An Overview of Parkinsons Disease: Causes, Connections and Cures?

Parkinsons disease is a progressive neurological disorder. It causes nerve cells in the brain to degenerate and die, leading to a variety of symptoms. The physical manifestations of Parkinson's are numerous, and the symptoms and signs exhibited by individual patients differ enormously. The nature of the disease, presentation of such a variety of symptoms and signs and ranging severity and progression, creates a much more complex and challenging research scenario. The disease affects large numbers of the population and ultimately results in devastating consequences for patients, their caregivers and loved ones. The race is on to explore and uncover the biological mechanisms responsible for the disease, the causes leading to deviations in normal biological functioning and to establish the most effective treatment plans with the aim of curing this cruel and complicated disease. There are numerous lines of research into Parkinsons disease across the UK alone and progress has undoubtedly been made over many decades. However, a full understanding and hence cure is yet to be uncovered. Having a full understanding of the normal functioning of the body and the apparent biological structural changes and changes in mechanisms within the body of a Parkinson's patient can and has initiated the research journey into the causes.

Symptoms of Parkinsons include problems with movement, typically slow movement (known as bradykinesia), muscle stiffness, tremors, impaired balance, speech problems and loss of autonomic movements. An early symptom can also be lack of facial expression. Patients with the disease can demonstrate a few or all these symptoms, but typically, such symptoms are progressive, becoming more apparent and increasing in severity.

According to Parkinsons UK, the condition is on the rise. They state in the UK alone, someone is 'diagnosed with Parkinsons every twenty minutes' (Parkinsons UK 2026). They also estimate that the number of people living with Parkinsons Worldwide will double to twenty-five million by the year 2050.

The concerning figures highlighting increasing incidence and prevalence of Parkinson's Disease, have prompted extensive and numerous research programmes, aiming to identify and understand the pathogenesis, causes and potential treatments and cures for the disease. To develop such programmes, understanding the structure and function of the brain, and how Parkinsons impacts such aspects is of paramount important, and can provide a platform on which to develop various research

programmes, techniques and experimentation. Understanding the complexities of brain functioning and performance is necessary to gain an insight into the interference of normal functioning because of Parkinsons. This is beyond the scope of this essay; however, the understanding of normal functioning allows a direct comparison to the malfunctioning in conditions such as Parkinsons Disease.

It has been established that many of the motor and non-motor symptoms associated with this disease are the result of loss of neurons responsible for production the chemical messenger dopamine. Decreased dopamine leads to impaired and irregular brain activity. It is also well accepted and publicised that people with Parkinson's also lose norepinephrine – another chemical messenger responsible for controlling many other body functions including blood pressure.

As symptoms and signs of this disease are non-specific and can vary between individuals, research obstacles exist. Additionally, a major barrier within such research models and developments into treatments and cures is that the exact cause of Parkinsons is unknown. However, it has been established that several factors are influential on disease development. Such factors include genetics (specific genetic modifications have been linked to Parkinson's head trauma, and environmental factors (including chemical /toxin exposure) potentially affecting neurones. There is currently a lot of interest and focus on the effects of contact sports and head injuries and the potential to develop such neurological conditions. Research by Kenbor, Rugbjerg et al 2015 examined the association between head injuries through life and the risk for Parkinsons disease in an interview-based case control study. They observed no association between head injuries occurring before the first cardinal symptom and risk for Parkinsons Disease and hence did not support the hypothesis that head injury increases the risk of developing the disease. They also suggested that studies in the future should focus on head injuries in combination with genetics or environmental factors. These factors and their impact on the brains ability to produce dopamine are still being continually investigated. The association of toxic exposure to non pesticidecompounds such as organohalogens, metals and solvents, have received strong support as risk factors. However, according to Caudle 2013 making a clear delineation as to the contribution of a class of compuounds or specific compound ‘to a particular suite of pathological and clinical synptoms remains to be achieved’.

As forementioned, Parkinsons is characterised by progressive loss of nerve cells (neurons) in part of the brain known as the substantia nigra, and these neurons produce dopamine.Therapy target refers to the biological mechanisms which contribute to the

development and progression of Parkinsons. There are many research programmes investigating the biological mechanisms and researchers are striving to find causes and treatments to counteract such processes with the goal of finding a cure. A study by Cramb, Kelly and Wade-Martins states that there is evidence to indicate impaired dopamine release can result from disruption to a diverse range of Parkinson's disease associated genetic and molecular disturbances and can be considered as a potential pathophysiological hallmark of Parkinson's disease. (Cramb et al, 2023)

There are several lines of investigations into the causes of neuron damage in this disease. Alpha Synuclein is an abundant protein identified in neurons. In Parkinsons, neurons begin manufacturing dysfunctional types of alpha synuclein and these coalesce and build up, leading to clumps called Lewy Bodies. The Lewy bodies interfere with the cells ability to function normally, and this leads to cell destruction and loss if not cleared. Researchers also believe that the clumps (Lewy Bodies) are transferable from neuron to neuron, leading potentially to the spread of Parkinsons across the brain. It is the presence of alpha synuclein and Lewy bodies which is considered the hallmark and driving force of Parkinson's.

Extensive research is underway and ongoing into finding compounds with potential to breakdown or prevent the development of Lewy bodies with the idea of altering and receding the progression of the disease. The results are so far inconclusive and variable.

The accumulation of waste, ability of breaking down waste material within cells are also important functions influential on the maintenance of good health of a neuron. Excessive accumulation of waste and persistence can lead to dysfunctional structure and mechanisms. It is thought that in people with Parkinsons, the neurons' normal processes for discarding waste may be faulty and can lead to increased toxicity. One study found a Parkinson's Disease linked mutation in a gene called Endophilis A1 blocked the process by which the body and brain recycle waste. (Beademosi, 2023).

Another potential consideration is the effect of chronic neuroinflammation. Inflammation is an important part of the body's immune defence, but when sustained or prolonged, there becomes potential for damage and atrophisation of normal healthy cells. Additionally, there are thought to be several pathways implicated in promoting neuroinflammation in Parkinsons. Some include overproduction of inflammatory molecules called inflammasomes, over activation of specialised immune cells in the

brain and it is even thought that chronic inflammation elsewhere in the body such as the gut could initiateneuroinflammation.

Several research programmes are ongoing to ascertain whether reducing neuroinflammation in Parkinson's could prevent of hinder the progression of the disease. A study by Tansey and Goldbery (2009) found the link between inflammation oxidative stress and PD has ‘become less controversical due to an overwhelming number of proofs of principle studies that strongly implicate inflammatory processes in progressive loss of nigral DA neurones. ‘

Having some knowledge of the biological processes involved in the pathogenesis of Parkinsons has initiated treatment plans. Treatments for Parkinson’s disease are aimed to improve the physical symptoms of the condition. Treatments offered to individuals tend to be personalised and combine medication, exercise therapy, surgery and complimentary options with the aim of maximising the management of symptoms. Treatment tends to be tailored to an individual's symptoms via a shared decision-making process with healthcare professionals.

With regards to medication, there are several drugs prescribed for Parkinson's. As discussed, Dopamine is a chemical messenger made in the brain, and one is aware that when the dopamine levels become low the symptoms of Parkinsons develop. The reduction in dopamine is a consequence of the neurones in the brain ceasing normal functioning. Taking dopamine as a drug is not effective as it cannot cross the blood brain barrier. Adaptations have therefore had to be implemented regarding the use of drugs to increase dopamine.

Most drug treatments work by doing one or more of the following things: -

- Increasing the amount of dopamine in the brain
- Replicating the action of dopamine through stimulation of areas of the brain where dopamine works.
- Blocking the action of enzymes that break down the dopamine.

Several drugs are available for treatment of Parkinsons. Anticholinergics are one type and these block the chemical messenger acetylcholine, which is found in the brain and body. These drugs are rarely used however; they have been found to be beneficial in

only a small number of patients. In Parkinson's patients the effect of acetylcholine is stronger, and this leads to brain overactivity which causes tremors. These can be used to help with rigidity, slowness of movement tremor, speech and writing difficulties and gait.

Apomorphine is a liquid drug and is a dopamine agonist. This drug works by tricking the brain into thinking they are dopamine, which can hence reduce symptoms. These tend to be prescribed for sudden changes in symptoms, including swallowing difficulties.

Levodopa drugs are another option for treatment. Levodopa is a chemical building block that the body converts into dopamine (in the brain). Levodopa drugs boost the supply of this and results in neurones making more dopamine. This drug tends to be the most popular and commonly prescribed.

Mao – B inhibitors are another alternative. These assist the nerve cells to make better use of the existing dopamine. MAO B is an enzyme which breaks down dopamine that is not being utilised in the brain. The MAO B inhibitors stop the enzyme so that more dopamine becomes available to treat the symptoms.

In conclusion to this overview of Parkinsons Disease, it is evident that there are many lines of investigation, some relating to the apparent misfunctioning and impairment of normal biological mechanisms because of chemical exposure, traumatic injury and genetics. The main theory behind the cause of this devastating disease is thought to be due to a loss of nerve cells in the Substantia Nigra, which are ultimately responsible for producing the chemical dopamine. Treatment aims tend to be focused on replenishing the dopamine within the brain, some drugs mimicking dopamine whilst others boosting the supply. Potential risk factors and causes are being researched thoroughly, but results can be highly variable and therefore inconclusive. Despite significant progress in research, there are still many hurdles to overcome in the quest for uncovering a cure. The fact that the disease presents a variety of different symptoms, with varying progression and severity may also cause more difficulty in producing definitive and conclusive solutions. More recently there have been some theories presented on associations between Parkinsons Disease and other neurodegenerative disorders, such as the eye disease glaucoma. Studies by Zhao, Cheung and Malvankar- Mehta , investigating the risk of Parkinsons disease in glaucoma patients, unfortunately were

inconclusive, but more research into the potential link between Parkinsons Disease and Glaucoma , for example, may prove significant and beneficial in aiding both diagnosis, management and treatment plans for Parkinson's Disease. This area most definitely is worth further exploration.

Thanks to the large number of fundraising agencies within the UK and beyond, such as the Biotechnology and Biological Sciences Research Council (BBSRC), The Cure Parkinsons Trust, The Dunhill Medical Trust, Medical Research Council and Neuroscience Research foundation research continues to produce progress. Such foundations have a strong emphasis on funding translational and clinical research. With continued financial support and perseverance, it is hopeful that an imminent and complete breakthrough will come.

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