

Perceiving Parkinson's

Synopsis - Established And Experimental Treatments In Parkinson's (Day 98)

Currently, oral dopaminergic medications, particularly levodopa, are the mainstay of treatment in Parkinson's. Yet there are many other ways to tackle the condition; let's go over them once more.

(1) Cueing Strategies In Parkinson's

The motor symptoms of Parkinson's can be improved using **cueing strategies** that focus conscious attention to a task, thus using pathways that bypass the abnormal basal nuclei. It is possible to "think" your way to improving your motor symptoms, and at the end of the day **you have nothing to lose** by trying. To avoid falls, one cueing strategy should never be forgotten - always feet first!

(2) Mind-Body Interventions In Parkinson's

The mind-body interventions with strong evidence showing that they provide benefits in Parkinson's are **treadmill exercise, aerobic exercise, resistance exercise, dance**, and **Tai Chi**, followed by Lee Silverman Voice Training LOUD, yoga, singing, boxing, BIG therapy, conventional physiotherapy, and Nintendo Wii. Pick two of them and **pursue them with passion**. Most are available in Hamilton. Please contact Parkinson's Community Educator **Janine Mair** to find out more.

(3) Dopaminergic Infusions

After several years, the honeymoon phase with dopaminergic oral medications ends and motor fluctuations and dyskinesias can become a real problem in people with Parkinson's, yet there is still the option of one of the dopaminergic infusions. **Subcutaneous apomorphine** is indicated for people under 70 years of age, with normal cognition, who have disabling motor fluctuations. Subcutaneous apomorphine is available in Hamilton - speak to Parkinson's nurse **Linda Gilbertson** to find out more. **Duodenal levodopa** is indicated for people of any age, with normal cognition or mild or moderate cognitive difficulties, who have disabling motor fluctuations and/or dyskinesias. Duodenal levodopa is not yet available in New Zealand, but with some luck that will change in the next several years.

(4) Deep Brain Stimulation

Deep brain stimulation can be a godsend in Parkinson's - in carefully selected people, it **surpasses** the best medical therapy to date for improving motor symptoms, motor complications, and quality of life. These benefits last for ten years or more, although the Parkinson's still progresses. By far, the most important factor for a successful outcome in deep brain stimulation is **careful patient selection**. The person who will do well with deep brain stimulation has the following characteristics:

- Age no more than 70 years at the time of surgery.
- Presence of medically refractory motor fluctuations, dyskinesias, or tremor.
- Excellent “on” response to levodopa.
- No significant mood disorder or cognitive difficulty.
- No other serious medical condition.

If you would like **more information** about deep brain stimulation in New Zealand, see the link below.

<http://www.parkinsons.org.nz/sites/default/files/page/Publications/DBS.pdf>

(5) Nicotine, Caffeine, And Marijuana Compounds

The scientific evidence for nicotine, caffeine, and marijuana compounds is weak. The best evidence for **nicotine** is a very small observational study showing that transdermal nicotine patches **slightly improved motor symptoms** after 17 weeks. The evidence for **caffeine** is stronger, with one randomized controlled trial showing that caffeine supplements **slightly improved motor symptoms** over six weeks. Even if the benefits of nicotine and caffeine are real, they are small. Regarding **marijuana compounds**, the best evidence to date is an observational study showing **improved motor symptoms** as well as **improved sleep and pain scores** after smoking marijuana. It seems marijuana compounds can produce a great improvement in some people, yet we must recall the 1960s, when levodopa was also a “miracle drug” until its side-effects were discovered years later. Like levodopa, the long-term risks of marijuana compounds may be significant; more research is needed.

(6) Assaulting Alpha-Synuclein

Strategies that assault alpha-synuclein include drugs that **block the intracellular aggregation of alpha-synuclein** (still in the early experimental stages), and **immunotherapy drugs that limit the spread of extracellular alpha-synuclein** (vaccines and antibody infusions). These therapies are all based on the assumption that alpha-synuclein is a “bad guy” in Parkinson’s, an assumption that has never been verified and may be flat-out wrong. If the assumption is correct, these therapies could be the next big thing in Parkinson’s. If the assumption is wrong, these therapies will go nowhere.

(7) The Neurotrophic Factor Saga

Neurotrophic factors are proteins that direct and support the survival, growth, specification, and maturation of various populations of neurons, including the dopaminergic neurons of the substantia nigra that are heavily damaged in Parkinson’s. To date, two dopaminergic neurotrophic factors have been studied in humans - **glial cell line-derived neurotrophic factor (GDNF)** and **neurturin (NRTN)**. Although initial uncontrolled studies suggested that neurotrophic factors might benefit people with Parkinson’s the later randomized controlled studies showed that they provided **no benefit** for people

with Parkinson's. The jury is not out yet, and neurotrophic factors are still tantalizing as a potential treatment for Parkinson's, but they have yet to live up to their initial promise, if they ever do.

(8) Cell Transplant Therapies

There is much excitement over cell transplant therapies in Parkinson's, yet they suffer from two huge problems at the outset. Parkinson's is **a disease of neurons**, including neurons throughout the autonomic and enteric nervous systems, and it **damages non-dopaminergic neurons**, including the ones that store a person's unique memories. Even in theory, cell transplant therapies cannot bypass these two problems. There are more problems, depending on the donor source:

- The ethical issues surrounding **fetal dopaminergic neurons** and **embryonic stem cells** are simply too contentious to ever allow them to be reliable tissue sources.
- **Induced pluripotent stem cells** circumvent the ethical issues, but it is scientifically arrogant to believe that researchers can fully control the fates of stem cells - to control life.
- **Directly induced dopaminergic neurons** may be the most appealing out of all the cell transplant therapies, if clinically effective transplants are ever shown to be feasible in people with Parkinson's.

There are still more cell transplant therapies out there, but **none have shown great promise**. For these reasons and more, we must not wait in hope for cell transplant therapies to solve Parkinson's.

Some of the above therapies are already known to be beneficial for people with Parkinson's, whereas others lack sufficient evidence. This is not to say that the evidence will never come, but **we do need more research** to ascertain whether they will deliver something real or not.

There is one glaring problem with all these therapies, which is that **none of them** really has the capacity to fully tackle the multiple facets of the condition that is Parkinson's:

- Parkinson's is a **disease of neurons** throughout the body.
- It is characterized by a **disturbed gut microbiota**.
- It is characterized by **mitochondria dysfunction**.

There is only one potential therapy that can tackle Parkinson's on all three levels - **diet**. Indeed, diet is the **elephant in Parkinson's**, a very big elephant, an elephant that for various reasons has been neglected far too long.

Diet has been completely **maligned and misunderstood** for centuries. Paradoxically, diet has probably been maligned and misunderstood more in the last few decades than at any other point in history.

We can change that, and we must change that. While many people wait in hope for magical cures that may never happen, the most powerful of all therapies in Parkinson's **may be right in front of us**.

There are many non-believers, and that is fine. However, I am of the firm opinion that determining whether a change in diet can potentially improve or slow down neurodegenerative diseases is **one of the most pressing issues of our time**.

Next week, I shall be emailing those people who met all the inclusion and exclusion criteria for the Waikato Hospital Parkinson's Dietary Study - these folks will be the **real stars**, people who are willing to undergo a significant dietary change for eight weeks to determine whether diet has a role in treating the complex neurodegenerative condition that is Parkinson's.

No matter what happens, we will **provide answers** to this question, which we must.

This is the last article in the Perceiving Parkinson's email series. It has been a **sincere pleasure**, and I hope you have found them informative. We will be posting the entire email series on a website soon, and when we do, I shall email the website address to everyone.

Remember, you have more power to improve your Parkinson's than you may believe. Your greatest weapons are available to you right now, and they always were - **knowledge**, and the **will to act on it**.

Take care,

Matt (Neurologist, Waikato Hospital).