

# Clinical Roundup

## Selected Treatment Options for Parkinson's Disease

### Integrative Therapies

Parkinson's disease (PD) is a neurodegenerative motor disorder affecting 2% of the North American population over 60 years of age.<sup>1</sup> Several processes are hypothesized to be involved in the pathogenesis of PD, including microglial inflammation, oxidative damage, and iron and protein accumulation. Naturopathic therapies offer a variety of options that target multiple processes simultaneously.

Care for patients with PD, at the Integrated Healthcare Centre (IHC), in Toronto, Ontario, Canada, is initiated by assessing them for depression and anxiety. Given that the core of therapy is centered on exercise, compliance is crucial and low mood can be a significant obstacle. The initial treatment includes bright-light therapy, for 30–40 minutes each day at a set time, with the maximal light intensity tolerated by the patient, to improve mood and energy.

A pilot study using 1000–1500 lux of daily bright light therapy for 60–90 minutes for 2 weeks demonstrated reduction in bradykinesia and muscle rigidity.<sup>2</sup> Concurrent weekly scalp electroacupuncture has been shown to result in modest gains in mobility and tremor management, as well as improvements in scoring on the Unified Parkinson's Disease Rating Scale (UPDRS), as demonstrated by Lam et al.<sup>3</sup> Together, these treatments offer enough improvement to regain some of the patient's confidence in his/her physical ability and to initiate a conversation about exercise.

While providing information on some basic exercises that the patient can do at home, the importance of joining a class on *t'ai chi*, Nordic Walking or tango, and/or seeking physiotherapy is emphasized strongly. There is a substantial amount of evidence reporting a very significant impact of various forms of exercise on PD symptoms, progression, and quality of life.<sup>4</sup> Of these studies, *t'ai chi*, Nordic Walking, and Argentinean tango offer diverse options to patients with mild–moderate PD.<sup>5</sup>

*T'ai chi* has been shown to improve balance significantly, which is often difficult to address with other therapies. However, this practice has not been shown to improve gait significantly.<sup>6</sup> Nordic Walking has been shown to increase walking

speed and the ability to stand up from sitting and to make turns.<sup>7</sup> However, this technique often proves challenging to master. Argentinean tango has been shown to improve UPDRS scores, increase walking velocity, reduce bradykinesia and tremor, and improve balance. The ideal regimen includes 1 hour of training, twice a week for 10–52 weeks.<sup>8</sup> Given that the greatest benefit of exercise is achieved through the more-challenging and intense regimens, the patient may require supervision to replicate these safely.

Nutritional and botanical therapies focus on targeting oxidative damage and apoptosis, while reducing adverse effects associated with L-dopa treatments. Preclinical studies have demonstrated antiapoptotic, iron-chelating, and antioxidative effects of a green tea extract, (-)-epigallocatechin-3-gallate (EGCG), in animals with PD.<sup>9</sup> Other preclinical studies with acetyl-L-carnitine and  $\alpha$ -lipoic acid have produced similar results. However, when combining these three antioxidants, clinicians and patients should be aware of the synergistic effects of these compounds, as well as potential drug–herb interactions. One of the long-term adverse effects of levodopa is an increase in serum homocysteine, which has been linked to subsequent loss of bone mineral density in patients with PD. A small clinical trial demonstrated that 1500  $\mu$ g of methylcobalamin supplementation may result in statistically significant preservation of BMD ( $P < 0.05$ ).<sup>10</sup>

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## Integrated Rehabilitation Strategies

Parkinson's disease (PD) is a complex neurodegenerative disorder with wide-reaching implications for patients and their families.<sup>1</sup> The initial clinical signs appear after the degeneration of ~ 60% of the dopaminergic neurons of the substantia nigra.<sup>2</sup> This degeneration produces motor dysfunction that manifests with a tetrad of primary symptoms—resting tremors, bradykinesia, muscular rigidity, and postural instability. Nonmotor symptoms may also occur and precede motor dysfunction by several years.<sup>3</sup> Progressive in nature, PD tends to worsen with time, leading to a general decrease in activity,<sup>4</sup> an increased risk of falling, immobility, and cognitive impairment.<sup>5</sup>

Management of PD has been conventionally centered on drug therapy, with levodopa viewed as the “gold standard” treatment.<sup>6</sup> However, even with optimal medical management, patients with PD experience deterioration in body function and have a reduced ability to participate in daily activities.<sup>7</sup> For this reason, support has been increasing for the inclusion of rehabilitation therapies as adjuvants to pharmacologic and neurosurgical treatment.<sup>7,8</sup> Exercise therapy is the conventional rehabilitative approach for PD; exercises may include aerobic exercises, balance training, and resistance training.<sup>9</sup>

Another rehabilitation approach, Pilates therapy, may also be an alternative therapy. Pilates is a type of exercise therapy that is aimed to improve flexibility and axial stability by strengthening the core musculature of the body. This therapy is based on the performance of coordinated movement sequences rather than on simple repetitive movements, as in other exercise programs.<sup>10,11</sup> The positive effects of Pilates therapy on balance in elderly individuals has been reported.<sup>12,13</sup> Pilates therapy has also been found to be beneficial for postural stability in elderly patients with idiopathic PD.<sup>14</sup> In clinical practice, Pilates therapy can be performed in 30–45-minute sessions, three times per week.

The Alexander Technique (AT), another complementary therapy to treat PD, is a learned method that is believed to change

movement habits in daily or specialized activities. Proponents of AT believe that it helps patients to discover balance in the body and mind by releasing unnecessary muscular tension through a series of learned patterns and postures. AT is usually taught in individual or small group lessons in which the teacher uses many modes of communication including skilled hand contact, talking, visual aids, imitating, modeling, mirrors, and text. With AT, it is possible for an individual with PD to cope with increased muscle tension and to improve his/her quality of life.<sup>15</sup>

Finally, virtual reality (VR), a popular alternative treatment method in the field of neurorehabilitation in recent years, can also be integrated into treatment for patients who have PD. VR is a computerized simulation that allows users to interact with images and virtual objects that appear in the virtual environment in real-time through multiple sensory modalities.<sup>16</sup> VR offers augmented feedback about performance, enables individualized repetitive practice of motor function, and stimulates both motor and cognitive processes simultaneously. This therapy provides a suitable context for learning new motor strategies of movement and relearning motor functions that have become impaired. VR also provides a safe and motivational environment for practice, thus making this therapy a useful tool for intervention in patients with neurodegenerative conditions such as PD.<sup>17</sup>

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## Anma Massage (Japanese Massage) Therapy

*Anma* massage (Japanese massage) therapy (AMT) is the complementary and alternative medicine most commonly used by patients with Parkinson's disease (PD) in Japan,<sup>1,2</sup> and it is reported that 29.8% of neurologists recommend this massage for alleviating rigidity, movement disorders, and pain in these patients.<sup>1</sup>

AMT, which originated from *Do-in* and *Ankyo* in ancient Chinese medicine, was brought from China in the sixth century and later developed into the present clinical approach. *Ankyo* involves meridian-based massage therapy, whereas *Do-in* involves movement therapy with breathing exercises. AMT incorporates whole-body massage with brief joint exercises. The focus of AMT is generally not on meridians, but rather on anatomy—especially muscle anatomy. Standard AMT techniques involve mainly kneading, with lesser amounts of stroking and pressing through clothing using rhythmic massaging motions. Stimulation intensity is adjusted according to each patient's comfort level.

In studies of outpatients with PD (Hoehn and Yahr stages II–IV),<sup>3,4</sup> AMT alleviated severity of subjective symptoms of muscle stiffness, movement difficulties, pain, and fatigue; and improved motor functions of the upper and lower limbs, and range of motion (ROM) of the shoulder joints. Moreover, in a study of 10 patients in nursing homes for elderly people; those who had more severe PD (Hoehn and Yahr stage V),<sup>5</sup> AMT significantly improved ROM of shoulder abduction on both the severely affected and less-severely affected sides of the shoulder joints, which were asymmetrically stiff and resistant to limb movement.

These results suggest that AMT is beneficial not only for patients with PD but also for nursing-care providers; if patients can move their limbs by themselves even if only

slightly, it can help reduce the workload of nursing-care providers. Because AMT is performed over clothing, patients do not need to take off and put on clothing before and after treatment. Thus, AMT is accessible for patients who have PD with movement difficulties.

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## Arm Swing Exercise Therapy Using a Video Monitor

The effects of an arm swing–based home exercise program on gait in Parkinson's disease (PD) patients has been reported.<sup>1</sup> The design of this study was approved by an ethics review board, and informed consent was obtained from all patients. This study suggested that an arm swinging–based home-exercise therapy using a video monitor was effective for helping patients with PD.<sup>1</sup>

In general, gait impairments involving reductions in speed and step length are common in PD. Decreased arm swing is the most frequently observed motor dysfunction, and loss of arm swing is a major predictor of falls in patients with PD.<sup>2,3</sup> Although various types of exercise therapy are used to alleviate these symptoms,<sup>4–7</sup> few studies have assessed arm swing exercises in patients with PD.<sup>1,8</sup>

A study was performed involving 22 outpatients who had Hoehn and Yahr stages II–IV PD. A video DVD was prepared in which a trainer performed an arm swing exercise or steps in synchrony with a metronome at a frequency of 92 and 100 cycles per minute.<sup>1</sup> The training program consisted of four parts: (1) arm swing in the seated position for 3 minutes; (2) arm swing in the upright position without stepping for 3 minutes; (3) arm swing with stepping for 5 minutes; and (4) walking on the floor for 1 minute. Patients with Hoehn and Yahr stages II–III PD performed 100 arm swings per minute, while patients with stage IV PD performed 92 arm swings per minute because these patients tended to fall frequently during walking.

The patients performed the arm swing exercise while watching a video monitor for 12 minutes and walked for 15 minutes every day. After following the program for 3–4 weeks, these patients showed significant improvements in 20-meter walking time (10 meters out, 10 meters back) and step length.

Loss of arm swing in PD may be associated with disturbances in the internal rhythm-formation process. Arm swing exercise is a therapeutic technique that uses rhythmic cues and may improve rhythm formation.

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## Integrated Yoga Therapy Approach

Parkinson's disease (PD) is a complex neurodegenerative disorder of the basal ganglia and brainstem, with both motor and nonmotor symptoms characterized by resting tremors, rigidity, bradykinesia, and postural instability.<sup>1</sup> It is estimated that ~ 7 million people have PD worldwide, affecting all ethnicities and cultures.<sup>2</sup> Onset is usually over age 60, but it is estimated that 1 in 10 people are diagnosed before age 50, with slightly more men than women affected.<sup>2</sup>

A cross-sectional study of 45 patients with PD (mean age = 66.1 years; 33% female) showed that higher levels of physical activity were associated with significantly less fatigue, and there was a trend for less apathy and depression and greater positive affect (experience of feeling or emotion).<sup>3</sup> It was reported that most patients with PD preferred moderate intensity exercise, performed in the morning, and including varied activities.<sup>3</sup> One of the preferred activities was yoga.<sup>3</sup>

Yoga—an ancient science incorporating physical activity, instructed relaxation, and interoception—is emerging as a useful rehabilitation tool for addressing chronic neurologic ailments.<sup>4</sup> Yoga has been shown to decrease oxidative stress,<sup>5</sup> improve neurocognitive function and mood,<sup>6</sup> enhance sensory motor performance,<sup>6</sup> increase dopamine and serotonin secretion,<sup>7</sup> and reduce cortisol secretion.<sup>7</sup> Increased endogenous dopamine release in the ventral striatum during *Yoga Nidra* meditation has also been reported.<sup>8</sup>

Case studies have shown beneficial effects of yoga in PD.<sup>9,10</sup> In one study of a 69-year-old female with PD for 8 years, it was noted that an 8-week period of weekly 60-minute yoga classes resulted in improvement in the scores on Berg Balance Scale and Timed Up and Go (TUG) tests during the intervention phase, and, subjectively, the participant reportedly gained much enjoyment and relaxation from the yoga classes.<sup>9</sup>

Another case study reported use of an integrated yoga program with physical therapy exercise in a male patient with PD.<sup>10</sup> The intense 1½-hour program incorporated strengthening, balance, agility, and yoga exercises twice weekly for 12 weeks. At the end of the program, it was observed that the patient's score on the Parkinson's Disease Questionnaire improved 16 points and his score on the High Level Mobility Assessment tool improved 11 points. There were also improvements in upper- and lower-extremity muscle strength and dynamic balance, and, later, the patient continued to work full time up to 29 months.<sup>10</sup>

The following yogic practices may be useful for managing PD.<sup>11</sup> The program starts with loosening practices (15 minutes), followed by yogic breathing (10 minutes), physical postures (15 minutes), meditation (15 minutes), and finally, relaxation in the corpse posture (5–10 minutes). This makes an integrated yoga module to be practiced for approximately 60 minutes, once daily for 3–5 days weekly, depending on the individual's capacity and comfort. The details of this program are as follows:

- (1) Loosening practices (*Shithilikaranavyāyāma* for approximately 15 minutes):
  - (A) Standing practices—loosening of fingers (*Anguli*

*shakti vikāsaka*), loosening of wrists (*Manibandha shakti vikāsaka*), loosening of elbow (*Kaphoni shakti vikāsaka*), shoulder rotation (*Skandha tathā bāhumula shakti vikāsaka*), and drill walking (*Pādasan-cālana*)

- (B) Sitting practices—neck bending (front and back, side-ways and rotation, *Grivā shakti vikāsaka*), half butterfly (*Ardha titali āsana*), full butterfly (*Purna titali āsana*), and ankle bending (*Gulphashaktivi-kāsaka*)
- (C) Supine practices—straight leg raising (*Padautt-hāsana*)
- (D) Prone practices—locust pose (*Salabhāsana*) breathing and cobra pose (*Bhujangāsana*) breathing
- (2) Breathing practices (*Prānāyāma* for ~ 10 minutes): Hands in and out breathing; ankle stretch breathing; hand stretch breathing; hare breathing (*Shashānkāsana Prānāyāma*); tiger breathing (*Vyaghrāh Prānāyāma*); dog breathing (*Svāna Prānāyāma*); sectional breathing (*Vihhāgiya Prānāyāma*); alternate nostril breathing (*Anuloma Viloma Prānāyāma*); bellow breathing (*Bhas-trikā*); and humming bee breathing (*Bhrāmari*);
- (3) Physical postures (*Āsanas* for a total of ~ 15 minutes):
- (A) Standing *āsanas*—tree pose (*Vrikshāsana*), half waist rotation pose (*Ardhakatichakrāsana*), hand to foot pose (*Pādahastāsana*), eagle pose (*Garudāsana*), and triangle pose (*Trikonāsana*)
- (B) Sitting *āsanas*—twisted pose (*Vakrāsana*) and fish pose (*Ardhamatsyāsana*)
- (C) Prone *āsanas*—cobra pose (*Bhujangāsana*) and locust pose (*Salabhāsana*)
- (D) Supine *āsanas*—upside down seal (*Viparithkarani-āsana*) and wind-releasing pose (*Pavanmukthāsana*).
- (4) Meditations (for ~ 15 minutes): *Om* chanting (*Prānāv-ajapa*), *Sahaja* yoga<sup>6</sup> meditation, *Yoga nidrā*,<sup>8</sup> and Kundalini yoga.<sup>7</sup>
- (5) Guided relaxation: Corpse pose (*Savāsana*)<sup>11</sup> for 5–10 minutes at the end of *āsanas* and *Prānāyāma*.

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## High-Dose Thiamine

In July 2011, Costantini et al. treated a 47 year-old man affected by spinocerebellar ataxia type 2 (*SCA2*) with parenteral high doses of thiamine.<sup>1</sup> In this patient, fatigue as well as motor symptoms were reduced after thiamine administration. Therefore, the hypothesis was formulated that, in some inherited and degenerative diseases of the nervous system, the pathogenesis of the symptoms could be linked to a focal thiamine deficiency caused by a dysfunction of the intracellular transport of thiamine or to structural enzymatic abnormalities. Such a dysfunction could be responsive to high-dose thiamine. Parkinson's disease (PD) has been related to mutations associated with *SCA2*.<sup>2</sup> Some reports have shown trinucleotide repeat expansions in the *SCA2* gene in patients with levodopa-responsive parkinsonism.<sup>2</sup> In addition, a number of factors link thiamine to PD pathology.<sup>3</sup> Recently, a considerable reduction of motor and nonmotor symptoms in patients affected by PD was observed with intramuscular (IM) daily doses of 100–200 mg of thiamine.<sup>3</sup>

Since July 2011, Costantini and colleagues have treated approximately 60 patients who have PD with 100 mg of IM thiamine two times per week. Some of the patients had been newly diagnosed with PD and were not under any therapy regimens.<sup>4</sup> Other patients were in a Hoehn and Yahr stage between 2.50 and 3.00. The latter group of patients were receiving therapy with carbidopa-levodopa- or dopamino-agonists, or with the aforementioned drugs taken together. Within 30 days from the beginning of the thiamine treatment, all patients presented with considerable reduction of all symptoms, in particular, an improvement in scoring on the motor component of the Unified Parkinson's Disease Rating Scale of 30% or more. Some pa-

tients had complete regression of all symptoms; however these findings have not been published.

Injection of high-dose thiamine was effective for reversing motor and nonmotor failures.<sup>5-7</sup> These results suggest that abnormalities in thiamine-dependent processes could be overcome by a diffusion-mediated process at supranormal thiamine concentrations.<sup>5-7</sup>

Although parenteral thiamine has a very high safety profile, the literature reports anecdotal evidence of possible inflammatory reactions or anaphylactic shock and cardiac arrest that may be associated with intravenous administration of thiamine.<sup>8</sup> However, during this and similar studies, collateral effects have not been observed as a consequence of IM administration of high doses of thiamine. ■

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