
Research Priorities of the New Zealand Parkinson's Community

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Purpose

To establish the research priorities of the New Zealand Parkinson's community.

To complete an audit of the research funding that had been directed towards Parkinson's research in the period 2015-2020 and to summarise the expertise of Parkinson's researchers based in New Zealand.

Executive Summary

Parkinson's disease is a complex and progressive neurodegenerative disorder with both motor and non-motor symptoms. Parkinson's is estimated to affect ~12,000 New Zealanders. Currently, there is no way to stop or slow the progression of the disorder, which results in increased levels of motor disability and for many declines in cognitive function.

This piece of research sought to canvas the New Zealand Parkinson's population to establish what areas of the disorder they most wanted research to focus on. Data was also collected from spouses and family members involved in supporting people with Parkinson's and also the clinical and research communities. The report also contains a summary of New Zealand researchers involved in Parkinson's research and an audit of grant funding directed towards Parkinson's-related projects during the period 2015-2020.

Common themes of survey responses included a desire for improvements in medications and treatments, ways to prevent progression of the disease and for a cure. These themes were shared across the survey response groups and represent the great challenges of changing the outcomes of complex disorders.

Interestingly, the core motor symptoms of Parkinson's were rated highly in terms of aspects of the disorder that research efforts should be directed towards. This highlights that these symptoms, which are required for the diagnosis and continue to decline throughout the course of the disorder, remain a primary source of morbidity for those living with Parkinson's.

Overall, there is good levels of support for a wide range of research approaches to be used in Parkinson's research and a good levels of willingness from people with Parkinson's to participate in research projects. Options to facilitate improved patient and family input into research design and ways to increase visibility of research in the community are discussed.

New Zealand has a small, but active Parkinson's research community that covers a wide range of research topics. Parkinson's focused research is routinely funded by the main funding agencies in New Zealand, however given that the success rate of funding applications can be quite low and in some instances more to do with available funding rather than quality of proposed research, it is likely that much more Parkinson's research could be carried out if more research funding was available in New Zealand.

Introduction

Parkinson's disease is the second most common neurodegenerative disorder and estimated to affect more than ~10 million people worldwide¹ and ~12,000 people in New Zealand^{2,3} (<https://www.nzbri.org/Labs/parkinsons/Epidemiology/>). Recent reports indicate that the number of people with Parkinson's is growing at an alarming rate^{1,4}. Age is the greatest risk factor for developing Parkinson's⁵ and with the ageing population, increased numbers of people with age-related disorders is expected. Whether the reported increase in numbers is above and beyond the ageing population remains unclear.

The hallmark motor symptoms of Parkinson's are rigidity (muscle stiffness), bradykinesia (slowed movements), and resting tremor. Gait disturbances and falls are also common as the disorder progresses. A wide-range of non-motor symptoms are common. They include neuropsychiatric symptoms of anxiety, depression, apathy, cognitive impairment and dementia, as well as, hallucinations and delusions. Sleep disturbances, pain and sensory impairment, and gastrointestinal and urogenital dysfunction are also common place^{5,6}.

The motor symptoms arise following the loss of the dopamine producing neurons in the substantia nigra *pars compacta* – an area deep in the brain⁵. More than half of these dopamine neurons are lost by the time a diagnosis is made. The loss of dopamine in the circuits controlling movement disrupts the flow of information within the circuits and results in the hallmark motor symptoms.

Management of the disorder is primarily through symptomatic treatment, largely via dopaminergic medications⁷. Levodopa is most commonly used and represents the attempt to replace the dopamine lost with the death of the substantia nigra dopamine neurons. Many people face unreliable responses to medications after a number of years, which can lead to increased disability⁷.

Methods

An online survey was developed to capture opinions on what aspects of Parkinson's people with Parkinson's and their support network would like research to focus on.

Information on, and a link to the survey was emailed to the client database of Parkinson's New Zealand, the Multiple Sclerosis and Parkinson's Canterbury (MSPD: local Canterbury Parkinson's support agency), and the research participant database at the New Zealand Brain Research Institute (NZBRI). There was no overlap between Parkinson's NZ and MSPD Canterbury databases but there would have been considerable overlap between the MSPD Canterbury and NZBRI database. In total between 1800 and 2000 people would have received the survey invitation email.

Email recipients were encouraged to pass the survey information onto their spouses or support networks and any others they knew who might be interested in the survey.

Parkinson's NZ provides support services to people with idiopathic Parkinson's, atypical forms such as multiple system atrophy (MSA), progressive supranuclear palsy (PSP), and corticobasal syndrome (CBS) and acquired forms such as vascular parkinsonism.

We also sought to gain opinions from clinical staff involved in the treatment and management of people with Parkinson's and researchers directly involved in Parkinson's-related research.

A wide range of clinicians involved in the treatment and management of Parkinson's were invited to complete the survey. Groups included the Parkinson's NZ community Educators/nurses, neurologists (emailed through the Australia New Zealand Association of Neurologists email list), and general practitioners with a special interest in older persons health (emailed through NZ College of General Practitioners).

Researchers were emailed via the Brain Research New Zealand email list, which covered the majority of researchers in New Zealand involved in neuroscience and clinical research relating to Parkinson's and neurodegeneration in the wider sense.

The email invitations were sent in early December 2019, with follow-up in February 2020. It is possible that the December timing of the email invitation may have impacted on the number of responses, especially in the Clinicians and Researcher groups as this is a known busy time of year followed by the annual summer holiday period. The response rate will have largely been unaffected by the emergence of covid-19 as New Zealand was covid free during the main collection period.

Results

Demographics of survey Respondents

Table 1. Demographics of Patient and Family Groups.

	People with Parkinson's	Family
Number of respondents	375	149
Gender		
% Female	40	72
Ethnicity (%)		
NZ European	86	87
Māori	4.8	7.5
Samoan	1.3	-
Chinese	<1	1.9
Indian	<1	3.8
Other	7	-
Region (n)		
Northland/Auckland	99	43
Waikato/Bay of Plenty	44	52
Gisborne/Hawkes Bay	13	2
Taranaki/Manawatu/Whanganui	37	2
Wellington	44	17
Nelson/Tasman/Marlborough	15	5
Canterbury/West Coast	102	43
Otago	22	14
Age (n)		
<50	4	26
51-60	34	21
61-70	145	40
71-80	153	46
>81	34	16

Table 2. Demographics of Clinician and Researcher Groups

	Clinicians	Researchers
Number of respondents	29	29
Gender		
% Female	76	41
Ethnicity		
% NZ European	69	75
Age (n)		
<40	4	13
41-50	6	5
51-60	11	6
>60	8	4
Region where services are provided/research conducted (n)		
Northland/Auckland	11	9
Waikato/Bay of Plenty	4	-
Gisborne/Hawkes Bay	5	-
Taranaki/Manawatu/Whanganui	1	-
Wellington	2	-
Nelson/Tasman/ Marlborough	3	-
Canterbury/West Coast	4	15
Otago	3	5
Years of experience		
<10	13	17
10-20	7	8
20-30	6	2
>30	3	1

Responses to individual survey questions

Below the responses to each of the survey questions are summarised with the main themes highlighted.

What symptom or aspect of your condition, currently, is the most disabling or has the greatest impact on your life?

People with Parkinson's were asked what aspect or symptom of the disorder was currently the most disabling or had the greatest impact on their lives. This question was a free-text response format.

The highest ranking responses were the classic motor symptoms.

- **walking/balance**
- **tremor/shaking**
- **movement/mobility slowness**
- **reduced ability** to carry out activities

Fatigue/lack of energy and changes in cognition were the next highest ranked symptoms.

Family respondents were also asked to identify what symptom or aspect of the condition they thought was having the most impact on the lives of people with Parkinson's.

Family respondents most commonly reported problems with

- **cognition**
- **mobility/walking/balance/falls**
- **tremor**
- **fatigue**

Family respondents were also asked what symptom or aspect of the disorder had the greatest impact on their life. The highest ranked aspects were,

- **cognition**
- **mood**
- having to move into a **caregiver role**
- **loss of the person and/or life** that they have had previously

The **loss of ability to do activities** and **communication problems** were the next highest reported aspects.

What specific Parkinson's-related questions or problems do you most want research to focus on?

When asked what specific questions or problems they wanted research to address, people with Parkinson's

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- **Treatments** – generally in reference to non-medication based treatments including wanting more information on diet, exercise, natural remedies, targeted treatment based on cause or subtype, and cannabis
 - A **cure** for the disorder
 - More knowledge about the **causes** of the disorder
 - **Medications** that are more effective or longer lasting and with less side effects
 - A way to stop or slow the **progression** of the disorder

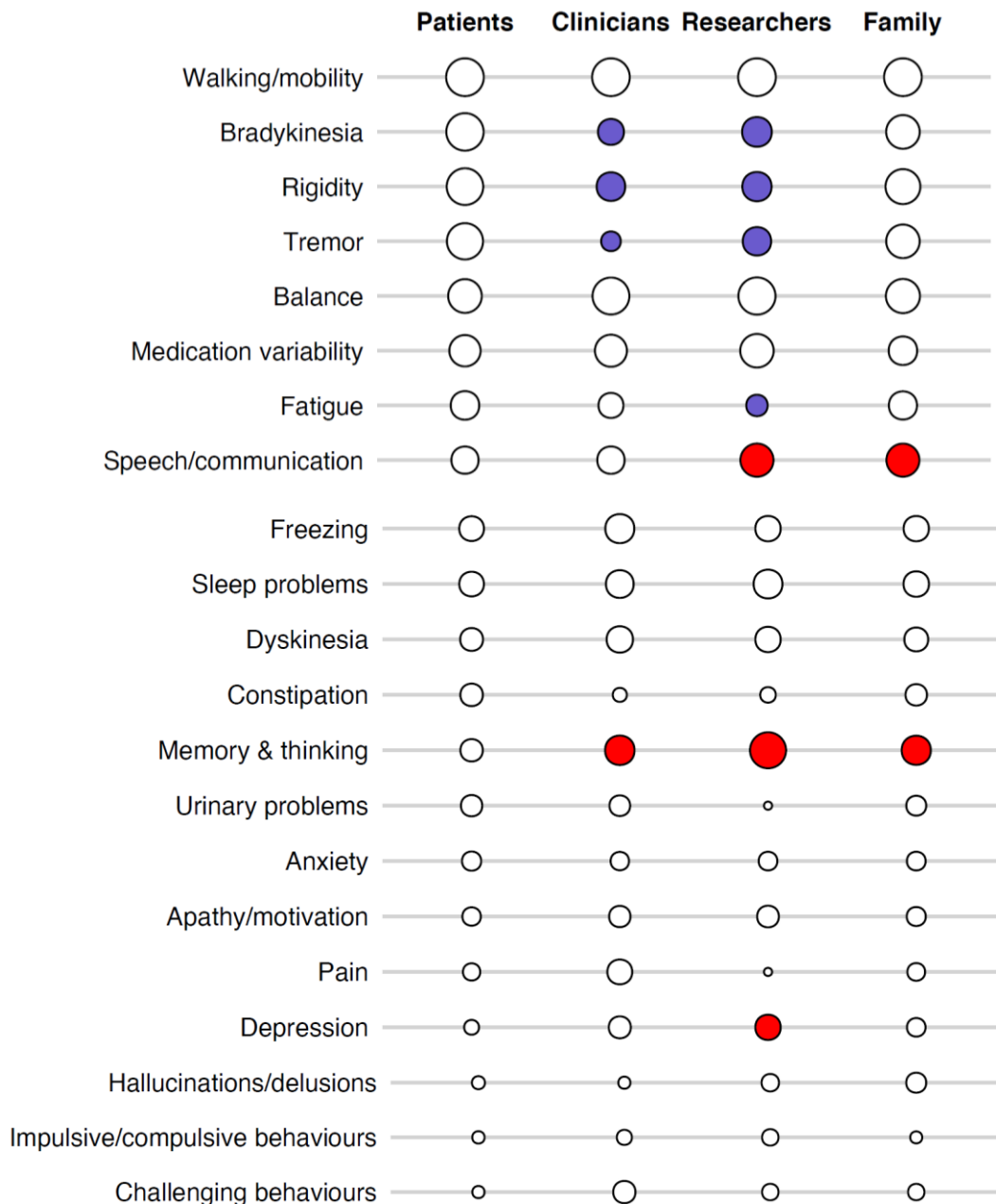
Following these more generalised topics, the specific symptoms of balance/walking and movement/mobility slowness were rated.

The wishes of families of those with Parkinson's were

- **Medications** that are more effective and with less side effects
- **Cognition** – how to delay or prevent onset of decline
- More knowledge about the **causes** of the disorder
- Better ways of controlling **tremor**
- A **cure** for the disorder

Symptoms of Parkinson's that research efforts should be directed towards

Respondents were presented with a list of 21 common symptoms associated with Parkinson's and asked to select up to five symptoms that they thought research should focus on. Figure 1 shows the responses of all four groups of survey respondents. The size of the circles indicates the relative number of responses and the symptoms are ranked according to the importance as determined by the people with Parkinson's responses. Not surprisingly, the responses of those with Parkinson's mirror the symptoms listed as having the greatest impact on daily life and are dominated by the classic motor symptoms. Interestingly, clinicians and researchers ranked bradykinesia, rigidity, and tremor as lower priority than people with Parkinson's. This could be due to these symptoms generally responding to medications and the subsequent perception that these symptoms 'are taken care of'. Clinicians, researchers, and family were all more likely to prioritise research into memory & thinking



Red indicates priority ranked higher than by patients, blue = lower.

Figure 1: Prioritisation of Parkinson’s symptoms for research efforts.

Parkinson’s symptoms are ranked in order of importance as indicated by the responses of those with Parkinson’s. Blue and red coloured circles indicate symptoms that were given a lower or higher ranking by other groups of respondents compared to people with Parkinson’s.

Life Changes due to Parkinson's

People with Parkinson's and their spouses/family were asked what the biggest changes in their life had been due to having Parkinson's or having a spouse/family member with Parkinson's.

People with Parkinson's most commonly reported

- **Job-related** impacts - with early retirement or changes in job or hours being prominent.
- **Hobbies** and physical activities - with changes in the ability (frequency or intensity) to do most commonly reported. Having to give up or change activities or hobbies was also commonly mentioned.
- **Driving** - with stopping and reducing distance of driving activities reported.
- **Relationships** - with breakdowns, increased stress, and changes in the nature of the relationships reported.

Also mentioned were loss of confidence, loss or changes in social activities, loss of independence, having to revise future plans, loss of ability to travel, and financial stress.

Spouses and family most commonly reported

- **Job-related** impacts – with early retirement reported most often followed by changes in the number of hours worked or the type of work.
- Move into a '**caregiver**' role - illustrating the changing nature of the relationships that often occur in these situations.
- Loss of **social interactions** - both within the home and outside of the home
- Loss of **freedom** to do their own activities
- Changes in **hobbies**
- Increased **domestic responsibility** – with changes in who carried out household chores and decisions.

Also mentioned were moving house, living separately (due to spouse being in care), and having to change future plans.

Research Advancements in Next 20 years

All respondents were asked to indicate one or two major advancements in Parkinson's they would like to see achieved in the next 20 years.

People with Parkinson's most commonly reported a desire for

- **Treatment and management improvements** - Some respondents directed their comments towards a specific aspect of the disorder with apathy, balance, cognition, depression, diet, drug trials, exercise, mobility/movement/motor, stem cells, and tremor all being mentioned independently.
- **A cure**

-
- **Medication improvements** - with improvements in effectiveness and less side-effects commonly mentioned.
 - **Slowing or stopping the progression** of the disorder – this was often seen as an acceptable achievement in the absence of cure. While most respondents use the term in general some did specially mention slowing or stopping the progression of memory problems.

Other themes with ten or more responses were increases in knowledge or research directed at specific aspects, earlier detection of the disease and better diagnostic accuracy, increased knowledge about causes, and information on prevention strategies.

Family members most commonly reported a desire for

- **Treatment improvements.** Suggestions included improvements in medications as well as treatments for specific symptoms.
- **Early diagnosis** and detection
- Slowing or stopping **progression**
- A **cure**

Advancement in knowledge of the causes of Parkinson's, prevention measures, and quality of life were also mentioned.

Clinicians predominantly wanted to see advances in **treatments** with disease modifying therapies, benefits of exercise, more effective medications, and stem cell treatments mentioned. Other advances were perhaps more directed at the health system with greater use of multidisciplinary teams, better access to surgical options, and better access to neurologists mentioned. Clinicians also wanted to see advancements in **early detection** and diagnosis and a way to stop or slow **progression**.

Researchers also most commonly reported advances in **treatment** as the most desired advancement with treatments ranking highest, with disease modifying therapies, more effective medications, and personalised treatments mentioned. Also mentioned was the ability for **early detection** of the disorder and the identification or **biomarkers** of the disorder.

Importance of Different Types of Research Approaches

Respondents were presented with a number of different research approaches that are commonly employed in the study of Parkinson's. Respondents were asked to rate the importance of each approach with options ranging from 'Not important' to 'very important'. The approaches presented covered a spectrum from 'bench to bedside'. Detailed explanation on how the approaches could be used was not provided so answers to this question are reflective of the respondent's prior knowledge. It is possible that with further explanation of how a specific approach may be used in the study of Parkinson's, the rating of some approaches would change.

Responses are shown in Figure 2. The top four approaches as rated by people with Parkinson's were 'new drug treatments', 'seeking patient knowledge to improve health care services and research', 'developing diagnostic tests', and 'identifying Parkinson's before motor symptoms start (prodromal Parkinson's).

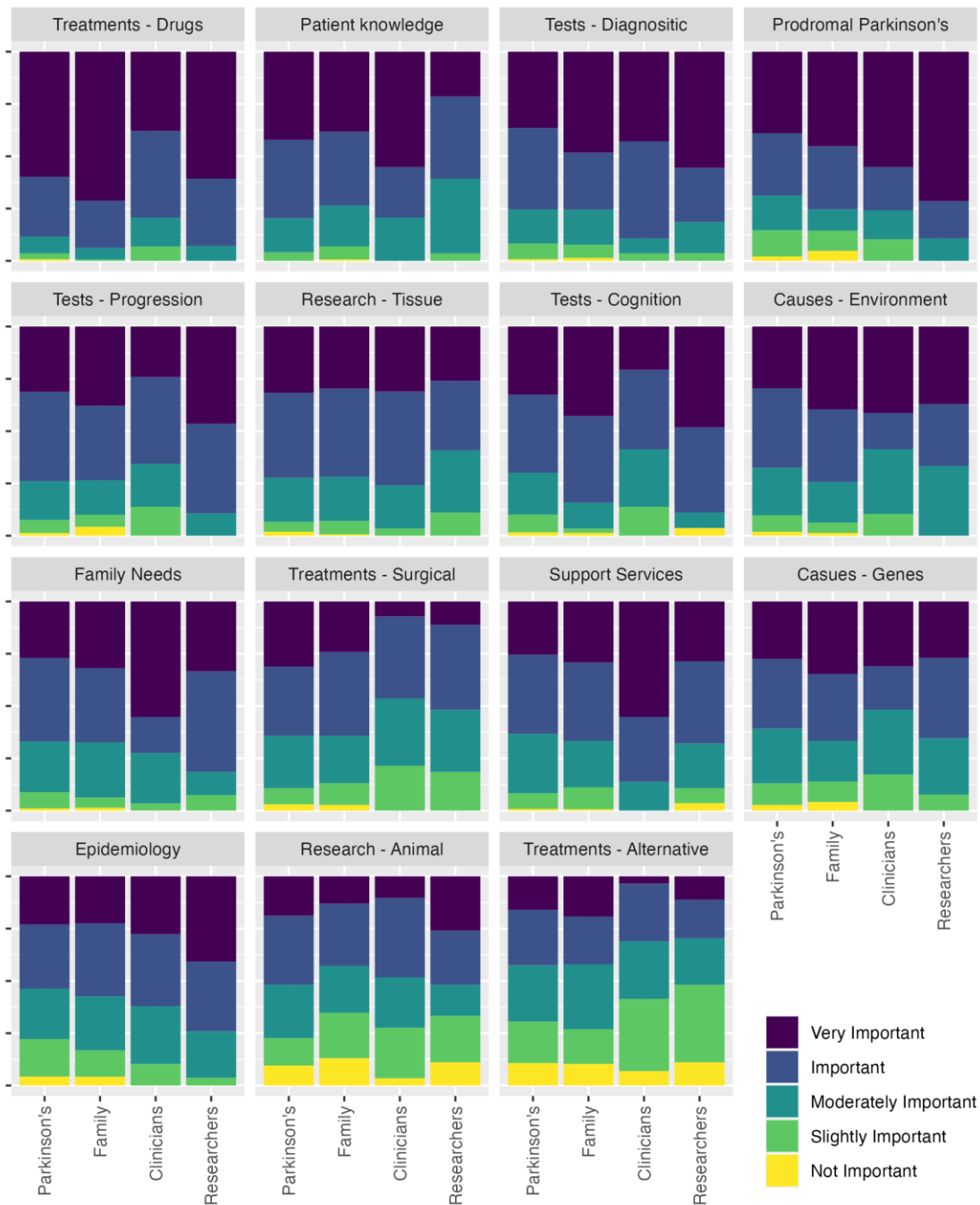


Figure 2: Importance of Research Approaches in Parkinson's research.

Research approaches are ordered by greatest to least proportion of people with Parkinson's endorsing the approach as being important.

Types of research people would be willing to participate in

Respondents with Parkinson's and family members were asked to consider 12 different types of research methodology that could be applied to the study of Parkinson's. They were asked to indicate which types of research they would consider taking part in, Figure 3. Overall there was generalised support for a wide range of research methodologies. Generally, support waned for the more invasive forms of research, such as collection of CSF samples via lumbar puncture and clinical trials of surgical interventions. This was, however, a hypothetical exercise and informed decisions could only be made once full details of a particular study are known.

A small proportion of people with Parkinson's reported no interest in participating in research. A larger proportion of the family group reported no interest in research participation, although some of this could be due to a lack of understanding of the importance of input from family in research projects. The family group showed strongest support for research into experiences of spouses and caregivers.

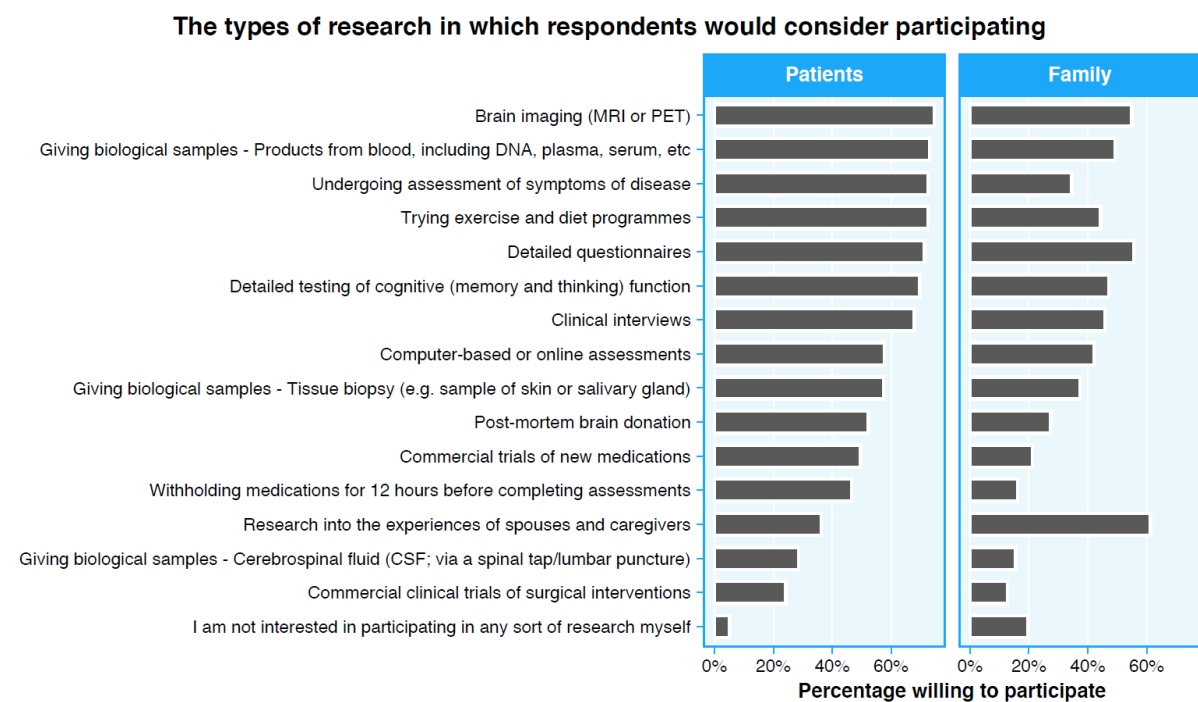


Figure 3: Types of research people would consider participating in

Interest in Research Outcomes and News of Developments

People with Parkinson's and their spouse/family were asked whether they followed research advances, and if they have previously been involved in research.

366 people with Parkinson's and 137 spouses/family endorsed following Parkinson's-related research developments. The majority of respondents were satisfied with access to information with 47% of people with Parkinson's and 40% spouse/family respondents rating access as 'sufficient'. 40% of people with Parkinson's and 50% of spouse/family respondents said access was ok, but would like easier access to scientific papers. 10-12% of respondents rated access as being poor and found it difficult to find reliable information.

Most people described the quality of language and information in sources they accessed to be adequate, ~10% described it as being too difficult to understand and ~10% too basic.

Respondents most commonly endorsed Newsletters or webpages of specialist organisations (e.g. Parkinson's NZ, Michael J Fox Foundation, Parkinson's UK, Neurological Foundation) as their source of information. This was followed by New Zealand Media (e.g. Stuff, NZ Herald, Listener), international media (e.g. BBC, New York Times), and Social Media groups or forums. People also reported getting information from books, attending seminars, having conversations with people, and reading scientific journal articles.

Research Participation

Previous research participation was reported by 145 (38%) people with Parkinson's and 32 (21%) spouse/family respondents. Those who had not previously participated in research were asked if there were any barriers that contributed to them not having participated.

Both groups reported the following barriers

- **Lack of contact** - never been asked to participate
- **Lack of knowledge** - don't know what opportunities are available or how to get involved
- **Geography** – not living in a city or near a university or hospital
- **Time** – not being able to fit requirements of research participation into already busy lives

People with Parkinson's also identified transport as a barrier as many rely on others to help get them around. Some had attempted to participate in research (most likely clinical trials) but were excluded due to co-morbidities or the results of pre-screening tests. Spouses/families also identified not knowing that they could be involved or useful in research.

Discussion – Survey results

Symptoms having the most impact

People with Parkinson's were most likely to report the classic motor symptoms (walking/balance, tremor/shaking, movement slowness) as having the most impact on their lives. Although no formal measure of quality of life was included in this study, previous studies have identified both motor and non-motor symptoms as key contributors to quality of life^{8,9}, however, a systematic review identified depression as being the symptom with the most impact on quality of life.¹⁰

Family were more likely to report cognitive issues as having an impact. This may be due to people with Parkinson's and cognitive problems not recognising the full impact of the problems. Similarly, family rated anxiety and depression higher than people with Parkinson's.

Impacts on individuals with Parkinson's and spouses/family

Both people with Parkinson's and spouses/family reported significant life changes as a result of the Parkinson's diagnosis. These most commonly involved changes in employment, hobbies and roles within relationships. This survey was not designed to explore the impact of life changes from a psychological or emotional way, but it is likely that the overall wellbeing of people with Parkinson's and their family have been negatively impacted, at least in the short-term, by the changes enforced by the presence of Parkinson's. The extent of these impacts will be dependent on a number of factors including age at diagnosis, the personality, and the stage of life of those diagnosed and their spouses or family. Having accessible support services to help people with Parkinson's and their families through these changes could be beneficial. The exact nature of these services should be driven by the end users and open to all regardless of regional location.

One potential model could be similar to the Employee Assistance Programmes that many employers make available to their staff. These programmes grant a small number (e.g. 1-3) of free counselling sessions to staff, paid by the employer. The programmes can help avoid the long wait times and, at least initially, the costs associated with accessing private counselling services. Many counsellors are able to provide services through online call platforms, which could help with accessibility. There may need to be some upskilling of counsellors to ensure they are at least familiar with disorder-specific issues. Implementation of this type of service would obviously need a lead organisation and funding to support the service, neither are easily established. It could be possible to have this service available to a range of neurodegenerative conditions, which, although could potentially increase the required funding, may make it more attractive to potential funders, given the wider reach of the service.

Research focus and Outcomes in next 20 years

There was considerable overlap in the responses between the two questions asking what “research should focus on” and what “research advances in the next 20 years” people wanted to see.

The strong desire for improved medications and treatments (including non-medication options) from all response groups is likely due to the fact that not all symptoms of Parkinson’s are sufficiently controlled by currently available treatments and the diminished response to dopaminergic medication over time that some people experience. The other highly ranked responses of “a cure” and “ways to stop or slow progression” reflect the big challenges facing chronic conditions such as Parkinson’s. Family, Clinicians, and Researchers also wanted advances in the early detection of Parkinson’s, which would be necessary for the use of advances in the treatment, especially if they were of disease-modifying treatments.

Different research approaches

The top rating of ‘new drug treatments’ fits with the desire, indicated in other areas of the survey, for new or more effective treatments. This is likely driven by the decreased efficacy of treatment over time and variability of response. Seeking input from people with Parkinson’s to improve healthcare and research is also well supported by the clinician and family groups. This research could be seen as a beginning to having increased patient voices in the New Zealand Parkinson’s research. The desire for ‘diagnostic tests’ likely reflects the uncertainty many people face when presenting with mild symptoms that may prevent a diagnosis being made immediately. This is probably particularly relevant for people with early onset (<50 years) Parkinson’s as often in these cases Parkinson’s is not initially considered likely due to age. If a test was available, these people would likely get a definitive diagnosis early, enabling them to have more autonomy over their health journey at an earlier stage. Although there was good overall support for “increased knowledge about prodromal Parkinson’s”, Clinician and Researcher groups rated this higher than people with Parkinson’s or family members. This may reflect the increased research focus on this topic and the greater awareness that the prodromal period will likely provide the best window of opportunity for the administration of disease-modifying therapies. The Clinician group gave higher importance ratings to developing support services and understanding family needs than any other group.

The approaches that were rated of least importance were, ‘knowing more about the people who get Parkinson’s (epidemiology)’, ‘using animal models’, ‘testing of alternative or complementary treatments’. Epidemiology and animal models may have been more highly rated if more context was provided, e.g. stating how this knowledge could lead to advances. Sometimes the ‘line of sight’ or ‘pathway to impact’ can be difficult to see if it is not specifically stated. The low rating for alternative therapies likely reflects the range of views people have on this topic, while some people are strong advocates for drug alternatives, others are less concerned with this.

Potential to improve community engagement with research

The reported barriers to participation in research gives a very clear signal to researchers that more promotion of research activities would be desirable and where possible, consideration given to methodologies that would allow for the inclusion of participants from across the country and not just those located near universities.

Following experiences during covid-19 lockdowns, a much greater proportion of the population is familiar with online video calling. As such, telehealth and tele-research are much more feasible and acceptable now¹¹. There remains challenges with the accurate assessment of motor symptoms remotely^{12,13}, but in time, accepted methods to do this will emerge and become commonplace.

One possible solution to greater promotion of research activities is to have a central register for current research projects. The register could list all projects, including lab-based projects, enabling the community to see what research is being carried out in New Zealand. Those projects recruiting participants could list contact details and inclusion/exclusion criteria.

Ideally, this resource would be hosted by an independent organisation, the Aotearoa Brain Project (ABP) would be well-placed to do this and they could apply the model to all areas of research they support. Promotion of the resource could then occur through organisations that already have strong public relationships, such as the Neurological Foundation and Parkinson's NZ.

National Registry / Research Cohort

There may be some benefit to national Parkinson's research and the research community to having a large longitudinal Parkinson's cohort. This could be set-up using Fox Insight (<https://foxinsight.michaeljfox.org/>) as a model. Basic disease metrics (such as presence of specific non-motor and motor symptoms, medication etc) would be included and tracked over time as could access to specialist care and other aspects of healthcare services to provide data on how delivery of services could be improved or identify where gaps exist. Researchers could access data for analyses or if needed, specific data could be collected in response to requests from researchers. It would be beneficial to include DNA collection and genetic analyses, however this would require significant funding. The cohort could largely be run as an online project.

Such a cohort would help facilitate research participation for anyone who was interested regardless of geographical location. It could also help stimulate research by removing the barriers of recruitment and data collection, which are often the most time-consuming and expensive aspects of research. Data from this national cohort could be used alongside data from similar international cohorts to help provide replication of findings or to give greater international representation to analyses.

Individuals within the cohort could also indicate if they would be willing to be approached for participation in face-to-face research projects. This would assist recruitment for projects and be of benefit to researchers that do not readily have access to the Parkinson's population for recruitment purposes.

Patient/family Consultation and Co-design of Research

There is a noticeable change in the funding landscape whereby consulting with people with Parkinson's and/or their families during the research planning phase is more commonplace, its absence likely to be commented on by reviewers, and in some cases a requirement of the funding agency. Projects like the current one, are good for providing a broad overview of aspects of disease that are causing disability and desires for research achievements, however, many researchers would prefer to be able get direct feedback on specific research projects. This type of consultation would be especially useful if data collection methods are likely to raise questions (during scientific or ethics review) about their suitability.

One potential mechanism to facilitate this consultation could be to have a centralised patient/family advisory group that could provide feedback on research projects prior to grant submission. Some challenges to this would be achieving a representative group, especially given it would require additional commitments to already busy lives, providing administration support and training for the group so they fully understand their role, and compensation for the time contributed by group members. A fee could be charged to researchers using the service, although it should be acknowledged that not all researchers/groups would have discretionary funding available for this, although over time it could be factored into funding budgets. Regularity of meetings would need to be carefully considered, so as not to overburden the group but to also adequately service the research community. Quarterly meetings could be a starting point but may need to be revised in response to demand from researchers. Multiple committees could be established to help meet demand and reduce burden on committee members.

Cultural Consultation and co-design of Parkinson's-related Research

Cultural consultation is generally required for ethics approvals and for funding applications. Traditionally this consultation has focussed on Māori but increasingly applicants are asked to comment on whether consultation with Pacific communities has been completed.

There are well-established pathways, through universities, for achieving Māori consultation and researchers are well-versed in the requirements and expectations associated with Māori consultation in relation to health research. Such pathways for Pacific peoples consultation are less common and many researchers are less knowledgeable about specific cultural considerations in relation to Pacific populations, however, this is slowly changing.

Currently, there is little known about the presentation and progression of Parkinson's within the Māori and Pacific people groups. Few published studies have reported the ethnicity of participants and none to date have specifically targeted these ethnic groups. This gap is being addressed, in part, by a Michael J Fox Foundation grant held by Prof. Leigh Hale, University of Otago (www.otago.ac.nz/physio/research/experiences-and-impact-of-parkinsons-symptoms-for-maori-pacific-people-and-their-whanau). This

project includes tracking of general mobility and falls risk and also includes a kaupapa Māori design component.

The underrepresentation of Māori in Parkinson's research is potentially due to the comparatively low number of Māori with Parkinson's as indicated by our previous epidemiology research¹⁴.

The dearth of kaupapa Māori research projects aimed at Parkinson's may be due to a low number of suitably qualified researchers within the Parkinson's, neurodegeneration, or more widely, the neuroscience research space. It may also be a result of the low numbers of Māori with Parkinson's¹⁴ and as such it is not perceived as a critical health need requiring study within this population.

Activity in the Pacific peoples space is more advanced with the observation of a number of early-onset cases in those of Pacific descent and the subsequent confirmation of the overrepresentation of *PINK1* mutations in Pacific populations¹⁵.

Parkinson's Research in New Zealand – Overview

A list of New Zealand researchers actively involved in Parkinson's research is presented in Table 3. This list was generated by searching the expertise database of the universities/research institutes and substituted by knowledge of the authors. It is likely that some people have been missed, but we believe that the bulk of researchers at a senior level (Research Fellow and up) have been captured. From this list of >40, it has been determined that less than half (~13) have Parkinson's as their main area of research. The others, for example, have expertise in certain techniques/areas (e.g. molecular neuroscience, genetics, or neuro rehabilitation) but these are applied across disorders and while Parkinson's is or has been included in their research, it is not the main focus of their research activities.

The Parkinson's researchers in New Zealand cover a range of research fields from neurophysiology, drug delivery systems, neuroanatomy and molecular neuroscience, and clinical research.

The neurophysiology research utilizes animal models to assess activity in brain circuits involved in the control of voluntary movement and how activity changes in response to the loss of dopamine and other brain chemicals associated with Parkinson's. Dr Freestone from Auckland specializes in the role of endocannabinoids in normal and disease-related function.

Dunedin-based researchers have historically been strong in the neurophysiology field and have more recently moved into drug delivery system development (Prof. John Reynolds), gut-brain connections (Prof. Louise Parr-Brownlie), and molecular mechanisms (Dr Indranil Basak).

The Neurological Foundation Human Brain Bank in Auckland provides a valuable resource for study of post-mortem brain tissue. Research activities in Auckland, centered around the brain bank tissue, include investigations into brain inflammation, blood-brain barrier integrity, olfactory bulb structure, and alpha-synuclein sub-species. Prof. Maurice Curtis, Prof. Richard Faull, Prof. Mike Dragunow, and Dr Victor Dieriks are key PIs in this area of research.

Christchurch is a hub of clinical research and has a longitudinal cohort of patients that started in 2007³. Professors Tim Anderson and John Dalrymple-Alford are PIs for this cohort, with Assoc. Prof. Tracy Melzer leading the brain imaging research. The research focuses on describing the progression of the disease, the development of cognitive impairment, and identifying biomarkers of disease stage through investigations of saccadic eye movements, magnetic resonance imaging (MRI), biological samples (blood, DNA, tears), and quantitative EEG.

Christchurch also hosts a Parkinson's epidemiology research programme, which is monitoring the prevalence and incidence of the disorder, using health administration data. Other aspects of the disorder are being investigated using the data sources and risk factors via a HRC project grant. Drs Toni Pitcher and Daniel Myall are the PIs of this programme.

Outside of the traditional academic-led research, there are numerous Parkinson's-related clinical trials. These are pharmaceutical company-led, require a tertiary-level neurology service for completion and as such are generally limited to the metropolitan centres (generally Auckland and Christchurch). These trials are not considered in this report.

Table 3. New Zealand Based Researchers involved in Parkinson's research

Institution	PD main focus	Area of research
University of Otago, Dunedin		
Dr Indranil Basak	Y	Non-coding RNA, neurodegeneration
Dr Yusuf Ozgur Cakmak		Non-invasive electrostimulation, clinical research
Dr Nick Cutfield	Y	Clinical research, neurology, eye movements
Prof. Dirk De Ridder		Clinical research, neuromodulation, Neuroimaging
Prof. Leigh Hale		Physiotherapy, rehabilitation, exercise and physical activity
Prof. Brian Hyland	Y	Neurophysiology, animal models
A/P Hilda Mulligan		Rehabilitation, physical activity
Dr Sonja Seeger-Armbruster	Y	Neurophysiology, animal models
Prof. Louise Parr-Brownlie		Neurophysiology, motor control, animal models
Prof. John Reynolds		Neurophysiology, animal models
New Zealand Brain Research Institute (NZBRI)		
Dr Daniel Myall	Y	Clinical research, epidemiology, data science
Dr Kyla Horne	Y	Clinical research, neuropsychiatric symptoms
<u>University of Canterbury</u>		
Prof. John Dalrymple-Alford	Y	Neuropsychology, cognitive impairment
<u>University of Otago, Christchurch</u>		
Prof. Tim Anderson	Y	Clinical research, clinical trials
Dr Tracy Melzer	Y	Neuroimaging
Dr Toni Pitcher	Y	Clinical research, epidemiology, biomarkers

Prof. Martin Kennedy		Genetics
Dr Sarah Perry		Speech and language therapy - swallowing
Dr Campbell Le Heron		Motivation / apathy
University of Canterbury		
AP Roeline Kuijer		Health psychology, partner relationships
Prof. Megan McAuliffe		Speech production and perception
Dr Catherine Theys		Speech production, acquired neurological speech and language disorders
Victoria University		
No known researchers		
Massey University		
Dr Helen Fitzsimons		Molecular geneticist, memory, drosophila
Waikato University		
No known researchers		
University of Auckland		
Prof. Winston Byblow		Movement neuroscience, neurorehabilitation, neurophysiology
Dr Tara Coleman		Health geography
Prof. Bronwen Connor		Gene therapies, cell replacement therapies
Prof. Maurice Curtis		Neuroanatomy, post-mortem tissue, olfactory system
Dr Victor Dieriks	Y	Neuroanatomy, post-mortem tissue, olfactory system
Prof. Michael Draganow		molecular pharmacology, neuroscience, post-mortem tissue
Prof. Sir Richard Faull		Neuroanatomy, molecular neuroscience, post-mortem tissue
Dr Peter Freestone	Y	Neurophysiology, animal models, cannabinoids
Dr Jian Guan		Neuropharmacology
Prof. Nick Holford		Pharmacology
Dr Hannah Kersten		Optometry, optic nerve and retina changes in disease
Prof Ian Kirk		Neuroplasticity, memory and attention
Prof. Janusz Lipski	Y	Neurophysiology, animal models
Dr Duncan McGillivray		Oxidative stress, biological membranes
Dr Justin O'Sullivan		Genetics, systems biology

Prof. Suzanne Purdy		Audiology, speech, neuro-rehabilitation
Dr Malvinder Singh-Bains		Neuroanatomy, post-mortem tissue
AP Lynette Tippett		Clinical psychology, cognition, emotional processing
AP Henry Waldvogel		Chemical neuroanatomy, GABA receptors
AP Deborah Young		Gene therapies

Auckland DHB

Dr Barry Snow	Y	Parkinson's clinical trials
Dr Richard Roxburgh		Neurogenetic disorders
Dr Christina Buchanan		Neurogenetic disorders

Parkinson's Research Funding Audit

Information on successful research funding secured for Parkinson's-related research by New Zealand researchers was collected by searching the websites of funders or directly contacting funders. The information gathered is presented in Table 4 and included projects where "Parkinson's" was in the title, keywords or lay summary of the grant.

Funding allocated to projects, fellowships, and scholarships was considered in two ways. Firstly, the total awarded that was in some way related to or relevant to Parkinson's (e.g. projects where the outcomes could have been applied to more than one neurological disease) and secondly, for Parkinson's-specific projects. Information from 12 funding sources were considered, five of these funders pay overheads and this money is included in the reported totals. It was not possible to determine the amount of money allocated to overheads, but the universities generally charge a rate between 100 and 115 percent, which is applied to all academic salaries. Some funders, such as the Michael J Fox Foundation have a set overhead rate (8-15%) applied to salaries.

During the audit period of 2015-2020 period total Parkinson's-related funding was \$23M and Parkinson's-specific funding was \$20M. The Health Research Council (HRC) and the Neurological Foundation were the top two funders of Parkinson's-specific research awarding ~\$2.9M each. A notable difference between these two funders is that HRC is an overhead paying funder and Neurological Foundation is an overhead exclusive funder; as such, the money awarded by Neurological Foundation is all going directly to salaries and research costs. The average project grant awarded by HRC is valued at \$1.2M with a duration of three years, whereas the average project

grant from the Neurological Foundation is ~\$150K over two years, thus, the number of projects funded by each funder, within the same dollar amount is different.

For the Neurological Foundation we were able to compare the amount of funding received by Parkinson's in relation to other neurological disorders for the 3-year period 2018 to 2020. During this time Parkinson's research received ~\$1.39M in funding, which equates to ~12% of the total funding awarded by them during this period; this is compared to ~19.7% going to Alzheimer's/dementia research, ~10% to stroke and ~9% to brain cancers.

During the audit period, Brain Research New Zealand (BRNZ) contributed ~\$2.8M (overhead inclusive) funding to Parkinson's-specific research. Unfortunately, this funding stream is not available beyond 2020, due to the failure to secure ongoing Tertiary Education Commission funding through the Centre of Research Excellence (CoRE) funding stream. BRNZ will be a missed funding source in the coming years for Parkinson's research.

The Health Research Council (HRC) and the Marsden fund award some of the highest valued grants. During the audit period, there were two Parkinson's-specific project grants and two career awards funded by HRC and two projects funded by the Marsden fund. It must be acknowledged that these are highly competitive funding streams and cover very broad areas of research. A notable absence is the lack of a Parkinson's-specific programme grant in the 2010-2020 period and perhaps represents a missed opportunity, although eligibility to submit a programme application is complicated and requires two current or recent HRC projects (or similar sized grant from other national or international funders).

One international funding agency that is freely available to New Zealand-based researchers is the Michael J Fox Foundation (MJFF). Two Auckland groups have been successful at obtaining funding from this source in the 2015-2020 period (five NZ projects in total from 2007 to 2020). MJFF have targeted funding streams, rather than accepting general applications, as such, the frequency at which one could apply is limited, as you would need to fit within the specifications of the funding stream.

Outside of the traditional competitive funding rounds, Parkinson's research in New Zealand has also been supported by bequests and fundraising driven by private citizens and charitable organisations.

The Neuro Research Charitable Trust was formed in 2013 with the goal of raising \$1M for Parkinson's research. This goal has been reached and the trust now seeks to continue providing funding for neurological research, with an emphasis on Parkinson's. All funds raised by the trust are directed to the Centre for Brain Research, Auckland University to support the research of Sir Prof Richard Faull and Prof. Maurice Curtis. The annual amounts listed in Table 2 have been extracted from the charity's annual reports and although we do not know exactly what this money has been used for, we have allocated it to Parkinson's-specific funding.

Parkinson's research in Christchurch has been supported by a \$1M bequest from a private citizen. This money was used during 2014-2018 to support the continuation of the longitudinal cohort and other Parkinson's research activities. In addition to this bequest, the New Zealand Brain Research Institute (NZBRI) has supported Parkinson's research by providing institutional support and salary short-fall coverage.

We have been unable to capture the total number of grant applications submitted and as such are unable to comment on the overall success rate of Parkinson's grant applications. Given our overall knowledge of the funding landscape and personal experiences, it is however likely that as many as five grant applications have been submitted for every successful grant.

Although this summary covers the main funding sources for neurology and neuroscience research in New Zealand it does not cover all potential funders. Money from internal university funding streams and other international funding agencies are missing. Also, money provided by Ageing Well National Science Challenge has not been included. This funding source appears to target higher-level projects and although Parkinson's may be considered in the research, it is unlikely to be the focus. It is possible that some Parkinson's-related funding distributed by MBIE is not represented in this summary. The information provided by MBIE did not always allow for the identification of research areas, either due to commercial sensitives, bulk funding provided to other funds, such as Science Challenges, or data collection methods. We do believe we have captured information from funders who provide the vast majority of the money that is directed towards Parkinson's research in New Zealand.

Travel grants have been excluded in this summary, however, these are important funding streams and like other sources of funding can be incredibly difficult to secure. Although academic staff (Lecturer/Research Fellow and above) will often receive departmental funding which covers or mostly covers attendance at one international conference annually, post-docs are often not afforded this level of support and can find it difficult to secure funds to support conference attendance. The level of support at all employment levels will differ between departments and institutions. A lot of importance is placed on conference attendance, specifically international conferences, for career development and networking. Funders such as the Neurological Foundation, Canterbury Medical Research Foundation (CMRF), Auckland Medical Research Foundation (AMRF), and Maurice & Phyllis Paykel Trust (MPPT) all provide travel funding, with some being directly linked to funded projects.

Funding success of Parkinson's projects continued beyond those reported in Table 4. In 2021, an additional four Parkinson's-focused projects were funded to the tune of ~\$2.2 million and a \$5 million neurodegenerative disorders programme grant was also successful. In 2022, one project, worth \$534k was awarded and in 2023, a Sir Charles Hercus Fellowship (~\$500k) and MBIE programme (\$5 million) were awarded.

Table 4. Parkinson's Research funding in New Zealand 2015-2020

Agency	2015	2016	2017	2018	2019	2020	2015-2020 (Total)	2015-2020 (PD-specific)
HRC	-	\$120,000	\$1,686,366	-	\$1,199,417	\$2,527,518	\$5,533,301	\$2,995,527
Marsden	-	-	-	-	-	\$1,914,000	\$1,914,000	\$1,914,000
MJFF	-	-	-	\$226,000	\$221,000		\$447,000	\$447,000
CMRF	\$82,630	-	-	\$94,948	\$96,983	\$109,226	\$383,787	\$383,787
AMRF							\$772,063	\$772,063
BRNZ	\$1,146,176	\$508,143	\$959,550	\$156,333	-	\$95,328	\$2,865,530	\$2,865,530
NF	\$713,171	\$530,787	\$222,395	\$284,517	\$669,723	\$943,264	\$3,363,857	\$2,954,717
MBIE	-	\$5,466,663	-	-	-	-	\$5,466,663	\$5,466,663
Lotteries	-	\$27,418	-	\$226,955	-	-	\$254,373	\$254,373
NZBRI	\$200,000	\$200,000	\$200,000	\$200,000			\$800,000	\$800,000
MPPT	-	\$12,000	-	-	\$23,000	\$12,000	\$47,000	\$22,000
Neuro Trust	\$100,000	\$200,000	\$300,000	\$420,000	\$200,000		\$1,220,000	\$1,220,000
							\$23,067,574	\$20,095,660

HRC = Health Research Council, MJFF = Michael J Fox Foundation, CMRF = Canterbury Medical Research Foundation, AMRF = Auckland Medical Research Foundation, BRNZ = Brain Research New Zealand, NF = Neurological Foundation of New Zealand, MBIE = Ministry of Business, Innovation, and Employment, Lotteries = Lottery Health Research, NZBRI = New Zealand Brain Research Institute, MPPT = Maurice & Phyllis Paykel Trust, Neuro Trust = The Neuro Research Charitable Trust.

Awarded years were not provided by the AMRF so totals are listed only. ‘–’ indicates years with no funding of interest awarded, and greyed cells indicate years where data was not collected. Total funding includes projects that included Parkinson’s but also other neurodegenerative disorders. PD-specific is funding granted for projects directly relevant to Parkinson’s.

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