biology and life sciences forum

MDPI

Proceeding Paper

Guidelines for the Diagnosis and Treatment of Parkinson's Disease †

Tarek Elshourbagy [1,*], James Robert Brašić [2] and Alveena Batool Syed [3]

[1] Faculty of Medicine, Cairo University, Giza 12613, Egypt
[2] Section of High Resolution Brain Positron Emission Tomography Imaging, The Russell H. Morgan Department of Radiology and Radiological Science, Division of Nuclear Medicine and Molecular Imaging, School of Medicine, The Johns Hopkins University, Baltimore, MD 21287, USA; jbrasic1@jh.edu
[3] Cleveland Clinic, Cleveland, OH 44195, USA; syeda11@ccf.org
* Correspondence: doctarek_medico@yahoo.com; Tel.: +1-551-5026-671
† Presented at the 1st International Electronic Conference on Clinical Medicine, 15–30 September 2021; Available online: https://eccm.sciforum.net/.

Abstract: Parkinson's disease (PD), the second most common neurodegenerative disorder afflicting 10 million people worldwide and the fourteenth leading cause of death in the United States, is caused by the death of dopaminergic neurons that regulate movement in the substantia nigra pars compacta. To facilitate an assessment framework for providers to apply precision medicine to develop treatment plans tailored to the specific needs of each person with possible PD and related conditions, we propose guidelines for the diagnosis and treatment of people with possible PD and related conditions based on review of available knowledge.

Keywords: deep brain stimulation; differential diagnosis; dopamine transporter; immunotherapy; movement disorders; neurodegenerative disorder; neurological examination; pathogenesis; physical examination; subthalamic nucleus

check for updates

Citation: Elshourbagy, T.; Brašić, J.R.; Syed, A.B. Guidelines for the Diagnosis and Treatment of Parkinson's Disease. *Biol. Life Sci. Forum* **2021**, *9*, 9. https://doi.org/10.3390/ECCM-10859

Academic Editor: Michele Roccella

Published: 15 September 2021

1. Introduction

Parkinson's disease (PD), the second most common neurodegenerative disorder afflicting 10 million people worldwide [1] and the fourteenth leading cause of death in the United States [2], is caused by the death of dopaminergic neurons that regulate movement in the substantia nigra pars compacta. Mechanisms contributing to the development of PD in vulnerable individuals include protein misfolding, protein aggregation, and mitochondrial dysfunction [3].To facilitate an organized approach for clinicians to utilize precision medicine to develop treatment plans to address the specific needs of individuals with PD and related conditions, we have developed guidelines for diagnosis and treatment based on the review of available knowledge [3].

2. Methods

We reviewed the key literature on the pathogenesis of Parkinson's disease on PubMed and Google Scholar to propose guidelines for the development of diagnostic and therapeutic interventions for people with Parkinson's disease and related conditions.

3. Results and Discussion

Clinicians can generate optimal care of people with possible PD and related disorders through systematic utilization of the established principles of clinical medicine, assessment of signs and symptoms of patients, development of a differential diagnosis, and usage of appropriate laboratory tools to rule in or out the disease. (Figure 1). Careful evaluation of persons with PD requires medical and family history [4], examination, structured movement assessments by visual observation [5,6], instrumentation [7], and neuroimaging [3].

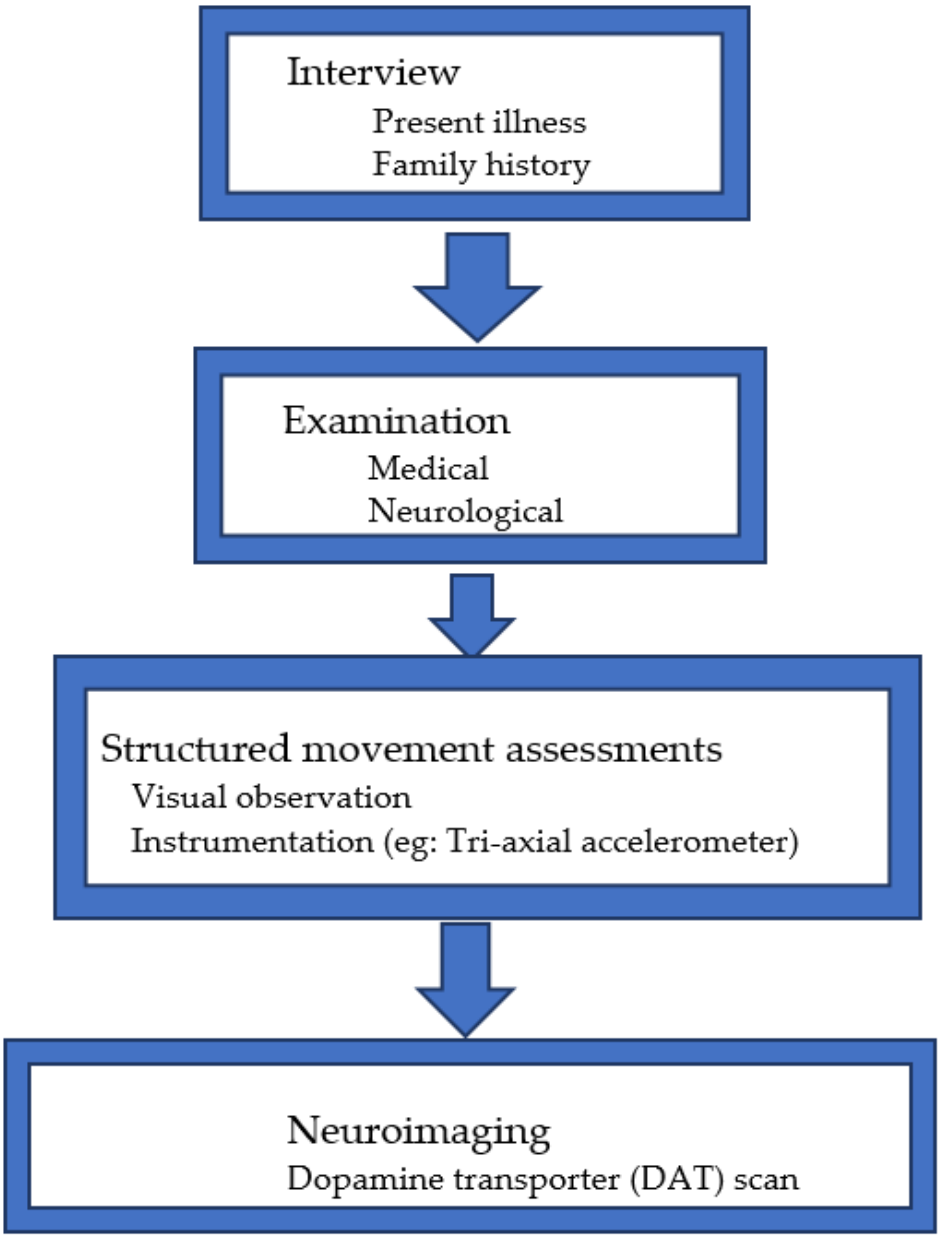

Figure 1. Guidelines for the diagnosis of Parkinson's disease (PD).

Clinicians will then benefit from the systematic consideration of potential therapies for PD to apply the principles of precision medicine to develop an optimal treatment plan (Figure 2).

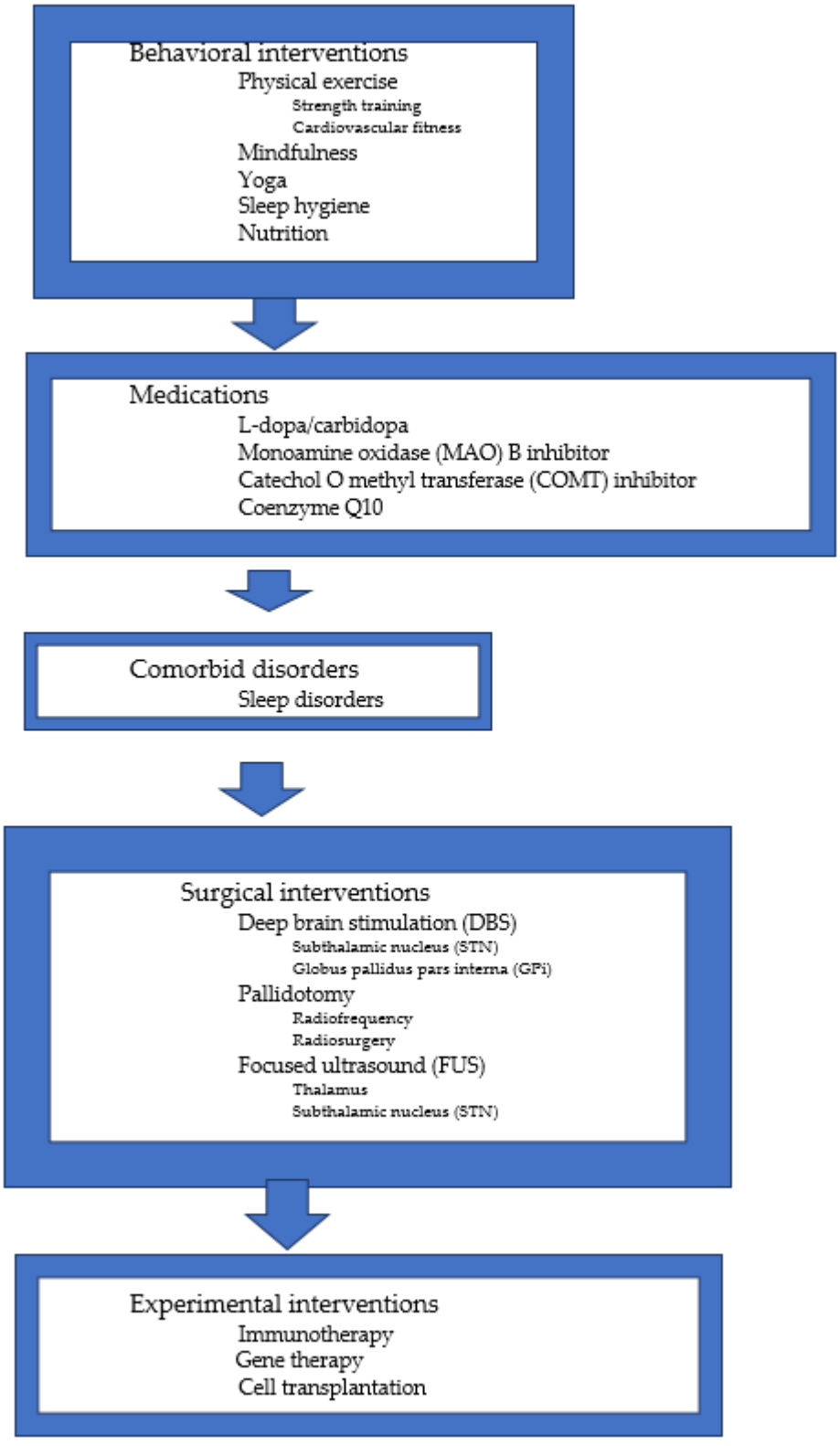

Figure 2. Guidelines for the treatment of Parkinson's disease (PD).

3.1. Behavioral Interventions

Physical exercise (strength training and cardiovascular fitness) plays a key role in the prevention and treatment of PD in addition to improving somatic and mental health [8].

3.2. Nutrition

Assessment of individuals is key to foster the use of beneficial dietary components and nutritional supplements and to discourage unfavorable ones [9].

3.3. Medications

People with PD generally benefit from a variety of pharmacological interventions including L-dopa/carbidopa [10], monoamine oxidase (MAO) B inhibitor, and catechol O methyltransferase (COMT) inhibitor [11]. Additionally, co-enzyme Q10, a co-enzyme for protein complexes 1, 2, and 3 of a mitochondrial electron transport chain, may selectively benefit genetic subgroups of people with PD [12].

3.4. Comorbid Disorders

People with PD merit assessment for specific sleep disorders to apply the principles of precision medicine to tailor a treatment plan specific to the needs of the individual [11].

3.5. Surgical Interventions

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) (Figure 3) [13] and the globus pallidus pars interna (GPi) are procedures that have benefited some people with PD who are refractory to medications [14]. Positron emission tomography (PET) has demonstrated that improvement in symptoms in people with PD with STN DBS was associated with cerebral glucose metabolism alterations including striatal decrements and cerebellar, parietal cortical, and temporal cortical increments as well as vesicular monoamine transporter 2 (VMAT2) decrements in the striatal, cortical, and limbic regions [13] (Figure 4).

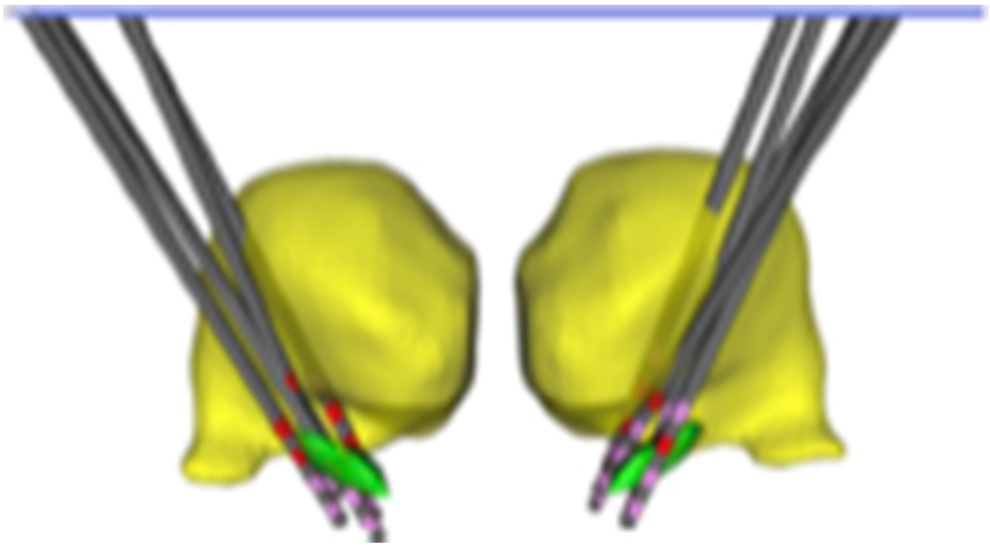

Figure 3. Diagram of electrode placements near and through the thalamus (yellow) with active cathodes (red) for bilateral subthalamic nucleus (STN) (green) deep brain stimulation (DBS) for Parkinson's disease (PD). Reproduced with permission [13].

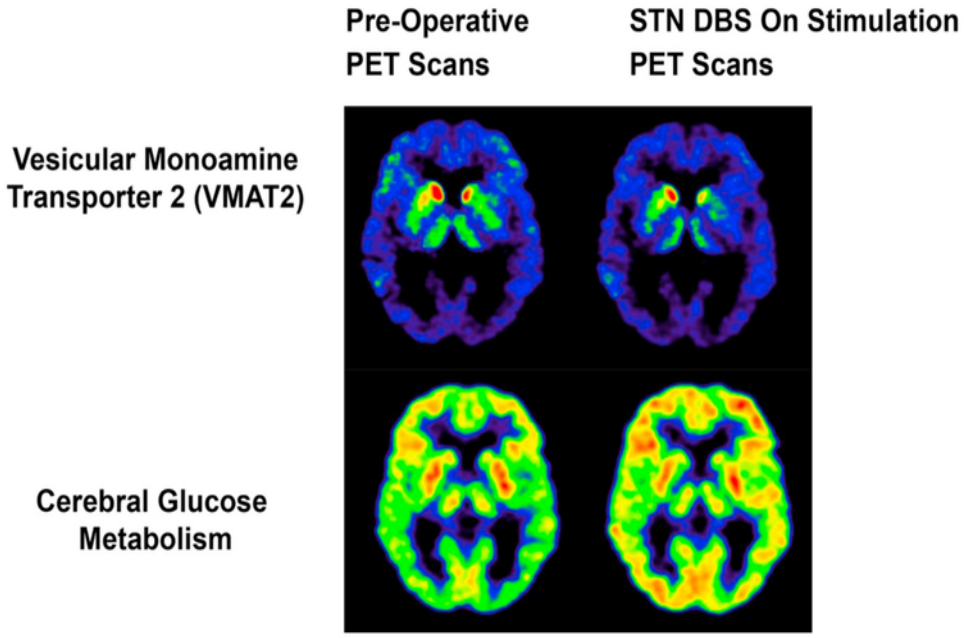

Figure 4. Positron emission tomography (PET) images of vesicular monoamine transporter 2 (VMAT2) and cerebral glucose metabolism of a 59-year-old man with Parkinson's disease before and during deep brain stimulation (DBS) of the subthalamic nuclear (STN). Brighter colors indicate higher activity. Darker colors indicate lesser activity. Reproduced with permission [13].

Pallidotomy by radiofrequency or radiosurgery represent other possibly beneficial surgical interventions for PD [15].

Focused ultrasound (FUS), a procedure that can be accomplished without the penetration of the brain through a craniotomy, may be applied to the thalamus and the subthalamic nucleus [15].

3.6. Experimental Interventions

Immunotherapy. Since inflammation produced by the immune system plays a major role in degeneration of the basal ganglia in PD, drugs targeting the immune microenvironment such as sargramostism are under trials. Sargramostism, a recombinant granulocyte monocyte colony stimulating factor, shows promise to protect the basal ganglia from degeneration [16].

Gene therapy. Drugs targeting genes responsible for the development of PD include non-disease modifying drugs which treat the symptoms by targeting dopamine synthesis and disease modifying drugs which slow PD progression such as glial cell-line derived neurotrophic factors [17].

Cell transplantation. Growing dopamine-secreting neurons from pluripotent stem cells using CRISPR technology and transplanting them into the degenerated part of the basal ganglia may offer a line for slowing PD progression and restoring basal ganglia functions [18].

In order to facilitate prompt and efficient diagnosis and treatment of PD, we propose guidelines for the diagnosis (Figure 1) and treatment (Figure 2) of PD.

4. Conclusions

We are pleased to propose guidelines for the diagnosis and treatment of Parkinson's disease (Figures 1 and 2) in order to provide a checklist of key items to consider in the development of a treatment plan for people who may have Parkinson's disease. Future investigations will measure and quantify the benefits produced by the guidelines. Additionally, future investigations will explore the development of handwriting analysis and other potential digital biomarkers other tools for the diagnosis of PD. We anticipate that

clinicians, administrators, policy planners, advocates, and other concerned individuals will benefit from the adoption of our guidelines for the diagnosis and treatment of Parkinson's disease and related conditions [3].

Author Contributions: Conceptualization, T.E., J.R.B. and A.B.S.; methodology, T.E., J.R.B. and A.B.S.; software, T.E.; validation, T.E., J.R.B. and A.B.S.; formal analysis, T.E.; investigation, T.E.; resources, T.E., J.R.B. and A.B.S.; data curation, T.E., J.R.B. and A.B.S.; writing—original draft preparation, T.E.; writing—review and editing, T.E., J.R.B. and A.B.S.; visualization, T.E., J.R.B. and A.B.S.; supervision, T.E., J.R.B. and A.B.S.; project administration, T.E., J.R.B. and A.B.S.; funding acquisition, T.E. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Data Availability Statement: All data is available in the indicated references.

Acknowledgments: The authors thank the Welch Medical Library of the Johns Hopkins University School of Medicine in Baltimore, Maryland, USA, for providing literature for this article.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. de Lau, L.M.L.; Breteler, M.M.B. Epidemiology of Parkinson's disease. *Lancet Neurol.* **2006**, *5*, 525–535. [CrossRef]
2. Parkinson Foundation, What Is Parkinson's? 2022. Available online: http://www.parkinson.org/parkinson-s-disease/pd-101/what-is-parkinson-s-disease (accessed on 5 March 2022).
3. Elshourbagy, T.; Syed, A.B.; Amer, M.A.M.; Brasic, J.R. Precision medicine to identify optimal diagnostic and therapeutic interventions for Parkinson's Disease. *Med. Sci. Discov.* **2021**, *8*, 514–519. [CrossRef]
4. Young, J.G.; Kaplan, D.; Pascualvaca, D.M.; Brasic, J.R. Psychiatric examination of the infant, child, and adolescent. In *Comprehensive Textbook of Psychiatry/VI*, 6th ed.; Kaplan, H.I., Sadock, B.J., Eds.; Williams & Wilkins: Baltimore, MD, USA, 1995; Volume 2, pp. 2169–2206.
5. Brašić, J.R. Treatment of movement disorders in autism spectrum disorders. In *Autism Spectrum Disorders*; Hollander, E., Ed.; Medical Psychiatry Series; Marcel Dekker, Inc.: New York, NY, USA, 2003; Volume 24, ISBN 0-8247-0715-X.
6. Brašić, J.R.; Mohamed, M. Human brain imaging of autism spectrum disorders. In *Imaging of the Human Brain in Health and Disease*; Seeman, P., Madras, B., Eds.; Academic Press, Elsevier Science: Oxford, UK, 2014; pp. 373–406.
7. McKay, G.N.; Harrigan, T.P.; Brašić, J.R. Alow-cost quantitative continuous measurement of movements in the extremities of people with Parkinson's disease. *MethodsX* **2019**, *6*, 169–189. [CrossRef] [PubMed]
8. Oliveira de Carvalho, A.; Filho, A.S.S.; Murillo-Rodriguez, E.; Rocha, N.B.; Carta, M.G.; Machado, S. Physical exercise for Parkinson's disease: Clinical and experimental evidence. *Clin. Pract. Epidemiol. Ment. Health* **2018**, *14*, 89–98. [CrossRef] [PubMed]
9. Mischley, L.K.; Lau, R.C.; Bennett, R.D. Role of diet and nutritional supplements in Parkinson's disease progression. *Oxid. Med. Cell. Longev.* **2017**, *2017*, 6405278. [CrossRef] [PubMed]
10. LeWitt, P.A. Levodopa therapy for Parkinson's disease: Pharmacokinetics and pharmacodynamics. *Mov. Disord.* **2015**, *30*, 64–72. [CrossRef] [PubMed]
11. Radhakrishnan, D.M.; Goyal, V. Parkinson's disease: A review. *Neurol. India* **2018**, *66* (Suppl. S1), 26–35. [CrossRef]
12. Prasuhn, J.; Brüggemann, N.; Hessler, N.; Berg, D.; Gasser, T.; Brockmann, K.; Olbrich, D.; Ziegler, A.; König, I.R.; Klein, C.; et al. An omics-based strategy using coenzyme Q10 in patients with Parkinson's disease: Concept evaluation in a double-blind randomized placebo-controlled parallel group trial. *Neurol. Res. Pract.* **2019**, *1*, 31. [CrossRef] [PubMed]
13. Stefani, A.; Högl, B. Sleep in Parkinson's disease. *Neuropsychopharmacology* **2020**, *45*, 121–128. [CrossRef] [PubMed]
14. Smith, G.S.; Mills, K.A.; Pontone, G.M.; Anderson, W.S.; Perepezko, K.M.; Brasic, J.; Zhou, Y.; Brandt, J.; Butson, C.R.; Holt, D.P.; et al. Effect of STN DBS on vesicular monoamine transporter 2 and glucose metabolism in Parkinson's disease. *Parkinsonism Relat. Disord.* **2019**, *64*, 235–241. [CrossRef] [PubMed]
15. Lee, D.J.; Dallapiazza, R.F.; De Vloo, P.; Lozano, A.M. Current surgical treatments for Parkinson's disease and potential therapeutic targets. *Neural. Regen. Res.* **2018**, *13*, 1342–1345. [CrossRef] [PubMed]
16. Gendelman, H.E.; Zhang, Y.; Santamaria, P.; Olson, K.E.; Schutt, C.R.; Bhatti, D.; Shetty, B.L.D.; Lu, Y.; Estes, K.A.; Standaert, D.G.; et al. Evaluation of the safety and immunomodulatory effects of sargramostim in a randomized, double-blind phase 1 clinical Parkinson's disease trial. *NPJ Parkinson's Dis.* **2017**, *3*, 10. [CrossRef] [PubMed]
17. Axelsen, T.M.; Woldbye, D.P.D. Gene therapy for Parkinson's disease, an update. *J. Parkinson's Dis.* **2018**, *8*, 195–215. [CrossRef] [PubMed]
18. Stoddard-Bennett, T.; Pera, R.R. Stem cell therapy for Parkinson's disease: Safety and modeling. *Neural Regen. Res.* **2020**, *15*, 36–40. [CrossRef] [PubMed]