Surgical management of camptocormia in Parkinson’s disease: systematic review and meta-analysis

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OBJECTIVE Camptocormia is a potentially debilitating condition in the progression of Parkinson’s disease (PD). It is described as an abnormal forward flexion while standing that resolves when lying supine. Although the condition is relatively common, the underlying pathophysiology and optimal treatment strategy are unclear. In this study, the authors systematically reviewed the current surgical management strategies for camptocormia.

METHODS PubMed was queried for primary studies involving surgical intervention for camptocormia in PD patients. Studies were excluded if they described nonsurgical interventions, provided only descriptive data, or were case reports. Secondly, data from studies describing deep brain stimulation (DBS) to the subthalamic nuclei were extracted for potential meta-analysis. Variables showing correlation to improvement in sagittal plane bending angle (i.e., the vertical angle caused by excessive kyphosis) were subjected to formal meta-analysis.

RESULTS The query resulted in 9 studies detailing treatment of camptocormia: 1 study described repetitive trans-spinal magnetic stimulation (rTSMS), 7 studies described DBS, and 1 study described deformity surgery. Five studies were included for meta-analysis. The total number of patients was 66. The percentage of patients with over 50% decrease in sagittal plane imbalance with DBS was 36.4%. A duration of camptocormia of 2 years or less was predictive of better outcomes (OR 4.15).

CONCLUSIONS Surgical options include transient, external spinal stimulation; DBS targeting the subthalamic nuclei; and spinal deformity surgery. Benefit from DBS stimulation was inconsistent. Spine surgery corrected spinal imbalance but was associated with a high complication rate.

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KEYWORDS sagittal bending; camptocormia; deep brain stimulation; repetitive trans-spinal magnetic stimulation; spine surgery; functional neurosurgery

Camptocormia, an abnormal uncontrollable forward flexion of the spine while standing or walking that corrects while lying flat, is relatively common in patients with Parkinson’s disease (PD). The incidence of camptocormia in PD is approximately 6.9%.16,47 Camptocormia is often debilitating and can result in the inability to ambulate or perform activities of daily living.89 Nonsurgical treatments include plaster corsets, levodopa, and botulinum neurotoxin or lidocaine injections, though the efficacy of these methods is unclear and outcomes can vary widely between patients.45 Although medical therapy is considered first-line therapy for camptocormia in PD, many cases of camptocormia are ultimately refractory to medications alone.47 For well-selected patients with camptocormia that is not adequately controlled by conservative management strategies, surgery may be indicated. Repetitive trans-spinal magnetic stimulation (rTSMS), deep brain stimulation (DBS), and spinal deformity surgery are surgical options, although the optimal intervention remains unclear.

To this end, we systematically reviewed the available

ABBREVIATIONS DBS = deep brain stimulation; GPi = globus pallidus interna; PD = Parkinson’s disease; rTSMS = repetitive trans-spinal magnetic stimulation; STN = subthalamic nucleus.

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surgical options for camptocormia in PD patients and associated outcomes. As a secondary aim, we conducted a meta-analysis of DBS treatment in PD patients with camptocormia to investigate potential predictors of successful outcomes.

**Methods**

**Systematic Review**

We searched PubMed with the following search terms: “Parkinson’s disease” and “camptocormia” in October 2017 (Fig. 1). Filters were used to include only articles involving human subjects and written in English. References of reviewed studies were examined for potential additional studies. The query resulted in 107 articles. Articles were excluded if they met any of the following criteria: 1) case report (in attempt to minimize publication bias, though some case reports were included as examples in the discussion); 2) review; 3) the article was not relevant; 4) the intervention was nonsurgical. Potential study biases were assessed and described when appropriate. Level of evidence was assessed for each study and criteria were based on previous methodology. Level of evidence was determined by the following criteria: 1) Level 1, randomized controlled trials; 2) Level 2, prospective observational or case-controlled studies; 3) Level 3, retrospective studies; 4) Level 4, case reports or series (< 10 patients). The literature search and study design adhered to preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines.

**Meta-Analysis of DBS Outcomes**

Studies describing only DBS therapy targeting the subthalamic nuclei from the systematic review were included in the meta-analysis if they met the following criteria: 1) minimum 6-month average follow-up; 2) clear quantitative sagittal bending angle measurements before and after DBS unit implantation; 3) studied 4 patients at minimum; 4) DBS was the only surgical intervention. Studies of DBS targeting the globus pallidus interna (GPI) were excluded to minimize confounding. Multiple variables, including age, sex, PD duration, camptocormia duration, and preoperative and postoperative sagittal bending angles, were collected.

**Data Collection**

The primary outcome measure was change in sagittal plane bending angle, which was dichotomized into either 1) a decrease of ≤ 15° versus > 15° or 2) a decrease of ≤ 50% versus > 50%. The following variables were collected if they could be unambiguously associated with a change in sagittal bending angle: age, sex, PD duration, camptocormia duration, and baseline sagittal plane bending angle. Variables were dichotomized for meta-analysis to look for possible predictors of outcomes, which is methodology similar to that used in past studies. Age and PD duration were dichotomized into ≤ 60 or > 60 years old and ≤ 10 or > 10 years, respectively, because the values were approximately characteristic of PD patients who developed camptocormia. Camptocormia duration was dichotomized into ≤ 2 or > 2 years because outcomes have been mixed for PD patients undergoing DBS if their duration of camptocormia was over 2 years. There was insufficient data to collect appropriate complication rates.

**Statistical Analysis**

Sagittal plane bending angle changes were dichotomized (i.e., ≤ 15° vs > 15°; ≤ 50% reduction vs > 50% reduction) and stratified by each variable via preliminary statistical analysis, which helped to identify variables potentially associated with outcomes. Measurements were done via either standing films or lateral photos. Student t-tests and chi-square tests were used to evaluate continuous and categorical data, respectively. Factors demonstrating a potential association with sagittal plane bending angle changes (i.e., a significance level of p < 0.05) after preliminary analysis were subjected to formal meta-analysis. Cochran’s Q and I² tests evaluated for study heterogeneity to determine whether a fixed or random effects model was appropriate. Mantel-Haenszel tests calculated odds ratios and 95% confidence intervals. Potential bias was assessed by visualizing odds ratio funnel plot asymmetry. Wizard Pro 1.8.28 was used for preliminary statistical analysis and Review Manager v5.3 (Nordic Cochrane Centre, Rigshospitalet, 2008) was used for meta-analysis.

**Results**

A total of 96 studies were excluded (5 based on the title; 54 based on review of the abstract; and 39 based on full-text review), yielding 9 included studies (Table 1): 1 of these studies described trans-spinal magnetic stimulation; 7 studies described DBS implantation targeting the subthalamic nucleus (STN); and 1 study described deformity surgery.

**DBS Meta-Analysis Results**

Five studies were included for meta-analysis. Two of the studies listed in Table 1 were excluded. There were no asymmetrical funnel plots. The prelimi-
nary data are summarized in Table 2. The total number of patients included was 66. The percentage of patients who had over a 15° absolute decrease in sagittal plane bending angle was 51.5% (34/66). The percentage of patients who had over a 50% decrease in sagittal plane bending angle was 36.4% (24/66). The mean sagittal plane bending angles prior to and following DBS surgery were 56.6° ± 5.1° and 38.4° ± 6.6° respectively. The mean sagittal plane bending angle change following DBS treatment was -18° ± 6.1°. Shorter camptocormia duration (i.e., ≤ 2 years) was predictive of a greater than 15° decrease in sagittal bend ing angle following bilateral STN DBS (OR 4.15, 95% CI 1.41–12.18, p = 0.01). Shorter camptocormia duration (i.e., ≤ 2 years) and younger age (i.e., ≤ 60 years) did not predict a 50% decrease in sagittal plane bending angle (Fig. 2).

Discussion

Here the current evidence for outcomes of surgical treatment in PD patients with camptocormia is reviewed and summarized, including the present meta-analysis for DBS treatment targeting the STN.

Characteristics of Camptocormia

Camptocormia is a postural deformity defined as severe forward flexion of the thoracolumbar spine that is

TABLE 1. Summary of studies describing surgical intervention for camptocormia in patients with PD

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Cases</th>
<th>Study Type</th>
<th>Evidence Level</th>
<th>Intervention</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arii et al., 2014</td>
<td>37</td>
<td>Randomized sham controlled trial</td>
<td>1</td>
<td>Single trial of rTMS</td>
<td>Transient avg decrease of 10.9° in treatment group (no significant decrease in sham group)</td>
</tr>
<tr>
<td>Asahi et al., 2011</td>
<td>4</td>
<td>Case series</td>
<td>4</td>
<td>Bilat DBS (STN)</td>
<td>75% of pts improved SB forward flexion by ≥12°</td>
</tr>
<tr>
<td>Capelle et al., 2011</td>
<td>3</td>
<td>Case series</td>
<td>4</td>
<td>Bilat DBS (STN)</td>
<td>All 3 pts improved by mean of 19% BFM subscore for trunk</td>
</tr>
<tr>
<td>Sakai et al., 2017</td>
<td>14</td>
<td>Retro obs cohort</td>
<td>3</td>
<td>Bilat DBS (STN)</td>
<td>6 of 14 pts had ≥50% reduction in SB angle following DBS surgery</td>
</tr>
<tr>
<td>Sako et al., 2009</td>
<td>6</td>
<td>Case series</td>
<td>4</td>
<td>Bilat DBS (STN)</td>
<td>Mean preop SB angle decreased by 78% after surgery (≥5 mos follow-up)</td>
</tr>
<tr>
<td>Schulz-Schaeffer et al., 2015</td>
<td>25</td>
<td>Retro obs cohort</td>
<td>3</td>
<td>Bilat DBS (STN)</td>
<td>13 of 25 (52%) pts had improvement of SB angle by ≥50% (≥6 mos follow-up)</td>
</tr>
<tr>
<td>Umemura et al., 2010</td>
<td>8</td>
<td>Case series</td>
<td>4</td>
<td>Bilat DBS (STN)</td>
<td>4 of 8 pts improved short term; 5 of 8 pts improved long term</td>
</tr>
<tr>
<td>Yamada et al., 2015</td>
<td>17</td>
<td>Prosp trial</td>
<td>2</td>
<td>Bilat DBS (STN)</td>
<td>Avg preop SB angle decreased significantly at 3 mos follow-up (~40.7%) &amp; last follow up (~34.8%)</td>
</tr>
<tr>
<td>Wadia et al., 2011</td>
<td>2</td>
<td>Case series</td>
<td>4</td>
<td>Spinal fixation</td>
<td>Subjective improvement of back pain following T3 to pelvis fixation w/ or w/o osteotomy at last follow-up</td>
</tr>
</tbody>
</table>

Avg = average; BFM = Burke-Fahn-Marsden; obs = observational; prosp = prospective; pts = patients; retrosp = retrospective; SB = sagittal bending.

TABLE 2. Summary of preliminary data results

| Variable | SBA Absolute Decrease | | | SBA % Reduction | | |
|-----------|------------------------|-----------------|-----------------|-----------------|-----------------|
|           | ≤15°                   | >15°            | p Value         | ≤ 50%           | > 50%           | p Value         |
| Age, mean ± SD | 65.2 ± 3.3 | 61.7 ± 4.1 | 0.192 | 66.0 ± 2.4 | 56.8 ± 5.8 | <0.001* |
| Sex | | | | | | |
| Male | 18 | 22 | 0.482 | 25 | 15 | 0.812 |
| Female | 14 | 12 | | 17 | 9 | |
| PD duration | | | | | | |
| ≤10 yrs | 7 | 10 | 0.484 | 8 | 9 | 0.099 |
| >10 yrs | 25 | 24 | | 34 | 15 | |
| Camptocormia duration | | | | | | |
| ≤2 yrs | 6 | 16 | <0.002* | 10 | 12 | 0.002* |
| >2 yrs | 26 | 12 | | 32 | 6 | |
| Baseline TL angle | | | | | | |
| ≤45° | 15 | 13 | 0.478 | 17 | 11 | 0.672 |
| >45° | 17 | 21 | | 25 | 13 | |

TL = thoracolumbar.
Change in sagittal plane bending angle (SBA) was dichotomized two ways: 1) absolute decrease of ≤ 15° versus > 15° or 2) percentage decrease of ≤ 50% versus > 50%. Data are presented as numbers of patients unless otherwise indicated.

* Statistical significance, leading to subsequent meta-analysis.
apparent during ambulation and improves in the supine position.\textsuperscript{9} There is no universal quantitative threshold to establish a diagnosis of camptocormia, but a widely accepted value is a sagittal plane bending angle greater than roughly 45\textdegree\textsuperscript{9,15} while standing. The deformity generally develops within 10 years of PD onset and responds poorly to levodopa treatment.\textsuperscript{9,15} The development of camptocormia is more likely in PD patients with advanced disease progression, more severe motor symptoms, and relatively high levodopa dose requirements.\textsuperscript{41,47}

The pathogenesis of camptocormia is unclear but considered to be multifactorial, with various mechanisms contributing to the overall condition.\textsuperscript{22,49} Although spinal surgery has been attempted to treat camptocormia, primary spinal deformity (rigid kyphoscoliosis) is likely not a primary driver of the condition, as the characteristic flexion disappears in the supine position\textsuperscript{26} and thus we do not recommend spinal surgery as an initial treatment.\textsuperscript{22} Camptocormia could be related to dopamine depletion as well, considering that levodopa medication can produce a mild improvement in camptocormia in some PD patients.\textsuperscript{12} However, levodopa has only had inconsistent results in patients with PD and camptocormia\textsuperscript{12} and thus low dopamine levels cannot be the only factor involved.

**DBS Targeting the Subthalamic Nuclei**

The most common form of surgical therapy used for treating camptocormia in PD patients is bilateral STN DBS. DBS is effective in treating motor symptoms in PD patients,\textsuperscript{31} though improvements in postoperative quality of life have only been shown in patients who are younger than 65 years.\textsuperscript{13} STN DBS may also reverse cognitive decline in PD patients,\textsuperscript{18,43} making DBS an important treatment option for patients whose symptoms are not adequately controlled by noninvasive therapy. The implantation procedure was traditionally done while the patient was awake, but “asleep” DBS surgery (i.e., surgery done under general anesthesia using intraoperative imaging) has been shown to be effective.\textsuperscript{28,32} How STN DBS works is still unclear,
but the prevailing hypothesis is that stimulation interferes with neuronal circuits and inhibits the production or release of neurotransmitters or hormones.8

Recently, there has been more evidence for using STN DBS to treat camptocormia secondary to PD.12 For example, a study of 14 PD patients showed that 42.9%—slightly under half—had at least 50% improvement in their sagittal plane bending after DBS stimulation.8 In contrast, 35.7% of the patients had no change in sagittal plane bending angle following surgery. Another study of 8 patients showed improvement in only 50% in the short term and 62.5% in the long term, although the exact postoperative time course was unclear.48 Though STN DBS is widely used for treating PD, there have been no established predictors of success for PD-associated camptocormia. A systematic review of studies describing patients undergoing DBS for the treatment of PD-related camptocormia found that 68% of patients (n = 32) showed significant improvement following DBS surgery.12 The authors concluded that DBS showed benefits but that the role of DBS and the optimal timing of surgery after the onset of camptocormia were unclear. Our analysis reveals that duration of camptocormia may be inversely related to the efficacy of STN DBS stimulation. Specifically, PD patients receiving STN DBS within 2 years of the onset of camptocormia had increased odds of achieving at least a 15° improvement in their sagittal plane bending angle as compared to patients with longer disease duration.

**DBS Targeting the GPi**

The globus pallidus was a target initially described for primary dystonia21 but has also been more recently been used to treat camptocormia.20,27,30 The GPi has been shown to be an appropriate target for DBS in PD patients to improve motor function. A randomized double-blind controlled trial showed that patients had significant improvement in motor function with either STN or pallidial stimulation, with low complication rates.31 A second randomized controlled trial demonstrated that there was no difference between STN and pallidial stimulation in terms of improved motor function for PD patients.19 It is posited that potential abnormal asynchronous activity in the globus pallidus medialis disrupts normal posturing via involuntary truncal flexion;30 stimulating the GPi is thought to resolve this activity and restore physiological posturing. Supporting this theory, an initial case report demonstrated markedly improved camptocormia in a 49-year-old woman following right pallidotomy.42 Further evidence is a case study describing 2 nonambulatory patients with dystonic camptocormia who underwent GPi DBS that allowed them to regain the ability to walk.20 However, evidence for GPi DBS in camptocormia is still scarce.

Although GPi DBS can have some efficacy in improving camptocormia secondary to dystonia, the evidence has been limited to mostly case reports for treatment of PD-related camptocormia.27,30,48 One case report described a 57-year-old PD patient who developed severe camptocormia and was successfully treated with high-frequency bilateral GPi DBS.48 Her camptocormia did not improve after optimization of her medications and thus she underwent asleep DBS unit implantation, which resulted in placement of the leads in the ventrodorsal GPi. Her camptocormia was substantially improved at 2 months and completely resolved at 1 year. Another case involved a 62-year-old PD patient with drug-resistant severe camptocormia that responded well to bilateral pallidal stimulation.27 At 14 months following the implantation, his camptocormia had almost completely resolved. Both of these examples described favorable outcomes, but case reports are subject to publication biases and are classified as providing a low level of evidence. Larger, prospective studies are required to determine the efficacy of GPi DBS in camptocormia secondary to PD.

**Repetitive Trans-Spinal Magnetic Stimulation**

Repetitive trans-spinal magnetic stimulation (rTSMS) may have a role in improving PD-associated camptocormia.1 A randomized placebo-controlled study showed that a single trial of rTSMS resulted in a transient decrease of thoracolumbar spinal flexion angle.2 Patients were randomly assigned to either a stimulation group (n = 19) or a sham treatment group (n = 18); the 2 groups had average angle decreases of 10.9° and −0.1° (an increase of 0.1°), respectively. The authors speculated that the effect of rTSMS was possibly due to a blockade of afferent sensory nerve fibers or disruption of akinetic corticostriatal activity. There are important limitations of this study. First, patients with sham stimulation did not experience the twitch sensation in their paraspinal muscles as did those undergoing rTSMS. Second, the sample size was relatively small. Last, results were transient.

**Predictors of Greater Improvement in Sagittal Plane Bending Angle Following DBS Surgery**

The results from our meta-analysis showed that a shorter camptocormia duration before DBS unit implantation was a significant predictor of a greater postoperative decrease in sagittal bending angle. A study showed that the duration of camptocormia may predict the efficacy of DBS.39 The study investigated 25 PD patients with camptocormia and found that 13 patients had at least a 50% decrease in their sagittal bending angle. Analysis showed that patients with shorter camptocormia duration (e.g., 1.5 years) were more likely than those with longer duration to benefit from DBS. We found a similar result in that camptocormia duration of 2 years or less was predictive of a decreased postoperative sagittal plane bending angle of at least 15° but camptocormia duration was not predictive of whether patients had at least a 50% decrease in sagittal plane bending.

**Spinal Deformity Surgery**

Evidence is limited with respect to spinal surgery for camptocormia correction. There are a few case reports and short series in the literature.33,49,50 Peek et al. described a 55-year-old man who had sagittal plane bending of 45° at the hip that resolved after lying supine.33 The patient initially underwent a T7-to-ilium posterior fixation that required a revision with multiple parallel rods and crosslinks when the posterior fixation rod disconnected from the iliac screw. He presented a few months later with loosening of
the L5 pedicle screw, which ultimately required a 2-stage revision with multiple interbody fusions. However, the long-term result was favorable, as the physiological sagittal plane bending angle was restored at 1 year after his last operation. The authors suggest that camptocormia can be treated via spinal fixation, but given the potential surgical risks, it may be considered only in the case that DBS and nonsurgical options have failed and the patient has the strong desire to remain ambulatory. Patients should be cautioned that the reoperation rate and complication rate are high.

Spinal fusion surgery for PD patients could be generally unfavorable due to high rates of complications.\textsuperscript{6,7,25,38} A retrospective review of 14 PD patients who underwent spine surgery showed that 12 of them required multiple operations (mean 2.6, range 1–11) and had a high rate of complications.\textsuperscript{6} Furthermore, DBS has been shown to be relatively effective for camptocormia, with low rates of morbidity,\textsuperscript{12} which is why patients and surgeons may opt against spinal fusion surgery as a first option. Indeed, a proposed algorithm for treating PD patients with camptocormia indicated that spinal surgery should be avoided completely if the patient does not have myelopathy or radiculopathy.\textsuperscript{39} However, DBS may fail to correct camptocormia (Fig. 3) and spinal surgery may be one of the few remaining treatment options. Moreover, the present study’s results showed that the longer duration of camptocormia resulted in lower efficacy of DBS for restoring physiological sagittal balance, and thus spinal fusion surgery may be the only remaining option for patients who have had camptocormia for long durations. Further research comparing the efficacy of DBS versus spinal fusion surgery in patients with longstanding camptocormia is necessary to clarify this hypothesis.

**Study Limitations**

There are a number of limitations to this study. First, only a small number of studies met the predetermined criteria. Moreover, the small number of studies used for meta-analysis—the secondary aim of this study—resulted in a small sample size, which likely lowered statistical power and increased the potential margin for error. However, we would expect a negative rather than positive result with a small sample size; thus our finding is likely still valid. Further meta-analyses will be required after more high-quality investigations are conducted. This may help to identify additional factors that portend better outcomes. Second, studies used different methods for measuring the sagittal bending angle; however, potential confounding should have been minimal since the comparisons were made between pre- and postoperative angles rather than between study comparisons. Future work may adopt widely accepted, valid, and reliable measurements to aid in across-study comparisons, such as the Schwab SRS (Scoliosis Research Society) classification system.\textsuperscript{40} Third, there are inherent limitations to meta-analysis, especially in neurosurgery.\textsuperscript{41} For example, only published data were available for analysis, and thus the results may be skewed toward more positive results (i.e., publication bias). Still, the funnel plots of odds ratios investigating bias did not reveal asymmetry, reducing the risk of this confounding effect, and the PRISMA guidelines for meta-analyses were followed. Fourth, the majority of studies found in our review did not meet the criteria for level 1 or 2 evidence. Additional high-quality studies investigating surgical options for camptocormia are necessary.

**Conclusions**

We systematically reviewed the existing literature on surgical treatment in camptocormia. The surgical options include rTSMS, STN DBS, or GPi DBS, and spinal deformity corrective surgery. In general, STN DBS therapy worked for some patients but was inconsistent in terms of benefit. A meta-analysis of available data found that a camptocormia duration of 2 years or less was predictive of a larger decrease in sagittal plane bending following STN DBS therapy. Evidence for GPi DBS is limited to case reports and should be interpreted using appropriate clinical judgment. Furthermore, evidence for spinal fusion surgery to correct sagittal imbalance due to camptocormia was limited, but spinal fusion was associated with a high complication rate in this population. Future directions for possible data collection include the use of large, prospective registries like the Quality Outcomes Database (QOD)—especially with coordination among centers that have both high-volume PD DBS and spinal deformity surgery practice settings—to facilitate larger scale studies and identification of more accurate predictors of outcomes for patients suffering from camptocormia.

**References**


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Author Contributions
Conception and design: AK Chan, Mummaneni. Acquisition of data: AK Chan, AY Chan. Analysis and interpretation of data: AK Chan, AY Chan, Mummaneni. Drafting the article: all authors. Critically revising the article: all authors. Reviewed submitted version of manuscript: AK Chan, Lau, Durcanova, Miller, Larson, Starr, Mummaneni. Approved the final version of the manuscript on behalf of all authors: AK Chan. Statistical analysis: AK Chan, AY Chan, Mummaneni. Administrative/technical/material support: Miller. Study supervision: Mummaneni.

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