motor fluctuation, what is known about its effect on speech, how much stimulation it delivers, and how large the evidence base actually is.*

Material and Methods: *Narrative review of randomised trials, crossover studies, physiological studies and society-level reviews indexed in PubMed and the major neurology, movement disorder and neurosurgery journals. No new patient data were generated; every estimate quoted is one published by the original investigators.*

Results: *In the founding crossover study of 8 patients, motor scores improved by 66.2 per cent unblinded and 49.7 per cent blinded against the unstimulated state, compared with 54.3 and 30.5 per cent on conventional stimulation; the advantage of adaptive stimulation was 28.7 per cent ($p = 0.03$) and 27.0 per cent ($p = 0.005$) respectively, achieved with 56 per cent less stimulation time. A later blinded randomised crossover trial in 4 patients using stimulation-entrained gamma oscillations reported improved motor symptoms and quality of life over conventional stimulation. Acute testing found fewer speech side effects with adaptive than conventional stimulation.*

Conclusion: *The physiological rationale is sound and the reported effects are consistent, but the entire randomised literature comparing adaptive with conventional stimulation involves fewer patients than a single arm of the trials that established conventional stimulation. This is a promising technology at an early stage, and should be described as such.*

Abbreviations: *aDBS – Adaptive Deep Brain Stimulation, cDBS – Conventional Deep Brain Stimulation, DBS – Deep Brain Stimulation, LFP – Local Field Potential, PD – Parkinson's Disease, STN – Subthalamic Nucleus, UPDRS – Unified Parkinson's Disease Rating Scale.*

Keywords: *Parkinson's Disease; Adaptive Deep Brain Stimulation; Closed-Loop Neuromodulation; Motor Fluctuation; Caregiver Burden*

Introduction

Deep brain stimulation of the subthalamic nucleus is an established treatment for Parkinson's disease with motor fluctuations. Randomised comparison against best medical therapy established benefit in quality of life and motor function [1,2], the benefit extends to patients with earlier motor complications [3], and the choice of target has been examined directly [4,5]. Long-term follow-up shows the motor benefit is durable while axial and non-motor features progress [6,7,8].

The therapy nonetheless has a structural mismatch built into it. Stimulation is delivered continuously at parameters set during a clinic visit, while the disease it treats varies across the day with medication cycles, sleep, activity and stress. The patient who is undertreated at the end of a levodopa cycle is overtreated at its peak, and the same fixed setting produces both.

Adaptive stimulation proposes to close that loop. A signal recorded from the stimulating electrode is used to estimate the patient's current state, and stimulation is adjusted in real time by a device that senses while it stimulates [35]. Beta-band oscillatory activity in the subthalamic nucleus was the original candidate signal, since its power tracks motor impairment and falls with effective treatment [9,10,11]. This review examines what has been demonstrated, what has been assumed, and how much evidence exists.

Material and Methods

Search strategy: PubMed and the archives of the major neurology, movement disorder and functional neurosurgery journals were searched for studies of closed-loop neuromodulation in Parkinson's disease. Search terms combined deep brain stimulation with adaptive, closed-loop, beta oscillation, local field potential, biomarker and motor fluctuation. Reference lists of narrative reviews of the field [12,13,14] were screened by hand for primary sources.

Eligibility: Studies were included if they compared adaptive with conventional or absent stimulation in patients, characterised a control signal in patients, or reported effects on speech, stimulation burden or caregiver-relevant outcomes. Trials of conventional stimulation are cited to establish the comparator and are identified as such.

Data extraction and handling: Design, sample size, target, control signal, duration of testing and reported outcome were extracted as published. Sample size and the duration of the adaptive condition are reported alongside every result, because both are small throughout this literature and both bear directly on how the findings should be read. No pooling or re-analysis was performed. Figures 1 to 4 and Tables 1 and 2 reproduce published values only. This is a narrative synthesis and was not registered as a systematic review.

Results

The founding study: Eight patients with advanced Parkinson's disease underwent brain-computer-interface-controlled adaptive stimulation of the subthalamic nucleus, with stimulation triggered by beta power recorded from the stimulating electrodes and compared against no stimulation, conventional continuous stimulation and random intermittent stimulation. Relative to the unstimulated state, motor scores improved by 66.2 per cent unblinded and 49.7 per cent blinded on adaptive stimulation, against 54.3 and 30.5 per cent on conventional stimulation (Figure 1) [15].

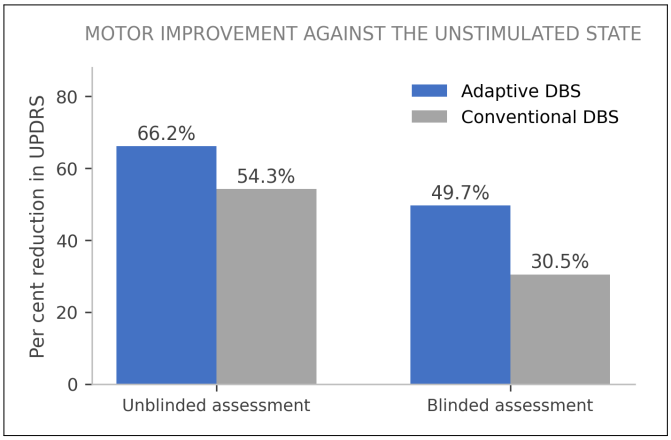

Figure 1: Reduction in UPDRS motor score against the unstimulated state, adaptive and conventional stimulation, in 8 patients [15]

The size of the difference: Expressed as the advantage of adaptive over conventional stimulation, the improvement was 28.7 per cent (p = 0.03) on unblinded assessment and 27.0 per cent (p = 0.005) blinded (Figure 2), and the effect persisted when rigidity scores were excluded [15]. Adaptive stimulation also outperformed random intermittent stimulation, which matters: it shows the benefit came from the timing of delivery rather than merely from delivering less.

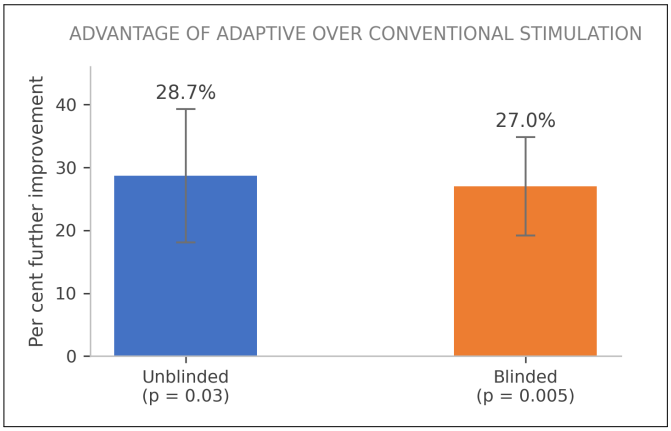

Figure 2: Further improvement with adaptive over conventional stimulation, with standard deviations [15]

Less stimulation, not more: Those improvements were achieved with a 56 per cent reduction in stimulation time and a corresponding fall in energy delivered [15]. Bilateral adaptive stimulation was subsequently shown to improve axial as well as limb symptoms with the stimulator active only about 45 per cent

of the time, and levodopa was tolerated during adaptive stimulation with further reduction in time on stimulation (Figure 3) [16]. Longer runs followed: eight-hour adaptive stimulation in freely moving patients [17], and control of levodopa-induced dyskinesia [18,19]. The same control principle has been applied outside Parkinson's disease, in Tourette syndrome [36].

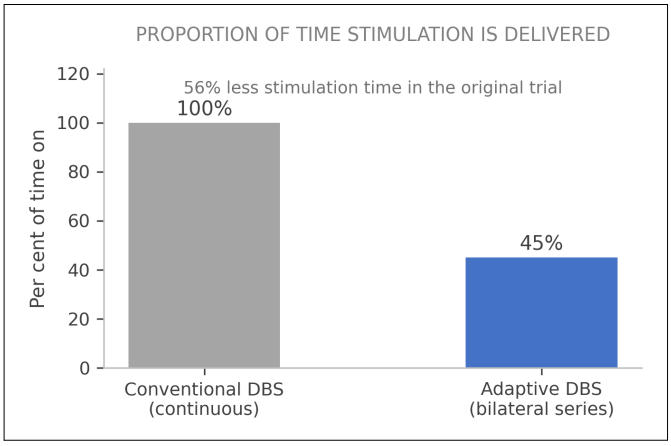

Figure 3: Proportion of time stimulation is delivered under conventional and adaptive control [15,16]

Study	Design and cohort	Principal reported finding
Little et al. 2013 [15]	Crossover, 8 patients, acute testing	aDBS 27-29% better than cDBS; 56% less stimulation time
Little et al. 2016 [16]	Bilateral aDBS series	Axial and limb benefit; stimulation on ~45% of the time
Little et al. 2016 [20]	Acute comparison, speech outcomes	Fewer speech side effects with aDBS than cDBS
Arlotti et al. 2018 [17]	8-hour aDBS, freely moving patients	Feasible and tolerated over a working day
Oehrn et al. 2024 [21]	Blinded randomised crossover, 4 patients	Gamma-driven aDBS improved symptoms and quality of life vs cDBS
Deuschl et al. 2006 [1]	RCT, 156 patients, cDBS vs medical therapy	Established quality-of-life and motor benefit of conventional DBS
Schuepbach et al. 2013 [3]	RCT, 251 patients, earlier disease	Benefit extends to patients with early motor complications

Table 1: Principal studies reviewed, with the finding as reported by the original investigators

Choosing the signal: Beta power is the best-characterised control variable, correlating with rigidity and bradykinesia and falling with treatment [9,10]. It is not the only option, and it has a known weakness: beta power falls physiologically before and during voluntary movement, so a beta-triggered system may withdraw stimulation at the moment the patient tries to move [12,22]. Alternatives have been explored, including kinematic control for tremor [23] and dual-threshold designs [24]. The most recent randomised work moved away from beta entirely: stimulation-entrained gamma oscillations in the subthalamic nucleus or motor cortex were the best predictors of each patient's most bothersome residual symptom, and were used to drive individually tailored algorithms [21].

The most recent trial: Four male patients already optimised on conventional stimulation over 11 to 31 months underwent a blinded randomised crossover comparison in their own homes, one month per condition. Adaptive stimulation improved motor symptoms and quality of life relative to conventional stimulation [21]. The design is notable for testing in real-life environments over weeks rather than in clinic over hours, which is the setting where fluctuation actually matters. It is equally notable for enrolling four patients, all of them men (Figure 4).

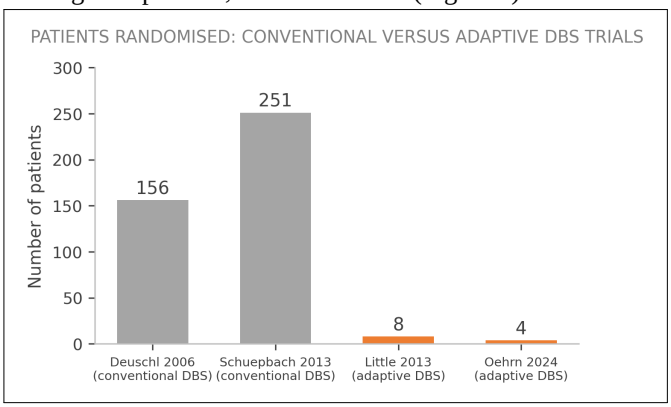

Figure 4: Patients randomised in the principal trials of conventional and of adaptive stimulation [1,3,15,21]

Speech: Speech deterioration is among the more troubling adverse effects of subthalamic stimulation, since it affects the thing patients use to maintain relationships. Intelligibility declines in a substantial proportion of patients after surgery, with contact location and voltage both implicated [25,26,27,28]. Acute comparison found fewer speech side effects with adaptive than with conventional stimulation, which is mechanistically plausible if current spread to adjacent structures is reduced when stimulation is intermittent [20]. This is a single acute study and has not been replicated over months.

The caregiver's side: Almost none of the adaptive literature reports caregiver-relevant outcomes, which is a gap rather than a finding. What is documented belongs to conventional stimulation: motor improvement does not reliably translate into improved family functioning, personality and mood changes are subjectively reported after surgery, and caregiver burden in Parkinson's disease tracks non-motor and neuropsychiatric features more closely than motor scores [29,30,31,32,33,34]. If adaptive stimulation reduces fluctuation and the unpredictability that comes with it, the effect on the household could be larger than the effect on the rating scale. That is a hypothesis, and no trial reviewed here has tested it.

Claim	Evidence status	Basis
Improves motor score vs cDBS	Demonstrated in small crossover studies	8 patients acute [15]; 4 patients chronic [21]
Delivers less stimulation	Well supported	56% less stimulation time; ~45% time on [15,16]
Benefit is from timing, not less current	Supported	Outperformed random intermittent stimulation [15]
Reduces speech side effects	Single acute study	Not replicated over months [20]
Beta is the right control signal	Contested	Beta falls with voluntary movement; gamma used instead [12,21,22]
Reduces caregiver burden	Untested	No adaptive study reports it [31,32]
Improves long-term outcomes	Untested	Longest randomised exposure is one month per arm [21]

Table 2: Claims made for adaptive stimulation and the current evidential status of each

Discussion

The rationale for adaptive stimulation is the strongest part of the case. A disease that fluctuates within the hour is being treated by a device that does not, and the cost of that mismatch is visible at both ends of every medication cycle. A system that reads the patient's state and responds to it addresses a real defect rather than an imagined one, and the physiological groundwork linking subthalamic beta activity to motor impairment was laid well before the engineering [9,10,11].

The results are also consistent. Every comparison reviewed here favoured adaptive over conventional stimulation, on motor scores, on stimulation burden, and in the one study that examined it, on speech [15,16,20,21]. Consistency across independent groups using different control signals is worth something.

What has to be said plainly is how little evidence this is. The founding study randomised eight patients in acute clinic testing. The most recent and most rigorous trial randomised four, all male, and describes itself as a feasibility trial [15,21]. By comparison, the trials that established conventional stimulation enrolled 156 and 251 patients [1,3]. The entire randomised comparison of adaptive against conventional stimulation involves roughly a dozen patients. Effect sizes derived from a dozen patients, in crossover designs where each patient is their own control and the assessment window is measured in hours to weeks, should be treated as evidence that the approach is worth testing properly, not as estimates of what it will deliver.

Two specific uncertainties deserve naming. The first is the control signal. Beta power was the founding biomarker and remains the most studied, yet it declines physiologically during voluntary movement, so a beta-driven system risks reducing stimulation exactly when the patient attempts to act [12,22]. The most recent trial abandoned beta for gamma, and did so on a per-patient basis, which is a substantial conceptual departure and means the two principal studies are not testing the same intervention [21]. The second is durability. Fluctuation patterns, medication and the disease itself change over years, and the longest randomised adaptive exposure reported is one month per condition.

Study limitations

The limitations belong to the underlying literature and are unusually severe. Sample sizes are single digit throughout [15,21]. The most recent trial enrolled only men, so nothing can be said about sex differences [21]. Testing periods range from hours to one month, against a therapy patients live with for a decade or more [17,21]. Crossover designs limit carryover assessment and cannot detect slow adaptation. Patients enrolled were already established on optimised conventional stimulation, so the comparison is adaptive against well-managed conventional care in patients who tolerated surgery, not against the general population offered stimulation. Blinding of the patient is imperfect when stimulation cycles perceptibly. Control signals and algorithms differ between studies to the point where pooling would be inappropriate [12,13,14]. And outcome measures are almost entirely clinician-rated motor scales, with speech examined acutely in one study and caregiver-relevant outcomes not examined at all [20,31].

Conclusion

Adaptive deep brain stimulation addresses a genuine defect in an established therapy: a fluctuating disease treated at a fixed setting. In the studies published so far it improved motor scores by roughly a quarter more than conventional stimulation while delivering around half as much current, and it appeared to spare speech in acute testing. Those findings come from eight patients and then four. The honest position is that the physiology is convincing, the early signals point the same way, and the randomised evidence is not yet sufficient to tell a patient what to expect. What the field needs is not another biomarker but a trial large enough, and long enough, to measure whether fewer fluctuating hours translates into a better life for the patient and for whoever lives with them.

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Conflict of Interest

The authors declare no competing interests.

Ethics Statement

This article reviews previously published studies only. No new patient data were collected and no participants were recruited, so ethical approval was not required.

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