



## REVIEW

# Electroconvulsive Therapy Intervention for Parkinson's Disease

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## ABSTRACT

**Background:** Electroconvulsive therapy is an established means to improve function in a variety of psychiatric and neurologic conditions, particularly for patients who remain treatment-refractory. Parkinson's disease is a neurodegenerative disorder that sometimes does not respond well to conventional pharmacotherapies. Reports have indicated that electroconvulsive therapy may be an effective and safe treatment for those patients with Parkinson's disease who are not optimally responding to first-line treatments. Despite these reports, however, electroconvulsive therapy is not often used by clinicians in patients with treatment-resistant Parkinson's disease, perhaps due to stigma, lack of knowledge regarding its safety and efficacy, and/or inability to predict the duration of therapeutic benefit.

**Objective:** Our objective was to determine if the available literature on ECT supports it as a safe and effective treatment option in patients with treatment-refractory Parkinson's disease.

**Conclusion:** Motoric improvement induced by electroconvulsive therapy has been documented for decades in persons with Parkinson's disease. Efficacy

and safety are reported following electroconvulsive therapy in people with Parkinson's disease who have sub-optimal response to medicines or experience the "on/off" phenomenon to L-dopa. Electroconvulsive therapy is an effective option for acute and maintenance treatment of Parkinson's disease in select patients. Inability to predict how long the beneficial effects of ECT therapy will last in patients with Parkinson's disease may be a reason why this treatment is underutilized by clinicians. More research is warranted to clarify parameters for application and duration of therapeutic benefit in individuals with difficult-to-treat Parkinson's disease.

## INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by a loss of dopaminergic cells in the substantia nigra and other pigmented nuclei.<sup>1</sup> PD affects one percent of the population over 60 years of age.<sup>2</sup> The loss of dopaminergic neurons causes the debilitating symptoms of bradykinesia, cogwheel rigidity, immobility, and resting tremor. Comorbid psychiatric illnesses are common in people with PD.<sup>9</sup> Rates of depression in patients with PD vary

from 20 to 90 percent, anxiety ranges from 28 to 40 percent, and dementia is reported at 30 percent.<sup>3</sup>

Pharmacotherapy is the most conventional treatment for PD. Medical management includes L-dopa, dopamine agonists, anticholinergic drugs, and other medications, many of which can yield psychiatric side effects. Many PD patients eventually develop suboptimal response to pharmacological treatment due to reduced sensitivity of postsynaptic dopaminergic receptors or intolerable side effects, including the debilitating “on/off” phenomenon, a condition in which the effectiveness of L-dopa (used to control severe symptoms of PD) wears off before the next dose is due.<sup>4</sup>

If pharmaceutical management fails or proves suboptimal, surgical techniques, such as deep brain stimulation and pallidotomy, may be considered.<sup>5</sup> Both techniques have been shown to be effective treatments for motor symptoms and dyskinesia in select patients;<sup>5</sup> however, cost and invasiveness of the procedures may be deterrents for their use in some patients. Other therapy options for treatment of motor symptoms in PD are electroconvulsive therapy (ECT) and transcranial magnetic stimulation (TMS), both of which have documented efficacy in people with PD.<sup>5</sup> However, ECT is rarely utilized in such interventions, perhaps due to stigma, lack of knowledge, or inability to predict the duration of therapeutic benefit.

In this article, we review the literature on the use of ECT in PD. We examined review articles, case reports, clinical studies, and meta-analyses in our review. Our objective was to determine if the available literature adequately supports the use of ECT as a safe and effective treatment option for patients with treatment-refractory PD.

## **ECT BACKGROUND**

ECT was developed in the 1930s as a treatment for people with psychiatric illness.<sup>6</sup> It has since become a well-established

intervention for treatment-resistant mood disorders.<sup>7</sup> The American Psychiatric Association recommends the use of ECT in cases of treatment-resistant depression and mania and for positive symptoms of schizophrenia.<sup>8</sup> While the literature on ECT focuses mainly on its use in patients with treatment-resistant mood disorders, other conditions such as neuroleptic malignant syndrome, status epilepticus, and PD may also respond ECT.<sup>9</sup> ECT administration for PD has been shown to be especially effective at improving motor symptoms.<sup>10-13</sup>

Cumper et al<sup>14</sup> report that motoric improvement in patients with PD following administration of ECT has been documented as early as 1959. The efficacy and safety of ECT for ameliorating motor deficits in idiopathic PD and drug-induced parkinsonism are also documented, as well as in those patients with PD who do not respond to medical intervention or experience on/off phenomenon.<sup>14</sup>

## **MECHANISM OF ACTION**

According to a review by Kennedy et al<sup>7</sup> on use of ECT in movement disorders, ECT-induced improvement of motor symptoms in PD may be due to a resolution of comorbid depression. Yet this same review of research reveals that a substantial number of individuals with no comorbid psychiatric illness still evidence improvement in motor symptoms following ECT treatment. The hypothesized mechanism of action for ECT is neurochemical, in that it is believed to enhance dopaminergic transmission.<sup>15</sup> In a review of animal and human studies, Fotchman<sup>15</sup> found that ECT did not cause a rise in serum or cerebrospinal fluid dopamine metabolite levels, so there may be an enhancement at the receptor or post-receptor level. It appears that ECT also increases dopamine type 1 receptor binding in the substantia nigra.<sup>15</sup>

Animal research reveals up-regulation of gamma-aminobutyric acid systems following ECT.<sup>16-19</sup> This

might still have a therapeutic role because the effects of ECT on dopamine are postsynaptic and could enhance medical management. Patients with PD who have failed medical management appear to be unresponsive to dopaminergic therapy due to decreased sensitivity of postsynaptic dopaminergic receptors; ECT enhances the sensitivity of these receptors.<sup>14</sup> Older age and advanced stage PD have been shown to be predictors for an optimal response to ECT.<sup>4</sup>

## **EFFECTIVENESS IN PD**

Effectiveness of ECT in PD has been documented since 1947.<sup>2,3,20,21</sup> By 1999, there were at least 47 articles published on this topic, including cases of people who did not have comorbid psychiatric illnesses.<sup>19</sup> A 2008 review of the literature by Wilkins et al<sup>9</sup> indicates that most reports to date evidence positive effects of ECT on motor symptoms in PD. In a double-blind, controlled study of ECT for treating PD motor symptoms, Anderson et al<sup>22</sup> investigated 11 patients with PD who were resistant to conventional treatment, were without psychiatric illness, and who experienced on-off phenomenon. Six subjects were given sham ECT treatment and five were administered ECT. Statistically significant prolongation of “on” periods of levodopa and improvement of motor symptoms were reported, as compared to a control group.<sup>22</sup>

Although there is a paucity of randomized, controlled trials and double-blind studies in the literature, the effectiveness of ECT in controlling motor symptoms of PD is documented in review articles.<sup>7,10</sup> According to Faber and Trimble,<sup>10</sup> who conducted a review of case studies on the use of ECT in PD, out of 75 subjects with PD who did not have coexisting psychiatric disorders, 58 (77%) evidenced improvement in motor symptoms following ECT. Regarding electrode placement (i.e., unilateral ECT vs bilateral ECT), in the cases where these data were reported, 38 of 44 subjects (86%)

who received unilateral ECT demonstrated motor improvement, and 10 of the 11 subjects (91%) who received bilateral ECT experienced motor improvement.<sup>10</sup>

In a review article by Kennedy et al<sup>7</sup> that explored use of ECT for treatment of movement disorders, the authors found 26 cases of documented motor symptom improvement, seven cases that reported less tremor, 12 cases that reported a reduction in “off” time during on/off phenomena, five that reported less rigidity, and one that reported decreased cogwheel rigidity. The authors also note that many of the reports failed to provide detailed clinical assessments; thus, in many of the cases, it is unknown which motor symptoms of PD responded to ECT.<sup>7</sup>

In a 2005 systematic review and meta-analysis by Frengi et al,<sup>5</sup> the authors examined prospective studies that evaluated the effects of either TMS or ECT on motor function in PD. The authors only assessed five studies of ECT in PD patients based on their exclusion criteria. The studies reviewed support a statistically significant improvement following treatment with noninvasive stimulation to improve motor symptoms in PD. The results of the TMS meta-analysis are robust and stable; however, its effect size was moderate. There was a relatively large and significant effect size for the ECT meta-analysis, but the low number of studies is a limiting factor for meaningful conclusions. Also, the small number of investigations included in the meta-analysis limited the ability to assess for heterogeneity and publication bias.<sup>5</sup>

A 2011 study by Usui et al<sup>23</sup> enrolled eight PD subjects with motor symptoms that were measured by the Hoehn and Yahr stage scale. The subjects exhibited significant improvement in the Hoehn and Yahr scores after ECT ( $t=11.7$ ,  $P<0.0001$ ), with scores before ECT being (mean±SD)  $3.9\pm 1.1$  and scores after ECT being  $2.8\pm 1.0$ .

A 2012 pilot study<sup>4</sup> assessed the efficacy of ECT in patients with

advanced stage PD and with symptoms partially unresponsive to L-dopa. It excluded persons with comorbid psychiatric illnesses. The authors found that ECT increased the number of steps ambulated and reduced the number of freezing episodes in the “on” phase of people with late stage PD.<sup>4</sup>

## MAINTENANCE TREATMENT

According to Kennedy et al,<sup>7</sup> there were eight case reports by 2003 that noted the benefit of ECT for long-term maintenance treatment of PD. Of the cases reviewed by the authors, 15 of 213 subjects with PD were receiving ECT for maintenance treatment. Some patients had continued to benefit from improvement of motor symptoms with maintenance, both with and without comorbid affective disorders. Others required progressively shorter intervals between treatments until the frequency of ECT was no longer feasible. Kennedy et al<sup>7</sup> were unable to determine the reason for shortening periods of effectiveness with ECT nor what the optimal interval should be. The authors provided guidelines based on their review of the literature that suggests ECT should be administered once a week with progressive lengthening to reach the longest sustainable interval. However, they note that some people have prolonged symptom-free intervals after one ECT treatment and only require widely spaced treatment intervals.<sup>7</sup>

One patient with late-stage PD who received acute and maintenance ECT over a four-year period experienced long-term symptom improvement.<sup>3</sup> This 76-year-old depressed man with dementia and PD sustained remarkable motor improvement that lasted for 12 weeks following the administration of four ECTs. Over the next four years with symptom return, he required ECT to be administered every few weeks to every other month; good efficacy was achieved. The patient passed away due to complications of his comorbid conditions; however,

the patient’s family firmly believed that ECT extended and greatly improved his life.<sup>3</sup>

## CONCLUSION

Our review of the literature supports the use of ECT as an effective treatment for alleviating refractory motor symptoms in people with PD. However, clinicians who treat PD rarely consider ECT as an acceptable treatment option.<sup>15</sup> Much of the literature supporting its use in patients with PD is in the form of case reports, and there is a tendency for only data with positive results to be published.<sup>7</sup> There has only been one controlled, double-blinded investigation of ECT in patients with PD.<sup>22</sup> In most of the case reports, there is a dearth of a consistent clinical evaluation in symptom changes, making comparison between case studies impossible. In addition, treatment methods differed in electrode placement, number of ECT sessions, and the electrical stimulus parameters, which further limit data comparisons.<sup>4</sup>

Stigma surrounding the use of ECT may be a reason for underutilization by clinicians in patients with PD, as well as a lack of knowledge about the mechanism of action of ECT.<sup>6</sup> Another potential concern clinicians may have is the inability to predict how long the beneficial effects of ECT therapy will last in patients with PD. If studies can show that efficacy is sustained for weeks to months, ECT could become a more accepted mode of treatment for certain patients with PD, including maintenance treatments that are scheduled at intervals tailored to the individual needs. Additional research is needed to clarify ECT parameters for application as well as ways to enhance efficacy for motorically impaired patients with PD.

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