

Parkinson's: symptoms, treatments and research

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Abstract

Parkinson's is a incurable progressive neurological condition caused by a degeneration of dopamine-producing cells. The most common symptoms of the condition include slowness of movement, tremor and muscle stiffness; other symptoms include sleep difficulties, depression and anxiety. Parkinson's is usually controlled by medication but other treatments and therapies, such as occupational therapy, physiotherapy and speech and language therapy, can also be effective in controlling and managing symptoms. The timing of this medication is key to the successful management of Parkinson's. Delays to initiating medication or missed doses can have serious consequences, and it can take some time for symptoms to stabilize.

Research into treatments for Parkinson's and, ultimately, finding a cure for the condition, is ongoing. Parkinson's UK researchers are working on projects to identify the causes of cell death and tests to detect the condition at its earliest possible stage. Current treatments can help to ease the symptoms but none can repair the damage in the brain or slow the progress of the condition; now, Parkinson's UK researchers are working to develop new treatments that can.

Key words: Parkinson's ■ Progressive neurological condition ■ Rigidity ■ Non-motor symptoms ■ Research developments

Parkinson's is a progressive neurological condition for which there is currently no cure. It is often perceived as a condition that affects older people, but one in 20 patients will be under the age of 40 at the time of their diagnosis.

Parkinson's can affect everyday activities such as talking, walking, swallowing and writing, and symptoms can include tremor, slowness of movement and muscle stiffness. Other less visible symptoms may include sleep difficulties, depression, anxiety and memory loss, and these are often the symptoms that are the most debilitating.

On top of any symptoms, many people with Parkinson's feel frustrated about their condition and the loss of skills and ability to do everyday things that are usually taken for

granted. Coupled with this, people with Parkinson's often feel very alone.

Parkinson's is a fluctuating condition; a person's symptoms can vary and change at any time, resulting in good and bad days. Symptoms can vary from day to day, or even from hour to hour.

Causes of Parkinson's

Parkinson's is caused by the loss of dopaminergic nerve cells in the brain, in the substantia nigra, which is located within the basal ganglia, deep in the lower region of the brain, on either side of the brain stem. Symptoms of the condition become apparent once around 70% of these cells are lost. The reason why these nerve cells die is not known but Parkinson's UK is committed to funding research into finding a cure and better treatments and supporting those affected by the condition.

Dopamine allows messages to be sent to the parts of the brain that coordinate movement. With the loss of the dopaminergic nerve cells, these parts of the brain are unable to work normally, causing the symptoms of Parkinson's to appear. The level of dopamine then continues to fall slowly over many years, causing symptoms to further develop and new symptoms to appear.

Main symptoms

The most common symptoms of Parkinson's are stiff, rigid or frozen muscles, slowness of movement and tremor. Contrary to popular belief, not everyone has a tremor – only around 70% experience this symptom. As well as affecting movement, people with Parkinson's often find that other issues, such as tiredness, pain and depression, can have an impact on their day-to-day lives.

Whereas these symptoms are typical of Parkinson's, the condition affects each person differently.

Motor symptoms

A tremor is an uncontrollable shaking movement that affects a part of the body, usually the hand. Anxiety or stress can make a tremor worse and drugs for Parkinson's, such as levodopa, can reduce or stop a tremor while the drugs are working.

Rigidity in Parkinson's means that the stiffness or inflexibility of the muscles can cause pain or cramping. Parkinson's can also prevent the muscles from stretching or relaxing. Simple movements, such as rolling over in bed or fastening buttons, can become difficult or impossible to manage. Freezing is also common – many people with Parkinson's describe freezing as feeling as if their feet are stuck to the floor.

Regular exercise can help patients maintain freedom of

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Figure 1. A pill timer



movement, strengthen muscles and, in some cases, increase their mobility so it is good to try to encourage regular movement. Parkinson's UK has recently awarded a research grant to Dr Cathy Craig at the School of Psychology, Queen's University Belfast, to investigate the potential benefits of patients using the Nintendo Wii. Many people with the condition have reported that using the Wii is a good way for them to exercise at home and has helped them with their balance, movements and mood (www.parkinsons.org.uk/wii).

Slowness of movement, also very common in Parkinson's, means that patients might find it difficult to start a movement, such as getting out of a chair. It might be difficult for people with Parkinson's to move as quickly as they would like, which can also be extremely frustrating. This can change quickly, and at times patients can move with ease, so it is important to give the right level of support and sufficient time for them to carry out activities.

Non-motor symptoms

Non-motor symptoms can include: incontinence and constipation; swallowing problems or loss of control of saliva; falls and dizziness; problems with sleeping, including excessive daytime sleepiness and intense or frightening dreams; depression and anxiety; pain; and hallucinations.

These symptoms may be less obvious than motor symptoms at first, but are the symptoms that patients often find the most debilitating. Former GMTV presenter, John Stapleton (a keen supporter of Parkinson's UK), recalls how his mother's Parkinson's symptoms became overwhelming:

'I know that when my mother was diagnosed neither of us thought very much of it. We thought she'd just have to put up with having shaky hands and not being able to open a tin of peas on her own. We had absolutely no idea of what lay in store.'

Parkinson's and dementia

Around one in three people with Parkinson's will go on to develop Parkinson's dementia within 12 years of diagnosis. People with Parkinson's dementia can show signs of confusion, which can often become worse at night or in the evening, and this can have a severe impact on, not only, the patient but also their family and carer(s).

Nurses should try to make patients with dementia feel as comfortable as possible and encourage them to keep engaging and interacting with other people. When speaking to patients with Parkinson's dementia, it often helps to use familiar phrases, speak clearly, listen well and give the person time to respond to you.

Treating Parkinson's

Drug treatment is the main way to control the symptoms of Parkinson's. Medications, such as levodopa and dopamine agonists (*Table 1*), aim to increase the levels of dopamine that reach the brain and stimulate the parts of the brain where dopamine works. Parkinson's affects patient differently and each person will have a different experience and different combination of drugs to help them manage their symptoms.

Parkinson's UK has recently updated its guide to the drug treatments used in Parkinson's (*Box 2*). The guide is an important resource to remind nurses what medications they may need and the often complicated nature of the treatment.

Medication: getting it on time

Parkinson's can affect different people in very different ways, with symptoms and severity varying from person to person. As a result each individual will have a carefully balanced combination of medication to control and manage his or her symptoms. The timing of this medication is crucial and is an important factor for any health professional working with patients with the condition. Patients with Parkinson's might need additional or slightly different care from other patients. It is likely that they will need medication at different times from the usual drug rounds, as patients can take up to 15 different tablets every day.

If people with Parkinson's do not get their medication on time, the consequences can be very serious. Their ability to manage their symptoms may be lost, for example they may suddenly not be able to move, get out of bed or walk down a corridor. It can take a long time to get symptoms under control again.:

'...one nurse forgot to give me my 8 o'clock medication. By 10 o'clock I began to feel an absolute wreck with the pain. I couldn't breathe. I said to him, 'I haven't had my 8 o'clock tablets have I?'. 'Oh no', he said, 'you haven't.

Box 1. Main types of drugs used to treat Parkinson's

Levodopa

One of the main drugs, and can be used at all stages of the condition. Levodopa is a chemical building-block that the body converts into dopamine, thereby replacing the dopamine lost from the neurons.

Dopamine agonists

Dopamine agonists act like dopamine to stimulate nerve cells. They can prevent side effects such as involuntary movements (dyskinesia).

Apomorphine

Apomorphine is a dopamine agonist administered subcutaneously. It is the strongest known dopamine agonist, and is usually prescribed to those who have had the condition for a long time.

Glutamate antagonists

The glutamate antagonist amantadine, is prescribed to treat Parkinson's disease symptoms. It is used infrequently and is likely to be given alongside other drug treatments. It can be used to treat tremor and stiff muscles, as well as unwanted involuntary movements.

Anticholinergics

These are less commonly used now and block the action of acetylcholine. Anticholinergics may be useful in the early stages of Parkinson's disease, when symptoms are mild, and tend to improve tremor.

Catechol-O-methyltransferase (COMT) inhibitors

These have to be used alongside levodopa and reduce symptoms by blocking an enzyme that breaks down levodopa, prolonging its effect.

Monoamine oxidase-B (MAO-B) inhibitors

MAO-B inhibitors prevent the breakdown of dopamine in the brain by inhibiting the enzyme monoamine oxidase type B (MAO-B). They are used to make the effect of levodopa last longer or to reduce the amount required.

Never mind. I didn't know.' And he lumped my 8 o'clocks together with the 10 o'clock medication and you can imagine what that did to me. I was violently sick on high dependency. And that was just through misunderstanding that if you miss a medication time you cannot double up later on to catch up. It's not a catch-up situation. It's about giving them on time.'
(Parkinson's UK)

When patients do not receive their medication in time, they are likely to require a higher level of care and possibly an extended hospital stay, at a significant cost in both time and resources. There is an increased risk of accidents and falls, and in some cases originally planned treatment may no longer be possible.

When staying in hospital, patients may ask to self-medicate. This can be an effective option as many people with Parkinson's are experts in their own condition, after having lived with it for many years. Other options to help them get their medication on time could include: using pill-timers (*Figure 1*) or alarms to remind staff about patients whose medication is due at different times to the usual drug-rounds; using a 'flagging' system to make it clear which patients have Parkinson's.

Parkinson's UK produces materials to help health and social care professionals to support their patients to get their Parkinson's medication on time, including a DVD entitled 'Medicine Management for Patients with Parkinson's'. The DVD is designed to give care home staff a vital insight into the condition. It also looks at how they can help people with Parkinson's and ensure they get the right medication at the right time whenever they go into any hospital or care home in the UK (*Box 2*).

Non-drug therapies

Therapies, such as occupational therapy (OT), physiotherapy and speech and language therapy, can be of huge benefit to patients and have a positive impact on their quality of life. Parkinson's affects each person differently and symptoms can vary hugely. It is, therefore, crucial that patients have an individually designed programme of therapy to help them overcome their symptoms as much as possible.

Occupational therapy

Occupational therapy (OT) can help patients cope with the impact of the condition on their day-to-day lives and helps them to live their lives as independently as possible. In some cases, OT can also help take the pressure off their carers by helping those they care for retain some independence.

Many patients find their condition frustrating, especially when it comes to everyday things that they find it increasingly difficult to carry out. OT can be valuable in helping those who experience problems such as walking or with getting in and out of bed, moving in bed, using steps and stairs and maintaining balance, by working with the patients to help them find ways of making a difficult task easier. Treatment can be effective right from diagnosis and through all stages of the condition.

Parkinson's UK, together with the College of Occupational Therapists, has produced a guide called 'Occupational Therapy for People with Parkinson's'. The guide covers a variety of topics such as initiating and maintaining movement, supporting participation and end-of-life care.

Physiotherapy

Initially, physiotherapy can assess how patients have been affected by their condition. This can be helpful for those who are newly diagnosed, as well as those who have been living with the condition for a long time.

Physiotherapy can teach patients techniques that can help make their movements easier. As mentioned, everyday activities can become ever more difficult as the condition progresses but these can be greatly improved through physiotherapy.

Parkinson's UK, along with AGILE (Chartered Physiotherapists working with Older People) and ACPIN (Association of Chartered Physiotherapists Interested in Neurology), has developed Quick Reference Cards (UK) for physiotherapists working with people with Parkinson's.

Speech and language therapy

Around 50% of patients will develop problems with their speech and communication, and speech and language therapy can help patients maintain a sense of independence and improve quality of life as the condition progresses. It can teach techniques to strengthen the volume of the voice and enable patients to continue to participate in conversations and socializing, as well as helping with problems with swallowing.

Deep brain stimulation

Deep brain stimulation (DBS) is a surgical technique used to treat some of the symptoms of Parkinson's. Although it is not suitable for all patients, it can help to alleviate slowness of movement, stiffness and tremor. It can also enable drug dosages to be lowered, which can lead to a reduction in the involuntary movements (dyskinesias) caused by some medications.

In DBS signals from an electrical implant in the brain help reduce symptoms, such as tremor and stiffness. This type of brain surgery can be an effective treatment option for up to 5% of people with Parkinson's, in particular those whose symptoms are no longer adequately controlled by medication, and who have particular unwanted side effects.

Recent research has shown that DBS significantly improves quality of life for some people with the condition more than medication alone. These findings came from a 10-year trial, co-funded by Parkinson's UK, the Medical

Research Council and the Department of Health, which was coordinated by the Birmingham Clinical Trials Unit at the University of Birmingham.

The trial compared the effects of DBS with the best drug therapy in 366 people with advanced Parkinson's who were considered suitable for surgery (Williams et al, 2010). They were divided into two groups: those who received immediate surgery and medical therapy; and those who received just medication for 1 year.

After 12 months follow-up the researchers found:

- The surgery improved quality of life and motor function in patients with advanced Parkinson's, compared with those receiving medical therapy only
- On average, the people who received DBS found that their symptoms improved, whereas those who received medication alone stayed the same
- The people who received DBS needed about one-third (34%) less medication to control their symptoms than those who did not undergo surgery.

Finding a cure: developments in research

'The research is our hope. Finding a cure would give me back my life.' (Richard, who has Parkinson's)

Scientific research has transformed the treatment, services and care for people living with Parkinson's around the world. There is now a range of medications, better surgical treatments, and therapies that allow the complex and fluctuating symptoms to be managed more effectively.

But researchers still have much work to do to find a cure. No current treatment can slow or stop the development of Parkinson's; they can only help in managing and controlling the symptoms. And as the condition progresses, these symptoms become more complex and the impact on people's lives can be devastating.

Bill has been living with Parkinson's for more than 20 years:

'My tremor became worse and my whole body would shake uncontrollably. I was finding it more and more difficult to do simple tasks such as buttoning my shirt or tying my shoelaces. Walking was a struggle. Without warning, my feet would feel glued to the ground. I would be helpless and unable to take another step for minutes.'

But there is hope. Breakthroughs in our understanding of what causes Parkinson's and advances in innovative new therapies over the last 10 years have brought us closer to a cure than ever before. And this momentum must be capitalized on. Parkinson's UK is funding 90 research projects worth £15million to accelerate progress towards a cure by tackling the fundamental challenges of the condition. This vital research is detailed below.

Understanding why nerves cells die

Parkinson's occurs when nerve cells in the substantia nigra are gradually lost but the reasons as to why these nerve cells stop working and die are unknown. Parkinson's UK

KEY POINTS

- Parkinson's is a progressive neurological condition, caused by a lack of dopamine, for which there is no cure
- The most common symptoms of Parkinson's are tremor, rigidity and slowness of movement. Many also experience non-motor symptoms, including constipation, swallowing problems, depression and hallucinations
- Parkinson's is usually treated with medication. The timing of this medication is extremely important. If people with Parkinson's do not get their medication on time, their ability to manage their symptoms may be lost and it can take a long time to get symptoms under control again
- Non-drug therapies, such as occupational, speech and language and physiotherapy, can be of huge benefit to people with Parkinson's and improve their quality of life

researchers are working to understand the chain of events that lead to cell death, which will pave the way for the next generation of treatments that can stop, slow or reverse the progressive loss of these precious cells.

Earlier diagnosis

There is currently no definitive test for Parkinson's. Neurologists make a diagnosis based on a person's symptoms, his or her medical history and sometimes by using brain scans. But these may give uncertain results and people can be wrongly diagnosed.

Parkinson's UK is funding research to develop tests to identify Parkinson's at the earliest possible stage. This would give the opportunity to protect the remaining nerve cells or save damaged cells.

Tackling the 'non-motor' symptoms

Although tremor, slowness and stiffness are usually the most

obvious symptoms of the condition, the most distressing problems often go unseen. Depression, sleep problems, hallucinations and dementia are as much a part of the condition as loss of mobility.

Patricia has been living with Parkinson's for 5 years:

'My specialist only asked about my physical symptoms. But I also had dreadful feelings of fear and panic. I was prescribed medication that improved my mobility but the anxiety continued and made my life a struggle.'

Parkinson's UK researchers are investigating what causes these debilitating 'non-motor' symptoms and are working on treatments to prevent them.

Developing the next generation of treatments

Current treatments for Parkinson's can help to ease the symptoms but none of them can repair the damage in the brain or slow the progress of the condition. Now, Parkinson's UK researchers are working to develop new treatments that can.

Stem cells offer great hope because they have the ability to become any cell type. Stem cell research aims to understand more about how an organism develops from a single cell and how healthy cells can replace damaged cells in adults. The idea is to repair the Parkinsonian brain – using new healthy cells to replace the nerve cells that have died.

Gene therapy is another area of great potential. It works by introducing normal genes into people with certain disorders to overcome the effects of defective genes that may cause their condition. Scientists use genes to re-programme the dying nerve cells to help them work better and survive for longer.

This treatment is likely to be used to treat people in the early stages of the whose nerve cells are still alive but this research is still in its infancy.

Conclusion

By working together to build on existing discoveries and explore these innovative areas of research, it is hoped that a cure for Parkinson's will be found.

Parkinson's UK offers support for everyone affected,, including people with the condition, their family, friends and carers, researchers and professionals working in this area. **BJN**

For more information about Parkinson's UK's support for professionals or to join the Professionals' Network—an online network, offering professionals access to the latest information and support on Parkinson's—visit parkinsons.org.uk/professionals.

Conflict of interest: Deiga Heisters is National Education Advisor for Parkinson's UK

Williams A, Gill S, Thelekat V, Jenkinson C, Quinn N, Mitchell R et al (2010) Deep brain stimulation plus best medical therapy versus best medical therapy alone for advanced Parkinson's disease (PD SURG trial): a randomised, open-label trial. *Lancet Neurology* 9(6): 581–91

Box 2. Resources

Parkinson's UK professionals' network: www.parkinsons.org.uk/professionalsnetwork

Professionals Guide to Parkinson's: www.parkinsons.org.uk/advice/publications/professionals/professionals_guide.aspx

Medicine Management for Patients with Parkinson's DVD: www.parkinsons.org.uk/hospitaldvd

Caring for your patient with Parkinson's: www.parkinsons.org.uk/advice/publications/professionals/caring_for_your_patient.aspx

Visit parkinsons.org.uk/getitontime for more information or to order a copy of the DVD.

The Drug treatment guide is available to order from www.parkinsons.org.uk/professionals, as a pocket guide or in a poster format.